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P1

Infusion of sodium sulfide improves myocardial and endothelial function in a canine model of cardiopulmonary bypass

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Hydrogen sulfide is produced endogenously by a variety of enzymes involved in cysteine metabolism. Clinical data indicate that endogenous levels of hydrogen sulfide are diminished in various forms of cardiovascular diseases. The aim of the current study was to investigate the effects of hydrogen sulfide supplementation on cardiac function during reperfusion in a clinically relevant experimental model of cardiopulmonary bypass. Twelve anesthetized dogs underwent hypothermic cardiopulmonary bypass. After 60 minutes of hypothermic cardiac arrest, reperfusion was started after application of either saline vehicle (control, $n = 6$), or the sodium sulfide infusion (1 mg/kg/hour, $n = 6$). Biventricular hemodynamic variables were measured by combined pressure–volume–conductance catheters. Coronary and pulmonary blood flow, vasodilator responses to acetylcholine and sodium-nitroprusside and pulmonary function were also determined. Administration of sodium sulfide led to a significantly better recovery of left and right ventricular systolic function ($P < 0.05$) after 60 minutes of reperfusion. Coronary blood flow was also significantly higher in the sodium sulfide-treated group ($P < 0.05$). Sodium sulfide treatment improved coronary blood flow, and preserved the acetylcholine-induced increases in coronary and pulmonary blood ($P < 0.05$). Myocardial ATP levels were markedly improved in the sulfide-treated group. Thus, supplementation of sulfide improves the recovery of myocardial and endothelial function and energetic status after hypothermic cardiac arrest during cardiopulmonary bypass. These beneficial effects occurred without any detectable adverse hemodynamic or cardiovascular effects of sulfide at the dose used in the current study.

P2

Cytoprotective and anti-inflammatory effects of hydrogen sulfide in macrophages and mice

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The aim of the current study was to test potential cytoprotective and anti-inflammatory effects of the novel biological mediator hydrogen sulfide in murine models. Murine J774 macrophages were grown in culture and exposed to cytotoxic concentrations of nitrosoglutathione, or peroxynitrite (a reactive species formed from the reaction of nitric oxide and superoxide). Pretreatment of the cells with sodium sulfide (60–300 μM) reduced the loss of cell viability elicited by the nitric oxide donor compound (3 mM) or by peroxynitrite (3 mM), as measured by the MTT method. Sodium sulfide did not affect cell viability in the concentration range tested. In mice subjected to bacterial lipopolysaccharide (LPS, 5 mg/kg i.p.), treatment of the animals with sodium sulfide (0.2 mg/kg/hour for 4 hours, administered in Alzet minipumps) reduced the LPS-induced increase in plasma IL-1β and TNFα levels. These responses were attenuated when animals were pretreated with the heme oxygenase inhibitor tin-protoporphyrin IX (6 mg/kg). The current results point to the cytoprotective and anti-inflammatory effects of hydrogen sulfide, in cells exposed to nitrosative stress, and in animals subjected to endotoxemia.

P3

Epithelial cell apoptosis is similar but hypoxic-inducible factor expression is weaker in acute acalculous cholecystitis than in calculous cholecystitis

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Introduction It has been previously shown that the two forms of acute cholecystitis, acute acalculous cholecystitis (AAC) and acute calculous cholecystitis (ACC), have significantly different histopathological features suggesting that AAC is a manifestation of systemic critical illness whereas ACC is a local disease of the gallbladder. A balance between cell proliferation and cell death is essential for cell homeostasis. The purpose of this study was to compare the markers of apoptosis, cell proliferation, and expression of hypoxic-inducible factor alpha (HIF-1α) in AAC, ACC and normal gallbladders.
Methods The AAC group consisted of 30 patients who underwent open cholecystectomy due to acute acalculous cholecystitis during their ICU stay. The ACC group consisted of 21 hospitalized patients who underwent cholecystectomy due to acute calculous cholecystitis. The control group consisted of nine samples taken from normal gallbladders extirpated during pancreatic tumor surgery. The immunohistochemical analysis was done according to the manufacturer's recommendations and they consisted of Ki-67 (proliferation), M30 (apoptosis) and HIF-1α antibodies. Cell proliferation and degree of apoptosis were expressed as the percentage of positive cells. HIF-1α expression was expressed as absent or weak (Score 1) or strong (Score 2).
Results Apoptosis (median, 25th, 75th percentiles) was significantly increased in AAC 1.3% (1.0%, 3.3%), $P = 0.001$ and ACC 0.93% (0.40%, 3.25%), $P = 0.011$ compared with controls 0.32% (0.20%, 0.40%). Proliferation rate was also significantly increased in AAC

8.0% (4.0%, 17.0%), $P < 0.001$ and ACC 14% (7.5%, 26.5%), $P = 0.001$ compared with controls 1.0% (1.0%, 3.0%). Strong HIF-1α staining was observed in 100% of ACC, in 57% of AAC and in 44% of control specimens ($P < 0.001$). Strong HIF-1α expression was associated with increased cell proliferation ($P = 0.002$).

Conclusions Cell proliferation and apoptosis were increased in AAC and ACC. The expression of hypoxic-inducible factor was, however, stronger in ACC compared with AAC.

P4

Effect of prostaglandin E_2 on ATP-induced Ca^{2+} responses in human THP-1 monocytic cells

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Introduction To clarify the relation between ATP and prostaglandin E_2 (PGE_2) in the immunologic system, we investigated the acute and chronic effects of PGE_2 on activation of purinergic signaling in monocytes by measuring the ATP-induced elevation of intracellular Ca^{2+} ($[Ca]_i$) in fura-2-loaded THP-1 monocytes.

Method THP-1 monocytes were grown for about 2 days. To examine the chronic effects, PGE_2 and dibutyryl cAMP (dbcAMP) were added and incubated for another day. The cell suspensions were washed, loaded with fura-2-AM, and transferred into a quartz cuvette and placed in the thermostat-regulated sample chamber of a dual excitation beam spectrophotometer. To examine the acute effects, ATP was added immediately after PGE_2 and dbcAMP into the cuvette. In the chronic experiment, ATP alone was added into the cuvette. Fura-2 fluorescence emission was measured at 510 nm. The $[Ca]_i$ was calculated from the ratio of the fluorescence at the two excitation wavelengths.

Results ATP induced a transient increase in $[Ca]_i$ followed by a sustained elevation of $[Ca]_i$. Acutely, PGE_2 inhibited both the transient and sustained ATP-induced elevations of $[Ca]_i$. However, this acute inhibitory effect diminished gradually with time and chronic PGE_2 accelerated the transient and sustained ATP-induced $[Ca]_i$ elevations for 24 hours. Both the acute and chronic effects of PGE_2 were mimicked by dbcAMP. In Ca^{2+}-free solution, ATP did not induce the sustained elevation of $[Ca]_i$ in control cells or cells pretreated for 24 hours with dbcAMP. This indicates that the ATP-induced sustained elevation of $[Ca]_i$ was due to Ca^{2+} entry. In addition, receptor-operated Ca^{2+} channel blockers inhibited the sustained ATP-induced elevation of $[Ca]_i$ in control cells and cells pretreated with for 24 hours dbcAMP.

Conclusion Acute PGE_2 inhibited the ATP-induced activation of monocytes. On the other hand, chronic PGE_2 accelerated monocyte activation by upregulation of receptor-operated Ca^{2+} channels (ROCs). If this mechanism exhibits a physiological role, ROC inhibitors should be developed as new anti-inflammatory agents.

P5

Interferon gamma levels are reduced by adenosine 5′-triphosphate in lipopolysaccharide-stimulated whole human blood

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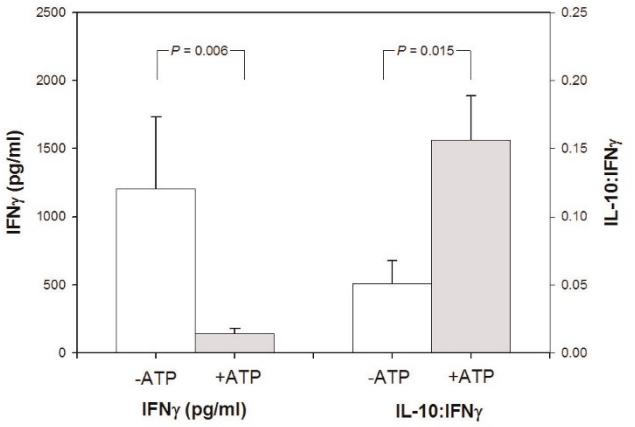
Introduction Extracellular release of ATP is an important modulator of immune response. ATP plasma concentration is increased in sepsis [1]. IFNγ plays a critical role in host defense by promoting Th1 phenotype and bacterial clearance. Low IFNγ levels are associated with the Th2 phenotype consistent with critical illness anergy [2]. It has been reported that 100 and 300 mM ATP increased LPS/PHA-stimulated IL-10 secretion in human blood [3]. Higher IL-10/IFNγ ratio shifts the immune phenotype from Th1 to Th2 response. We studied the effect of ATP on LPS-stimulated IL-10 and IFNγ secretion in a standardized *ex-vivo* whole human blood culture.

Figure 1 (abstract P5)



Methods Venous blood from 10 healthy volunteers was drawn into tubes containing 10 ng LPS/ml (ILCSÒ; EDI GmBH, Reutlingen, Germany) and incubated with or without 100 mM ATP, respectively, at 37°C for 24 hours. The supernates were separated and frozen at −20°C. Cytokine levels were analysed on a robotic workstation (epMotion 5075; Eppendorf AG, Hamburg, Germany) in duplicate using the ELISA Cytokine kit (Luminex; Biosource Int., Camarillo, CA, USA).

Results Added ATP reduced the mean concentration of IFNγ in LPS-stimulated blood from 1,206 ± 1,667 pg/ml to 140 ± 128 pg/ml; $P = 0.006$. There was no consistent effect of ATP on IL-10 secretion in our study (21.6 ± 16.9 pg/ml to 17.2 ± 18.8 pg/ml). Interestingly, three subjects of Indian/Indonesian origin had IL-10 levels below the assay detection limit. The mean IL-10/IFNγ ratio was increased from 0.05 ± 0.04 to 0.16 ± 0.09 in the remaining Caucasian subjects ($P = 0.015$). See Figure 1.

Conclusions Our results suggest an immunosuppressive effect of extracellular ATP that is evident by the decrease of IFNγ and therefore the relative shift of the immune response towards Th2 phenotype. Although this may represent a self-protective mechanism, it may contribute to critical illness anergy.

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P6

Tyrosine phosphorylation modulates rat vascular response to experimental endotoxemia *in vivo* and *in vitro*

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Introduction Endotoxemia is characterized by vascular hyporeactivity, hypotension and microcirculatory changes that are partially linked to the excess of nitric oxide production. The agents that can influence Ca^{2+} transport (affect Ca-ATPase) or modulate Ca^{2+} sensitivity of the smooth muscle contraction (modulate phosphorylation) may theoretically influence some of the above-mentioned effects.
Methods We evaluated the effects of tyrosine phosphatase or kinase inhibitors, sodium orthovanadate (SOV) or genistein (GEN). The effects of these agents were examined *in vitro*, in a model of vascular hyporeactivity of sepsis, in rings of rat aorta (RA), with or without endothelium (±ENDO), or in human mesenteric artery (HMA). *In vivo*, the intestinal microcirculation (terminal ileum) of endotoxemic rats (LEW.1A) that received i.v. lipopolysaccharide (LPS), 15 mg/kg BW, was examined using intravital microscopy.
Results *In vitro*. The nitric oxide production inhibitor L-NAME (5×10^{-4}) and cGMP inhibitor ODQ (5×10^{-5}) abolished LPS-induced hyporeactivity. GEN attenuated maximal tension (T_{max}) while SOV increased the response to PE; T_{max} (kg/g, dry muscle): controls vs SOV, RA (–ENDO): 0.87 ± 0.19 vs 1.42 ± 0.23 (10^{-7}); 1.56 ± 0.28 (10^{-6}) and 2.33 ± 0.69 (10^{-5}); RA (+ENDO): 0.88 ± 0.21 vs 1.53 ± 0.35 (10^{-7}); 1.35 ± 0.30 (10^{-6}) and 2.55 ± 0.68 (10^{-5}); and HMA (+ENDO): 1.12 ± 0.23 vs 0.37 ± 0.14 (10^{-7}); 2.06 ± 0.21 (10^{-6}) and 3.00 ± 0.07 (10^{-5}).
In vivo. In the LPS group GEN increased mucosal functional capillary density (FCD, cm/cm^2; mean ± SD; LPS vs GEN, 105.5 ± 44.6 vs 174.7 ± 39.1; $P = 0.018$). SOV (7.5 mg/kg) increased FCD not only in mucosa (163.7 ± 40.0; $P = 0.024$) but also in the longitudinal muscular layer (LPS vs SOV, 111.9 ± 24.0 vs 172.2 ± 19.5; $P < 0.001$). Surprisingly, the SOV (15 mg/kg) alone (without LPS) increased leukocyte sticking in the venules V1 (LPS vs SOV, number of stickers/mm^2, 403.3 ± 113.9 vs 669.8 ± 150.8; $P = 0.027$).
Conclusions The tyrosine phosphorylation pathway may play an important role in modulation of the LPS-induced vascular hyporeactivity and could enhance terminal ileum microcirculation. This might be a result of both modulation of tyrosine phosphorylation by genistein and sodium orthovanadate, and/or plasma membrane Ca-ATPase inhibition by SOV.

P7

Glibenclamide dose response in patients with septic shock

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Introduction (K+ATP) channels are implicated in the pathophysiology of catecholamine tachyphylaxis in septic shock. This prospective, randomized, double-blinded, clinical study was designed to determine whether different doses of glibenclamide have any effects on norepinephrine requirements and cardiopulmonary hemodynamics in patients with septic shock.
Methods We enrolled 30 patients with septic shock requiring invasive hemodynamic monitoring and norepinephrine infusion ≥ 0.5 μg/kg/min to maintain MAP between 65 and 75 mmHg. Patients were randomized to receive either 10, 20, or 30 mg enteral glibenclamide. Systemic hemodynamics, global oxygen transport, arterial lactate concentrations, gas exchange, and plasma glucose concentrations were determined at baseline, and following 3, 6 and 12 hours after administration of the study drug.
Results Glibenclamide decreased plasma glucose concentrations in a dose-dependent manner, but failed to reduce norepinephrine requirements. None of the doses had any effects on cardiopulmonary hemodynamics. See Table 1.

Table 1 (abstract P7)

Plasma glucose concentration (mg/dl)

	Time			
Glibenclamide	0 hours	3 hours	6 hours	12 hours
10 mg	118 ± 13	110 ± 9	109 ± 10	107 ± 10
20 mg	117 ± 5	106 ± 4	93 ± 7*	98 ± 9*
30 mg	113 ± 6	86 ± 3*	89 ± 4*	98 ± 3*

Data presented as mean ± SEM. *$P < 0.05$ vs baseline (0 hours) within groups.

Conclusion Oral glibenclamide is an ineffective adjunct in the treatment of catecholamine-dependent human septic shock.

P8

Molecular mechanism of glutamine induction of HSP70 involves activation of the *O*-linked-*N*-acetylglucosamine pathway in murine embryonic fibroblast cells

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Introduction The purpose of this study was to determine whether glutamine (GLN)-mediated cellular protection is dependent on the *O*-linked-*N*-acetylglucosamine (O-glcNAc) pathway. GLN can protect against critical illness via induction of HSP70. The molecular mechanism by which GLN enhances HSP70 is unknown. GLN can increase flux through the hexosamine biosynthetic pathway and activate transcription factors by O-glcNAc. We investigated GLN's effect on O-glcNAc levels and nuclear translocation of SP1 and HSF-1, which are vital to HSP70 expression. To determine the importance of O-glcNAc, we used silencing RNA (siRNA) against *O*-linked-*N*-acetylglucosamine transferase (OGT), the enzyme that catalyzes addition of O-glcNAc to proteins.
Methods Mouse embryonic fibroblast cells were treated with 0 mM GLN (CT) or 10 mM GLN (GLN), heat stressed (HS) and allowed to recover for 20 minutes. Cells were stained and mean fluorescent intensities (MFIs) measured for total O-glcNAc and nuclear HSF-1 and SP1. For OGT silencing, cells were transfected with either no siRNA, siRNA to OGT, or negative control oligos (nc siRNA) and then treated as above (but with 4 hours recovery). HSP70 and OGT were evaluated by western blot.
Results Microscopy showed GLN treatment increased nuclear MFI for HSF-1 by 40% (HS-CT: 1,005 ± 146 vs HS-GLN:1403 ± 102, $P < 0.05$) and SP1 by 54% (HS-CT: 214 ± 14 vs HS-GLN: 330 ± 13, $P < 0.05$). Total O-glcNAc levels showed 44% MFI increase in HS-GLN compared with HS-CT (HS-CT: 360 ± 24 vs HS-GLN: 518 ± 51, $P < 0.05$). Following OGT silencing, HS-GLN showed a threefold increase in HSP70

($P = 0.04$). These increases were completely blocked by OGT silencing ($P = 0.02$ vs non-siRNA GLN groups). GLN-nc siRNA groups did not decrease in HSP70 production. OGT was knocked down 86% compared with controls (siRNA: 0.999 ± 0.19 vs CT: 0.131 ± 0.05). $N = 3$.

Conclusions These results show GLN can activate the O-glcNAc pathway and enhance nuclear translocation of HSF-1 and SP1. Inhibition of OGT blocked GLN-mediated induction of HSP70. Thus, it appears the mechanism of GLN-mediated HSP70 expression is dependent on enhanced O-glcNAc pathway activation.

P9

The effects of *N*-acetylcysteine on the levels of glutathione, serum TNFα, and tissue malondialdehyde in sepsis

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Objectives This study was designed to determine the effects of *N*-acetylcysteine (NAC) as an antioxidant agent on the free oxygen radicals and their plasma levels.

Methods In this study, 40 Sprague–Dawley rats were randomly divided into three groups as sham ($n = 10$), sepsis ($n = 10$), and sepsis + NAC (20 mg/kg/24 hours) ($n = 10$). An experimental sepsis model was performed by a cecal ligation and perforation (CLP). NAC was administered at 0, 8 and 16 hours after CLP. The blood samples were taken at 24 hours to determine the levels of serum TNFα and erythrocyte glutathione (GSH), and renal and liver tissue malondialdehyde (MDA).

Results The serum TNFα levels were significantly decreased in group 3 compared with group 2 ($P < 0.05$). The erythrocyte GSH levels significantly increased in group 3 compared with group 2 ($P < 0.05$). In group 3, the liver MDA levels were decreased compared with group 2, but not statistically significant ($P > 0.05$) In group 3, the renal MDA levels were significantly decreased compared with group 2 ($P < 0.05$). The lung tissue PMNL levels significantly decreased in group 3 compared with group 2 ($P < 0.05$).

Conclusion In an experimental sepsis model, with the administration of NAC as an antioxidant agent at lower doses, many meaningful positive effects were detected on the levels of erythrocyte GSH, serum TNFα, respiration function, and renal tissue MDA. In spite of the low dose, NAC therapies decrease the organ function abnormalities; these effects were not reflected in the histopathological investigations. These findings suggest that NAC could be a possible therapeutic agent for sepsis and its mortality. However, further studies are needed to elucidate the effects of these drugs at higher doses.

P10

Exogenous adrenomedullin reduces the arterial lactate concentration and mean pulmonary arterial pressure in ovine endotoxemia

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Introduction Sepsis-associated arterial hypotension may be complicated by inadequate systemic and regional oxygen delivery resulting in lactic acidosis and multiple organ failure. We hypothesized that exogenous administration of adrenomedullin (AM), a vasodilatory peptide hormone with anti-inflammatory properties, may improve the oxygen delivery–demand relationship, thereby limiting the increase in arterial lactate concentrations in ovine endotoxemia.

Methods Fourteen adult ewes were instrumented for chronic hemodynamic monitoring. Following 16 hours of endotoxemia (*Salmonella typhosa* endotoxin, 10 ng/kg/min) the animals received either a continuous infusion of AM at incremental doses (10, 50, 100 ng/kg/min; each for 30 min) or the vehicle (normal saline; $n = 7$ each).

Results Endotoxin infusion contributed to a hypotensive–hyperdynamic circulation characterized by decreases in mean arterial pressure (MAP) and systemic vascular resistance index as well as increases in heart rate (HR), cardiac index (CI) and arterial lactate concentrations. AM infusion at 100 ng/kg/min increased the CI (12.2 ± 0.8 vs 7.8 ± 0.5 l/min) and oxygen delivery index (1,734 ± 121 vs 1,075 ± 63 ml/min/m^2), thereby decreasing the arterial lactate concentration (0.7 ± 0.2 vs 1.7 ± 0.3 mg/dl) and mean pulmonary arterial pressure (18 ± 1 vs 24 ± 1 mmHg; each $P < 0.001$ vs control) noticed in the control group. However, AM infusion at 100 ng/kg/min was linked to a decrease in MAP (64 ± 2 vs 80 ± 4 mmHg, $P < 0.001$ vs control).

Conclusions Despite decreasing MAP, infusion of AM reversed pulmonary hypertension and improved the oxygen supply–demand relationship in a dose-dependent manner, as indicated by a reduced arterial lactate concentration. However, due to the vasodilatory properties of AM, it may be rationale to combine AM with a vasopressor agent.

P11

Angiopoietin-2 correlates with pulmonary capillary permeability and disease severity in critically ill patients

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Introduction It has previously been shown that angiopoietin-1 (Ang1) protects the adult vasculature against plasma leakage, whereas Ang2 and VEGF destabilize the vascular endothelium resulting in vascular leakage. Consequently they might be involved in the pathophysiology of acute lung injury (ALI) and acute respiratory distress syndrome (ARDS) in sepsis patients. We hypothesized that plasma Ang2 levels are associated with pulmonary capillary protein permeability, the lung injury score (LIS), length of stay on the ICU, the APACHE II score and survival in septic patients with ALI or ARDS.

Methods A prospective observational study was performed in an ICU of an university hospital on 112 patients: 38 after elective cardiac surgery, 26 after major vascular surgery, 24 with sepsis and 24 with trauma. Plasma levels of Ang1, Ang2 and VEGF were measured and a mobile probe system was used to measure the pulmonary leak index (PLI) (that is, the transvascular transport rate of gallium-67-radiolabeled transferrin).

Results Plasma levels of Ang2 and the PLI were significantly higher in patients with sepsis compared with other patient groups. In the sepsis group, a positive linear correlation was observed between plasma levels of Ang2 and length of stay on the ICU ($r_s = 0.509$, $P < 0.05$) as index for disease severity. For all patients together, Ang2 had a positive linear correlation with PLI ($r_s = 0.374$, $P < 0.01$), LIS ($r_s = 0.489$, $P < 0.01$) and APACHE II score ($r_s = 0.287$, $P < 0.01$). Furthermore, Ang2 was significantly increased

in nonsurvivors. Plasma Ang1 levels did not differ between groups. VEGF levels were undetectable in the plasma of the majority of patients.

Conclusions Our results suggest that Ang2 is a mediator of pulmonary capillary permeability and a marker of disease severity in critically ill patients. Furthermore, the plasma levels of Ang2 and the ratio between Ang1 and Ang2 are more important in pulmonary capillary permeability and disease severity than absolute levels of Ang1 and VEGF.

P12

Dose-dependent effects of octreotide on plasma activities of IL-6 and lung tissue levels of malondialdehyde in sepsis

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Background and aim Sepsis, a complex and rapidly progressing infectious disease with high levels of mortality, is widely regarded as the most challenging problem in intensive care. The lung is frequently the first failing organ during septic conditions. Although the etiology of sepsis is multifactorial, early release of proinflammatory cytokines and oxidative damage are probably most important factors that lead to cell damage, organ dysfunction, and death. This study aimed to determine the effects of treatment with octreotide (OCT), on plasma activities of IL-6 and tissue levels of malondialdehyde (MDA) in an experimental model of sepsis.

Methods Sepsis was induced in female Sprague–Dawley rats by cecal ligation and puncture (CLP) as previously described. Group 1 ($n = 10$), sham operated animals; Group 2 ($n = 10$), sepsis served as control; Group 3 ($n = 10$) and Group 4 ($n = 10$), respectively, OCT 50 μg/kg twice a day and OCT 100 μg/kg twice a day administered subcutaneously immediately after the induction of sepsis and at 12 hours. Rats were sacrificed 24 hours after the surgical procedure. Blood and lung tissue samples were taken 24 hours after sepsis induction. Plasma activities of IL-6 and lung tissue levels of MDA were measured.

Results The results showed that the plasma levels of IL-6, an inflammatory indicator, and tissue levels of MDA, an oxidative indicator, are significantly increased during experimental model of sepsis ($P < 0.05$). Increase in MDA levels and IL-6 activities after CLP-induced sepsis was significantly prevented by OCT (100 μg/kg, s.c.) administration ($P < 0.05$).

Conclusion Octreotide seems to have a dose-dependent antioxidative and immunomodulator effect in CLP-induced sepsis in rats. Further trials are necessary to reveal the therapeutic effect of OCT in sepsis. On the other hand, further studies should be performed aiming to reveal the optimal OCT doses. As a drug with a wide margin of safety and less adverse reaction profile, OCT merits consideration as a choice of treatment in sepsis and septic shock.

P13

Escherichia coli porcine peritonitis induces histological and transcriptome evidence of cardiac injury

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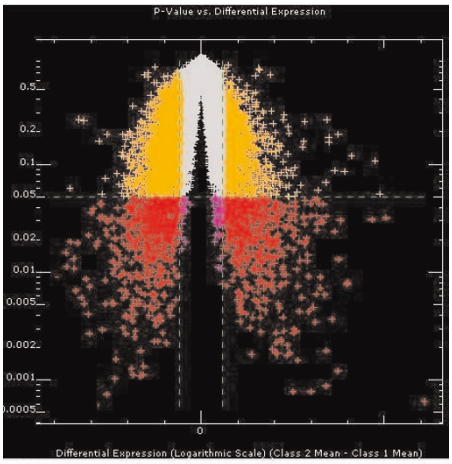
Introduction Cardiac dysfunction is a feature of sepsis. In order to gain insight into the fundamental mechanisms of this phenotype, gene expression analysis (Affymetrix) was applied to serial cardiac biopsies of sham ($n = 2$) and *E. coli* infected pigs ($n = 3$).

Figure 1 (abstract P13)



Methods Cardiac samples were taken basal and hourly after infection for gene analysis and at the end of the experiment for histopathological examination. Genes were determined to be differentially regulated at a greater than or less than twofold change and $P < 0.05$.

Results Sham pigs had stable heart rate, cardiac output (CO) and core temperature for the 5-hour period; infected pigs demonstrated an early elevation in CO and ventricular shortening and/or ejection (assessed by echocardiography) followed by development of hypodynamics. In infected animals, increasing numbers of genes were upregulated or downregulated (36, 278, 514, 842 and 1,238 at 1, 2, 3, 4 and 5 hours) (Figure 1) whereas sham infection altered fewer (247, 67 and 384 genes at 2, 3 and 4 hours). Comparing sham vs infected animals at the same time, numbers of significantly altered genes increased with time (32 at basal, to 74, 189 and 601 at 2, 3 and 4 hours post infection). In hematoxylin–eosin-stained sections, histopathological assessment revealed acute inflammation in pericardium and myocardium in infected pigs.

Conclusions These results will provide biomarker and mechanistic insights to pathogenesis of cardiac dysfunction of septic peritonitis and may also help identify some altered novel gene transcription pathways that can serve as new targets for diagnostic tools and therapeutic strategies. All candidate genes will be validated by quantitative PCR.

P14

Alkaline phosphatase treatment improves renal function in patients with severe sepsis or septic shock

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We previously demonstrated that upregulation of renal inducible nitric oxide synthase (iNOS) during systemic inflammation is

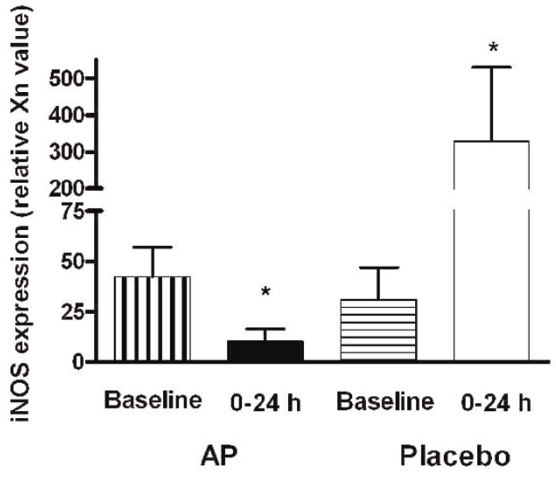
associated with proximal tubule injury. In several *in vitro* and animal studies alkaline phosphatase (AP) was found to be effective in attenuating the inflammatory response by dephosphorylating LPS and may prevent organ damage. The objective of this study was to investigate the effect of AP on renal iNOS expression and kidney damage in patients with severe sepsis or septic shock.

Fifteen patients (nine male/six female, age 55 ± 5 years) with Gram-negative bacterial infection, two out of four SIRS criteria (<24 hours) and acute onset of end-organ dysfunction (<12 hours) were included in a randomized, double-blind, placebo-controlled phase IIa study (2:1 ratio). An intravenous bolus injection of 67.5 U/kg bovine intestinal AP was followed by a maintenance dose of 177.5 U/kg for 24 hours. Arterial blood and urine were collected at different time points and analyzed for stable metabolites of NO. iNOS mRNA was determined by quantitative real-time RT-PCR using RNA isolated from renal cells in urine. The urinary excretion of the cytosolic glutathione *S*-transferase-A1 (GSTA1-1), a marker for proximal tubule damage, was measured using an ELISA. Data are depicted as the median (25–75% range).

NO metabolites in blood were not significantly different between AP-treated ($n = 10$) and placebo-treated ($n = 5$) patients. However, the urinary excretion of NO metabolites decreased by 80% (75–85) from 227 (166–531) at baseline to 41 (28–84) µmol/10 mmol creatinine ($P < 0.05$) after 24 hours of AP administration. After placebo treatment, the amount of urinary NO metabolites increased by 70% (45–570) (from 81 (64–419) to 628 (65–1,479) µmol/10 mmol creatinine, $P < 0.05$). Baseline expression levels of iNOS in renal cells were 42-fold induced at baseline (vs healthy subjects), and AP administration reduced this induction by 80 ± 5% (Figure 1). Creatinine clearance improved by 45% (30–180) in patients treated with AP and declined by 25% (15–35) in placebo-treated patients. During the first 24 hours the amount of GSTA1-1 in urine of AP-treated patients decreased by 70% (50–80), compared with an increase of 200% (45–525) in placebo-treated patients, which correlated with urinary NO metabolites, indicating NO-induced proximal tubular damage.

In conclusion, in septic patients, infusion of AP results in an attenuated upregulation of iNOS and, subsequent, reduced NO production in the kidney, associated with an improvement in renal function.

Figure 1 (abstract P14)



P15

Moderate hypothermia attenuates changes in respiratory system mechanics and cytokine production during low lung volume ventilation in rats

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Introduction Hypothermia was shown to attenuate ventilator-induced lung injury (VILI) in high end-inspiratory lung volume models of VILI [1-3]. Experimental evidence suggests that moderate tidal volumes may, under certain clinical conditions that induce alveolar instability, lead to a lung injury [4]. Recent studies have also suggested that insults like shock [5] or surgery [6] sensitize the lung to injury by priming for an exaggerated response to a second stimulus. The aim of this study was to investigate whether moderate hypothermia attenuates low lung volume injury during low PEEP, high FiO_2 and moderate tidal volume ventilation in animals sensitized to injury by previous anesthesia and surgery.

Methods Sixteen male adult Sprague–Dawley rats, instrumented under ether anesthesia with vascular catheters on the previous day, were anesthetized, tracheostomized, connected to a ventilator and randomly allocated to groups of normothermia (37 ± 0.5°C, group N, $n = 8$) or hypothermia (33 ± 0.5°C, group H, $n = 8$). After 2 hours of mechanical ventilation (FiO_2 1,0, respiratory rate 60/min, tidal volume 10 ml/kg, PEEP 2 cmH_2O) inspiratory pressures were recorded, rats were sacrificed, the P–V curve of the respiratory system constructed, and bronchoalveolar lavage and aortic blood samples obtained.

Results Group H animals exhibited in comparison with group N animals a lower increase in peak inspiratory pressures (0.7 ± 1.1 vs 2.4 ± 0.5 mmHg, $P < 0.001$), significant shift of the P–V curve to the left and lower total protein (113 ± 42 vs 201 ± 97 µg/ml, $P = 0.047$) and TNF (23.5 ± 8.0 vs 35.2 ± 8.5 pg/ml, $P = 0,022$) levels in BAL samples.

Conclusion Moderate hypothermia attenuated lung injury during low PEEP, high FiO_2 and moderate tidal volume ventilation in animals sensitized to injury by previous anesthesia and surgery.

Acknowledgement Supported by the Research project MZO 00179906.

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P16

Effects of neuronal nitric oxide synthase in ovine lung injury

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Introduction Excessive production of nitric oxide is a major factor contributing to acute lung injury and systemic inflammation after

burn and smoke inhalation injury. We hypothesized that the use of 7-nitroindazole (7-NI), a selective nNOS inhibitor, blocks molecular mechanisms in this pathogenesis.

Methods Eleven ewes were surgically instrumented and randomly allocated to either an injured untreated control group (40% total body surface area flame burn and 48 breaths of cotton smoke, $n = 6$), or an injury group treated with 7-NI (1 mg/kg/hour, $n = 5$).

Results This insult was associated with systemic inflammation and oxidative stress, as evidenced by a 2.5-fold increase in plasma nitrite/nitrate (NOx) levels, as well as sixfold, twofold, threefold and twofold increases in IL-8, myeloperoxidase (MPO), malondialdehyde (MDA) and poly-ADP-ribose-polymerase (PARP) lung tissue concentrations, respectively. These molecular changes were linked to severe pulmonary derangements. Compared with untreated controls, 7-NI significantly reduced NOx plasma levels (8.4 ± 1 vs 26 ± 10 μmol/l) and decreased IL-8, MPO (3.9 ± 0.2 vs 5.8 ± 0.7 U/g tissue), MDA (2.7 ± 0.3 vs 6.6 ± 1.1 nmol/mg protein) and PARP lung tissue content (3.4 ± 0.7 vs 6.7 ± 0.7), thereby decreasing pulmonary obstruction (12.4 ± 2.2 vs 28.7 ± 5.2 obstruction score) and increasing the PaO_2/FiO_2 ratio (456 ± 40 vs 313 ± 56, each $P < 0.05$).

Conclusions These data suggest that nNOS-derived NO plays a pivotal role in the pathophysiology of this double-hit injury and that selective nNOS inhibition may represent a useful approach to attenuate the degree of pulmonary damage.

P17

nNOS and Nox4 go nuclear: nNOS-derived and NADPH oxidase-derived reactive oxygen/nitrogen species promote oxidative nuclear damage in alveolar epithelial cells

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Emerging evidence implicates a role for angiotensin II (Ang II)-stimulated reactive oxygen and nitrogen species (ROS/RNS) formation in acute lung injury (ALI). However, details of the mechanism are lacking. We hypothesized that compartmentalized generation of superoxide (O_2^-) and nitric oxide (•NO) may be key events in the Ang II-stimulated progression of ALI. In the present study, we found that Ang II markedly enhanced ROS/RNS production 7.4-fold, an effect blocked by the specific nNOS inhibitor *N*(G)-propyl-L-arginine, the NADPH oxidase inhibitor apocynin, or small interfering RNA (siRNA)-specific gene silencing targeted against nNOS or Nox4. nNOS/Nox4 transiently co-immunoprecipitates, and co-localizes at the peri-nuclear region 15 minutes post Ang II stimulation. Subsequently, confocal and western blot analyses show that nNOS/Nox4 translocates to the nucleus, suggesting that nNOS/Nox4 may directly regulate nuclear signaling. Furthermore, PAR polymers, which are undetectable in resting conditions, were generated following Ang II stimulation, an effect blocked with apocynin or *N*(G)-propyl-L-arginine. In conclusion, these data suggest Ang II causes nNOS/Nox4 to co-localize at the peri-nuclear region of A549 cells, where superoxide produced by Nox4, and •NO produced by nNOS immediately react to form peroxynitrite, which leads to subsequent nuclear oxidative damage as evidenced by increased PAR polymer formation. Furthermore, these experiments demonstrate inflammatory-stimulated nuclear translocalization of nNOS/Nox4, which has important implications for direct ROS/RNS-mediated nuclear activities. Therefore, inhibition of nNOS/Nox4 may be an effective therapeutic target in patients with ALI.

P18

Dose effects of recombinant human IL-11 on the systemic hemodynamic function in hemorrhagic shock

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Introduction We have previously demonstrated that administration of recombinant human IL-11 (rhIL-11) during resuscitation improves the cardiovascular functions in a rodent model of hemorrhagic shock. The purpose of this study was to elucidate: (1) whether these beneficial effects were dose related, and (2) whether the effects of rhIL-11 could be reproduced in a large animal model.

Methods Swine ($n = 56$, weight = 25–35 kg) underwent 40% blood volume hemorrhage, and a 1-hour shock period, followed by resuscitation with 0.9% sodium chloride (three times the shed blood volume). The animals were randomized to receive: (1) group I, 5 μg/kg rhIL-11 ($n = 6$); group II, 20 μg/kg rhIL-11 ($n = 5$); group III, 50 μg/kg rhIL-11 ($n = 6$) – and then, (2) group IV, sham hemorrhage (sham, $n = 10$); group V, sham hemorrhage and 50 μg/kg rhIL-11 (sham + IL-11, $n = 6$); group VI, no drug (saline, $n = 15$); group VII, 50 μg/kg rhIL-11 (IL-11, $n = 14$). Blood samples and urine were obtained and analyzed at baseline, the end of hemorrhage, and at every hour.

Results (1) The mean arterial pressure was higher post-resuscitation (PR) in group III (62.9 ± 8.2 mmHg) than in groups I and II (54.9 ± 1.7, 53.9 ± 4.3 mmHg; $P < 0.01$). The urine output (I: 999 ± 428, II: 1,249 ± 180, III: 1,434 ± 325 ml) and the cardiac output (CO) (I: 3.01 ± 0.66, II: 3.30 ± 0.49, III: 3.43 ± 0.57 l/min) increased dose dependently. The volume of third space fluid loss of group III decreased significantly (I: 157 ± 32, II: 138 ± 32, III: 82 ± 21 ml; $P < 0.05$). (2) Mean arterial pressure was higher PR among groups IV, V and VII (71.4 ± 7.5, 71.0 ± 8.9, 72.9 ± 12.3 mmHg) compared with group VI (59.9 ± 10.9) and CO of PR was higher in group VII (3.46 ± 0.56 l/min) than group IV (2.99 ± 0.62; $P < 0.01$). Following resuscitation, the urine output was higher, and the urine specific gravity and third space fluid loss were lower in group VII (1,434 ± 325 ml, 1.0035, 82 ± 21 ml) compared with group VI (958 ± 390 ml, 1.0053, 125 ± 32 ml; $P < 0.05$).

Conclusion The effects of rhIL-11 on the cardiovascular functions were influenced by the dose of rhIL-11, although the relationship did not follow simple linearity. A 50μg/kg dose rhIL-11 significantly improves cardiovascular functions in a porcine model of hemorrhagic shock.

P19

Degradation of endothelial glycocalyx provides new insights in the pathogenesis of septic shock microvascular failure

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Introduction Glycocalyx (GLX) is implicated in mechanotransduction of shear stress and microvascular blood flow. We tested whether GLX loss accounts for the microvascular dysfunction in sepsis and whether activated protein C (APC) preserves endothelial GLX integrity.

Methods Endotoxin LPS (10 mg/kg) was infused in rats treated or not with APC (240 μg/kg/hour). Changes in GLX were assessed by circulating levels of hyaluronan (a GLX constituent) and by GLX

apparent thickness evaluated using intravital microscopy by comparing 4 and 150 kDa dextran distribution as markers of GLX permeable and impermeable tracers, respectively. Intravital microscopy was used to characterize mesentery functional capillary density. Because glycocalyx is extremely sensitive to free radical, oxidative stress was evaluated by oxidation of dihydrorhodamine (DHR) in microvascular beds and by concentrations of heart malondialdehyde (MDA) and plasma carbonyl proteins (CP).

Results LPS elicited a 4 hours later profound reduction in GLX layer thickness and increase in plasma hyaluronan levels. LPS rats had decreases in capillary continuous flow, and significant increases in intermittent and stopped flow capillaries compared with controls. The pressor responses to norepinephrine were greatly reduced, indicative of vascular hyporeactivity. *In vivo* oxidation of DHR and levels of heart MDA and plasma CP were all increased in LPS-treated rats. Interestingly, in LPS rats, APC reduced plasma hyaluronan levels and GLX destruction, which was accompanied with major improvements in vasopressor response and functional capillary density. APC treatment also prevented increases in biochemical and *in vivo* microvascular oxidative stress markers.

Conclusion In our model of septic shock, increased plasma hyluronan levels and reduction in endothelial layer thickness indicated GLX degradation. APC prevented vascular oxidative stress and limited GLX loss. GLX degradation plays a critical role in the septic vasculature and generation of free radicals during septic shock is potentially toxic to GLX function.

P20

Exhaled breath condensate mediators in mechanically ventilated brain-injured patients with no acute lung injury are mostly related to markers of systemic inflammation

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Introduction Mechanical ventilation may induce lung injury in patients with normal lungs. Application of PEEP appears protective. Lung injury is associated with the production and release of inflammatory mediators. Such mediators have been identified in patients' exhaled breath condensate (EBC) in various lung pathologies. In this study we identified EBC inflammatory markers in 27 mechanically ventilated brain-injured subjects with neither acute lung injury (ALI) nor sepsis.

Methods Patients were ventilated with 8 ml/kg tidal volume and were put either on PEEP = 0 (ZEEP, $n = 12$) or 8 cmH_2O (PEEP, $n = 15$). EBC was collected using the RTube device (Respiratory Research Inc., Charlottesville, VA, US) on the first, third, and fifth day of mechanical ventilation, and pH, IL-10, IL-1β, IL-6, IL-8, IL-12p70 and TNFα were measured. Applying mixed effects models, we further investigated potential relationships of the above EBC markers with indices of: i, lung injury (LIS score, PaO_2/FiO_2, detected pathologies on lung CT); ii, brain injury (ICP, CPP, GCS, serum (s) S100 protein, pentothal and mannitol administration); iii, endothelial injury (sICAM-1, sVCAM-1, von Willebrand factor antigen); iv, systemic inflammation (temperature, leukocyte counts and neutrophil counts in blood, albumin, soluble triggering receptor expressed on myeloid cells (sTREM), CRP, procalcitonin (PCT) and all above-mentioned cytokines in serum or plasma); and v, disease severity (APACHE II score, 24 hour ICU trauma score, presence of SIRS, mean arterial pressure).

Results No significant differences in EBC measurements were observed between the two groups except a time-dependent decrease in IL-10 ($P < 0.05$, by ANOVA) in the PEEP group. EBC pH and IL-10 showed no significant relationships (mixed effects models) with any parameter measured. All other EBC cytokines were inversely related to sTREM levels. Additional significant relationships were obtained between individual EBC cytokines and sIL-8 (IL-8, IL-12p70, TNFα), sIL-6 (IL-1β), PCT (IL-1β, IL-12p70), the existence of SIRS (IL-6, IL-8), sVCAM-1 (IL-6), and pentothal administration (IL-1β).

Conclusion In our population of mechanically ventilated, brain-injured patients with no ALI, ZEEP or applied PEEP did not induce detectable changes in most lung inflammatory mediators in EBC; the latter appear mostly related to markers of systemic inflammation (especially sTREM-1) rather than to indices of brain and endothelial injury.

P21

Reduced local inflammatory reactivity in septic patients compared with healthy controls

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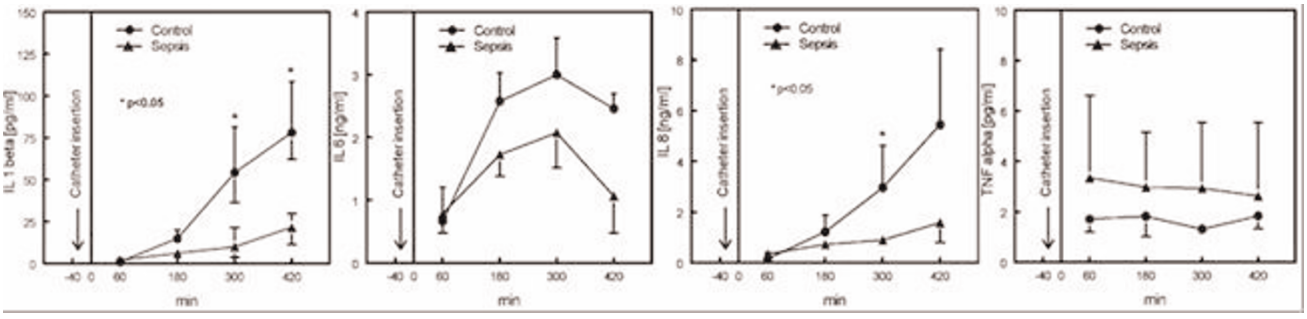
Introduction The aim of this study was to access the local inflammatory reactivity by measurement of the cytokine response

Figure 1 (abstract P21)



after catheter insertion into subcutaneous adipose tissue (SAT) of patients with severe sepsis compared with healthy volunteers.
Methods Eight healthy volunteers and 10 patients with severe sepsis were included. One 18-gauge open-flow microperfusion double-lumen catheter was inserted into SAT of the abdominal wall and perfused with an isotonic solution at a flow rate of 1 µl/min. Blood samples and probe effluent samples from interstitial fluid of SAT were withdrawn in two hourly intervals for a period of 8 hours and retrospectively analysed using a Multiplex ELISA system for IL-1β, IL-6, IL-8 and TNFα.
Results Concentrations of IL-1β, IL-6 and IL-8 were substantially higher in SAT (13.3 (11.2; 31.0); 1,934 (1,650; 2,730); 917 (656; 2,672) pg/ml; median (25th; 75th percentile)) than in serum (0.8 (0.6; 1.3); 49.2 (3.8; 67.6); 36.1 (6.3; 89.1) pg/ml) for both groups, whereas TNFα concentrations were similar in serum and SAT (Figure 1). Serum concentrations of all cytokines remained stable over time. However, a significant increase was observed for IL-1β and IL-8 in SAT in both groups. This increase was significantly in septic patients vs healthy controls.
Conclusion Insertion of a catheter into subcutaneous adipose tissue promotes a local inflammatory response in both healthy individuals and critically ill patients. The attenuated response in patients with severe sepsis might be caused by reduced inflammatory reactivity in this group.

P22

The evaluation of sivelestat sodium hydrate in acute lung injury/acute respiratory distress syndrome patients in the intensive care unit

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The onset mechanism of ALI/ARDS and subsequent tissue injury are considered to be associated with neutrophil elastase, and the main causes of ALI/ARDS are considered to be sepsis or aspiration pneumonia. In Japan, sivelestat sodium hydrate (Elaspol), a selective elastase inhibitor, was approved in 2002 for ALI/ARDS accompanied by SIRS, and this medicine has been evaluated in a clinical situation. In this study, we performed a retrospective comparison of the sivelestat sodium administration between two groups of patients: Group Elaspol, consisting of 308 patients(209 males and 99 females, aged 66 ± 15 years) with ALI/ARDS accompanied by SIRS who were treated with sivelestat sodium at a dose of 0.2 mg/kg/hour for 72 hours or more, after approval of this drug; and Group Control, consisting of 41 patients (28 males and 13 females, aged 66 ± 14 years) with ALI/ARDS accompanied by SIRS who were treated in the ICU under similar conditions, but using traditional methods for respiratory control, prior to approval sivelestat sodium. The APACHE II scores of Group Elaspol and Group Control were 23 ± 9 and 23 ± 8, SOFA scores were 8.7 ± 3.8 and 8.9 ± 4.1, and the lung injury scores were 2.1 ± 0.7 and 2.1 ± 0.6, respectively, with no significant differences between the groups. The initial PEEP value of Group Elaspol was 5.9 ± 3.3, which was significantly higher than that of Group Control (3.4 ± 2.7 cmH_2O). The PaO_2/FIO_2 ratios under mechanical ventilation management 24, 48 and 72 hours after the beginning of drug administration were 209 ± 87, 222 ± 92, and 222 ± 82 mmHg in Group Elaspol, and were 191 ± 91, 207 ± 91, and 211 ± 100 mmHg in Group Control. The ventilator-free days of Group Elaspol and Group Control were 18 ± 9 and 10 ± 12 days, respectively, and these values showed a significant difference ($P < 0.001$). Furthermore, the survival rate after 28 days was significantly higher in Group Elaspol than in Group Control (Group Elaspol: 75%, Group Control: 52%; $P < 0.001$). These results suggest that sivelestat sodium hydrate is a good option as a treatment strategy for neutrophil elastase-associated septic ALI/ARDS accompanied by SIRS.

P23

Pharmacological modulation with prolonged administration of moderate doses of steroid in a murine model of septic acute lung injury after burn insult

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Introduction Many patients who experience surgical stress including burn injury become susceptible to severe sepsis and septic organ dysfunction including acute lung injury (ALI), which remains the primary contributor to morbidity and mortality in burn patients. Proinflammatory cytokines including several chemokines are implicated in this process. The pharmacological modulation with steroid inhibiting the process of cytokine synthesis may serve as effective therapy for the prevention of tissue injury and the resultant organ dysfunction including respiratory failure. We developed a murine model of septic ALI after burn insult and examined the effects of prolonged administration of moderate doses of steroid.
Methods Male BALB/c mice were divided into three groups. Group I served for sham burns. In groups II and III, a 15% BSA full-thickness burn was made on the dorsum under ether anesthesia, followed by adequate fluid resuscitation. After the burn injury, 3 mg/kg prednisolone (PSL) in group III was administered subcutaneously daily for 10 days. On the 11th day, 10 mg/kg lipopolysaccharide (LPS) was injected intravenously. In the first experiment, we observed the survival within 72 hours after LPS injection in each group ($n = 10$). In the second experiment, we sacrificed the animals at 12 hours after LPS injection, then obtained plasma and lung tissue to determine the levels of TNFα and macrophage inflammatory protein-2 (MIP-2, a functional homologue of human IL-8 in mice) in these samples ($n = 8$, sandwich ELISA). We also determined gene expression ($n = 4$, MIP-2/GAPDH mRNA ratio by RT-PCR), myeloperoxidase activities (MPO, $n = 8$) and histopathological findings in the lung tissue.
Results The survival and production of cytokines are shown in Table 1. Histopathological findings in group III were obviously attenuated.

Table 1 (abstract P23)

Group	Survival (%)	Plasma TNF (pg/ml)	Plasma MIP-2 (pg/ml)	Lung MIP-2 (pg/mg)	Lung MIP-2/GAPDH mRNA ratio	Lung MPO (U/mg)
I (sham–LPS)	100	1,190	6,396	70.0	0.345	0.405
II (burn–LPS)	0†	3,024**	13,766**	142.5**	0.975‡	0.574**
III (PSL)	50*	749§	791§	11.6§	0.052§	0.244§

Mean values are presented. *$P < 0.05$ vs group II, **$P < 0.005$ vs group I, †$P < 0.01$ vs group I, ‡$P < 0.05$ vs group I, §$P < 0.005$ vs group II.

Conclusions In this animal model, a pretreatment with PSL as the cytokine synthesis inhibitor improved the survival and attenuated the production of cytokines. The complications associated with sepsis after burn insults, especially ALI, could be preventable by the pharmacological modulation with prolonged administration of moderate doses of steroid.

P24

Glucosamine enhances heat shock protein 70 expression *in vitro* and *in vivo* following injury

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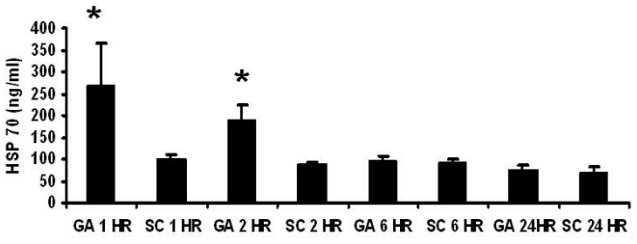
Introduction Enhanced activity of the *O*-glycosylation pathway (O-glcNAc) has been shown to enhance increase heat shock protein (HSP70) expression. Glucosamine (GA) is a vital intermediate in this pathway.
Methods Mouse fibroblast (MEF) cells underwent heat stress (HS) at 43°C for 45 minutes. GA doses from 1.25 to 20 mM were given immediately prior to HS. Cell survival was assessed via MTS assay. GA's effect on HSP70 expression *in vivo* was assessed using a mouse model of cecal ligation and puncture (CLP). Mice were given 0.26 g/kg GA i.v. 1 hour post CLP.
Results In MEF cells, 10 mM GA led to a 164% increase in HSP70 expression over control 4 hours post HS ($P < 0.05$ vs control). Further, GA treatment led to an increase in cell survival post HS injury at all doses tested ($P < 0.01$ vs control). Following CLP-induced sepsis, a single dose of GA led to an increase in lung and heart HSP70 at 1 and 2 hours post CLP vs saline control (SC). This effect was lost at 6 and 24 hours (see Figure 1, $*P < 0.05$ versus SC at each timepoint). Similarly, GA led to an increase in HSP70 in colon tissue as well, with the effect lasting to 6 hours ($*P < 0.05$ versus SC). The effect in colon was lost by 24 hours.
Conclusions To our knowledge, this is the first report that shows GA treatment can increase HSP70 expression both *in vivo* and *in vitro*. Previous data have demonstrated beneficial effects of GA treatment following ischemia/reperfusion injury and hemorrhagic shock early after injury. GA's effect on HSP70 expression in multiple tissues may help to explain these effects. Further, GA's effect on HSP70 expression may be an important factor involved in GA's benefits in arthritis and joint disease.

Figure 1 (abstract 24)



Lung heat shock protein (HSP70) expression in glucosamine vs saline following cecal ligation and puncture.

P25

Pharmacologic inhibition of cholinesterase improves survival in experimental sepsis

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Introduction Lethal sepsis occurs if an excessive inflammatory response evolves that cannot be controlled by physiological anti-inflammatory mechanisms. Vagus nerve stimulation showed improved survival in sepsis; however, this seems not to be feasible in septic patients. We therefore investigated the effect of activation of the cholinergic anti-inflammatory pathway by pharmacologic cholinesterase inhibition on survival and inflammation in a septic mouse model.
Methods To investigate the therapeutic effect of nicotine and physostigmine we performed cecal ligation and puncture (CLP) in female C57/B6 mice (each group $n = 21$). Substances were administered by intraperitoneal injection. Control groups received the same volume (50–180 µl) of LPS-free 0.9% NaCl (solvent). CLP was performed blinded to the identity of the treatment group. In addition to survival experiments we performed measurements of cytokines in plasma and the electrophoretic mobility shift assay (EMSA) for NF-κB in peritoneal skin, liver and kidneys.
Results (1) Animals treated with nicotine (400 µg/kg) or physostigmine (80 µg/kg) survived significantly better than control mice ($P < 0.05$). There was no difference between the treatment groups. (2) Dose escalation of physostigmine was not superior to the normal dose. Survival in the high-dose group, however, was still significantly better than in the control group. (3) Proinflammatory cytokine levels of TNFα, IL-6 and IL-1β were significantly reduced in animals treated with physostigmine ($P < 0.01$). (4) Cholinesterase inhibition with physostigmine in CLP reduced NF-κB activation in the peritoneum, kidney and liver compared with the control and sham-operated group ($P < 0.01$).
Conclusion We show that pharmacological cholinesterase inhibition with physostigmine improves survival in experimental sepsis, most probably by activation of the cholinergic anti-inflammatory pathway. One possible mechanism is modulation of the NF-κB pathway. Therefore, cholinesterase inhibition may have important implications for treatment of sepsis.

P26

Relationship between the presence of serum high-mobility-group box protein 1 and the injury severity score in trauma patients

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Introduction High-mobility-group box protein 1 (HMGB1) is a highly conserved, ubiquitous protein present in the nuclei and cytoplasm of nearly all cell types and, secreted into the extracellular milieu, acts as a proinflammatory cytokine. The function of HMGB1 has been widely studied for sepsis and inflammation. HMGB1 was reported as a late mediator in endotoxic shock and was known as an abundant protein present in nuclei and cytoplasm and involved in maintaining nucleosome structure and regulation of gene transcription. Moreover, elevated, circulating levels of HMGB1 also have been described in a case of human hemorrhagic shock due to abdominal aortic aneurysm without evidence of infection. However, the relationship between HMGB1 and trauma has not been studied except for the report of a rat model of burn.
Materials and methods The study cases consisted of 20 trauma patients who were admitted to the emergency room by ambulance. As soon as they arrived in the emergency room, their blood sample were collected, centrifuged, and stored at −80°C. The serum HMGB1 concentration was measured by ELISA. We compared the injury severity score (ISS), probability of survival values and the revised trauma score (RTS) of the patients with the presence of

serum HMGB1 (group A) and without the presence (group B). We therefore divided into two groups, high ISS group (≤25) and low ISS group (>25), and examined the relation with the serum HMGB1 level.

Results Our data showed that the number in group A was nine cases and group B was 11 cases. The ISS of group A was significantly higher than that in group B ($P = 0.0013$). The P value of group A was significantly lower than in group B ($P = 0.0131$). The serum HMGB1 level of the >25 ISS group was significantly higher than in the ≤25 ISS group.

Discussion These data suggest that HMGB1 seems to be a primary mediator of trauma-induced pathology. Because the ISS was significantly correlated with the presence of serum HMGB1, HMGB1 may be expressed in severe injuries and it may be a important parameter that indicates the severity of injury.

P27

Beneficial effects of antiplatelet drugs in patients with community-acquired pneumonia and in endotoxin shock in mice

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Aims Systemic inflammation and sepsis are associated with blood platelet activation, which may contribute to the development of organ failure. In this study we proved whether antiplatelet drugs have a benefit in patients who may develop sepsis as well as in a mouse model of endotoxin shock.

Methods Data obtained from 224 patients with community-acquired pneumonia (CAP) were retrospectively analysed for an association between prehospital treatment with long-acting antiplatelet drugs such as acetyl salicylic acid ($n = 36$) or thienopyridine ADP-receptor antagonists (clopidogrel or ticlopidin, $n = 8$) and clinical outcome. Use of statins was an exclusion criterion. BALB/c mice were pretreated with clopidogrel for 4 days prior to an intraperitoneal injection of LPS (*Escherichia coli* 0111:B4). For platelet counts and blood gas analysis, standard procedures were used. Lung tissues were stained with HE or a FITC-labelled anti-fibrin(ogen) antibody.

Results CAP patients with antiplatelet drugs ($n = 44$) were older than control patients ($n = 180$; 69 ± 7 vs 58 ± 13 years, $P < 0.00001$). At the day of hospital admission there were no differences in platelet or leukocyte counts, CRP and SOFA scores between both groups. However, patients on antiplatelet drugs developed organ failure less frequently than control patients (ICU admission: 9.1% vs 26.1%; $P < 0.02$). In the mouse model of endotoxin shock, clopidogrel reduced the drop in platelet count and the degree of lung injury. Compared with controls we found 20 hours after LPS injection in the clopidogrel-treated animals a lower number of thrombi in the lung vasculature (6.1 ± 2.3 vs 11.5 ± 4.4 thrombi per screen, $P < 0.025$) as well as higher blood pH and bicarbonate levels (7.01 ± 0.01 vs 6.93 ± 0.04, $P < 0.04$ and 10.2 ± 0.14 vs 7.3 ± 0.14 mmol/l, $P < 0.03$, respectively).

Conclusions Antiplatelet drugs may have a beneficial effect in systemic inflammation and sepsis, and could be a novel therapy option, at least in patients of low bleeding risk. One mechanism of their effects could be a reduction in the microvascular thrombus formation.

P28

Aggressive and moderate fluid resuscitation in septic pigs: consequences on morbidity

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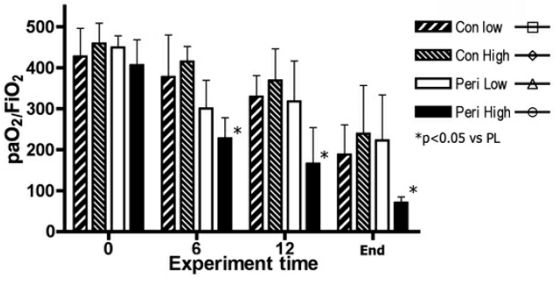
Critical Care 2007, **11(Suppl 2):**P28 (doi: 10.1186/cc5188)

Introduction While early aggressive fluid administration has been associated with improved outcome in sepsis [1], this approach may increase the risk of lung edema and abdominal compartment syndrome when capillary permeability is increased. The aim of this study was to test two different approaches of volume resuscitation in septic animals.

Methods Thirty pigs were anaesthetized and invasively monitored (systemic and regional flows and pressures). They were randomized to control, moderate volume (C; $n = 7$), control, high volume (CH; $n = 8$), peritonitis, moderate volume (P; $n = 8$) and peritonitis, high volume (PH; $n = 7$). Peritonitis was induced by instillation of 1 g/kg autologous faeces dissolved in glucose solution. Ventilation was adjusted to maintain an arterial pO_2 >100 mmHg. Groups CH and PH received 15 ml/kg/hour Ringer's solution plus 5 ml/kg/hour HES 6%, whereas groups C and P received 10 ml/kg/hour Ringer's solution. If clinical signs of hypovolaemia were present, additional boluses of HES 6% (maximally 100 ml/hour) were given. The animals were treated and observed for 24 hours or until death.

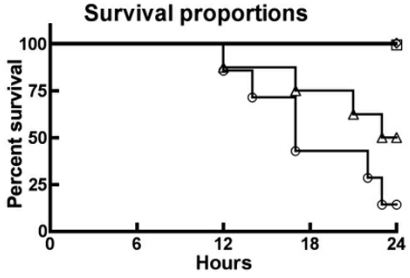
Results Cardiac output was higher in group PH as compared with the other groups ($P < 0.05$), while mean arterial pressure was

Figure 1 (abstract P28)



Oxygenation index.

Figure 2 (abstract P28)



Survival proportion.

similar in all groups. While the oxygenation index (paO_2/FiO_2) decreased in all groups, group PH had the lowest values after 6 hours and throughout the rest of the experiments ($P < 0.05$) (Figure 1). Survival was lowest in group PH, followed by group P, while all animals in the control groups survived until 24 hours (Figure 2).

Conclusion High-volume administration decreased oxygenation and survival in peritonitis but not in control animals. A high-volume approach may not be generally beneficial in abdominal sepsis.

Reference

1. Rivers E, *et al.*: *N Engl J Med* 2001, **345:**1368-1377.

P29

Effects of volume resuscitation on hepatosplanchnic oxygen consumption, liver mitochondrial function and mortality in endotoxemia

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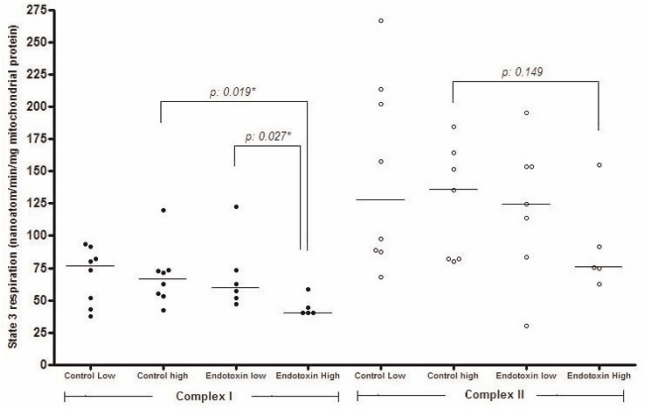
Introduction Fluid resuscitation is necessary in sepsis, but positive fluid balance may increase the risk of mortality. We tested the hypothesis that a volume resuscitation strategy may modify liver mitochondrial function and outcome.

Methods Twenty-nine anesthetized pigs received for 24 hours either endotoxin or placebo, and either Ringer's lactate 10 ml/kg/hour or 15 ml/kg/hour + 5 ml/hour HES. Systemic and regional hemodynamics were measured. Liver mitochondrial state 3 and state 4 oxygen consumption were determined.

Results Hepatosplanchnic oxygen delivery was similar in endotoxic pigs with high (2.97 ± 1.58 ml/min/kg) vs moderate volume administration (3.06 ± 0.6 ml/min/kg), but hepatosplanchnic VO_2 was lower in animals with high (1.32 ± 0.4 ml/min/kg) vs moderate volume administration (1.75 ± 0.3 ml/min/kg, $P = 0.019$). Endotoxin high-volume pigs exhibited a decrease in state 3 respiration for complex I and complex II (not significant) in comparison with control high-volume and with endotoxin low-volume pigs (Figure 1). They also had an increased mortality rate during the 24-hour study period (60% vs 0% in controls).

Conclusion A prolonged high-volume resuscitation approach during endotoxemia may be associated with impaired hepatosplanchnic oxygen consumption, liver mitochondrial dysfunction and high mortality. The impact of aggressive and prolonged volume administration on hepatosplanchnic oxygenation and mitochondrial function in human sepsis should be determined.

Figure 1 (abstract P29)



P30

Effect of C1-esterase inhibitor treatment on microcirculatory perfusion after superior mesenteric artery ischemia

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Multiple studies have stressed the importance of the contribution of activated complement to the pathology of reperfusion injury after tissue ischemia. Using intravital microscopy, this study explores functional consequences of the inhibition of the classical pathway of complement activation with C1-esterase inhibitor (C1-INH) in the context of superior mesenteric artery occlusion (SMAO)/reperfusion.

Thirty anesthetized, spontaneously breathing, male Sprague–Dawley rats underwent SMAO for 60 minutes followed by reperfusion (4 hours). C1-esterase inhibitor (100 IU/kg, 200 IU/kg body weight) or saline (0.9%) was given as a single bolus before reperfusion. Sham-operated animals ($n = 10$) without SMAO served as controls. Systemic hemodynamics were monitored continuously, arterial blood gases analyzed intermittently, and leukocyte/endothelial interactions in the mesenteric microcirculation quantified at intervals using intravital microscopy. Ileal lipid-binding protein (I-LBP) levels were measured from serum samples with an ELISA at the end of the experiments.

C1-INH restored microcirculatory perfusion of postcapillary venules to baseline levels in a dose-dependent manner and reduced leukocyte adhesion following SMAO/reperfusion to similar levels in both C1-INH-treated groups during reperfusion. Furthermore, C1-INH treatment efficiently prevented metabolic acidosis, and reduced the need for intravenous fluids to support blood pressure. Furthermore, I-LBP levels decreased in a dose-dependent manner, and were comparable with the levels of sham-operated animals at the end of the experiments. Survival rates were 100% in controls and after 200 IU/kg C1-INH, 90% after 100 IU/kg C1-INH, and 30% in saline-treated animals.

In the setting of mesenteric ischemia, C1-INH given as a bolus infusion shortly before reperfusion efficiently restored microcirculatory perfusion in a dose-dependent manner, reduced local and systemic inflammatory response, and improved outcome. I-LBP levels correlated well with the functional consequences of mesenteric ischemia/reperfusion and treatment at the end of the experiments.

P31

Dobutamine protects lymphocyctes against staurosporin-induced apoptosis via a receptor-independent and p38-independent pathway

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Introduction Since catecholamines have been shown to modulate various immunological functions, the goal of this work was to investigate their effects on staurosporin-induced apoptosis of Jurkat T cells, a well-established model for human T lymphocytes.

Methods Jurkat T cells passages 1–12 were used. Apoptosis was measured with a caspase-activity assay and with FACS analysis of annexin–propidium iodide double-stained cells.
Results Exposure of Jurkat T cells for 2 hours to staurosporin (2 μM) induced apoptosis: the number of apoptotic cells increased to 14.0 ± 0.8% versus 2.3 ± 0.4% in the control group. Pretreatment (4 hours) with dobutamine 100 and 500 μM decreased the staurosporin-induced apoptosis to 11.6 ± 0.6% and 8.7 ± 0.7%, respectively ($P < 0.01$, mean ± SEM, $n = 44$). Other catecholamines like epinephrine and norepinephrine (both up to 500 μM) had no effect on staurosporin-induced apoptosis. To investigate whether this protective effect of dobutamine was mediated via β-receptors, specific β-blockers were used: neither atenolol (β1) (100 mM), nor ICI 118,551 (β2) (10 mM) blocked the protective effect of dobutamine. Furthermore, dobutamine (1–500 μM) did not increase cAMP production in these cells. Therefore, the protective effect of dobutamine is not β-receptor-mediated. Since it was previously demonstrated that MAPKs p38 and JNK, but not ERK, are activated by dobutamine in Jurkat T cells, we investigated whether the activation of these MAPKs are involved in the protection by dobutamine: inhibition of JNK activation with SP 600125 (1 μM) did not influence the protective effect of dobutamine. Inhibition of p38 activation with SBI 202190 (5 μM) even seemed to reinforce the protection afforded by dobutamine.
Conclusions These experiments demonstrate that dobutamine pretreatment protects T cells from staurosporin-induced apoptosis. This protective effect is not β-receptor-mediated. Also, activation of MAPKs p38 or JNK by dobutamine is not responsible for the protective effect. The molecular mechanisms by which dobutamine exerts this protective effect remain to be elucidated.

P32

Serum vasopressin concentrations in critically ill patients in the intensive care unit

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Critical Care 2007, **11(Suppl 2):**P32 (doi: 10.1186/cc5192)

Introduction The aim of the study is the measurement of serum vasopressin concentrations in the mixed critically ill patients, 24 hours after admission to the ICU and just before the discharge.
Methods In this study there were included patients admitted to the ICU from June until November 2006 ($n = 22$; 12 males, 10 females), mean age 46.45 ± 22.03, APACHE II score 8.59 ± 4.76, length of stay 9.68 ± 6.52. Patients with central nervous system failure, neurosurgical patients and patients remaining in the ICU for no longer than 72 hours were excluded. Serum vasopressin concentrations were measured 24 hours after their admission to the ICU and just before their discharge. The control group was 20 healthy volunteers (blood donors). Vasopressin was measured by the radioimmunoassay method in pmol/l. The sensitivity of the method is 0.5 pmol/l and the specificity is 100%. The statistical analysis was done with the *t* test.
Results Vasopressin serum concentrations at 24 hours after admission were 32,618 ± 20,570 pmol/l. Vasopressin serum concentrations in critically ill patients were significantly higher than in the healthy control group (11,302 ± 31,002, $P < 0.001$). Serum vasopressin concentrations on admission compared with vasopressin concentrations at discharge were statistically significantly increased ($P < 0.001$).
Conclusions Serum vasopressin concentrations in critically ill patients in a mixed ICU are increased 24 hours after admission compared with the control group. The value at discharge is lower than the value on admission and it approaches the value of vasopressin in healthy volunteers. To confirm these results, more studies will be needed.

P33

Effects of simultaneously infused terlipressin and dobutamine in septic shock

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Introduction Terlipressin is increasingly used in the treatment of sepsis-associated hypotension. However, terlipressin may reduce cardiac output and global oxygen supply.
Methods We performed a prospective, randomized, controlled clinical study to determine whether dobutamine may counterbalance the depressions in cardiac index and mixed-venous oxygen saturation resulting from sole terlipressin infusion. We enrolled 60 septic shock patients requiring high doses of norepinephrine (0.9 μg/kg/min) to maintain mean arterial pressure at 70 ± 5 mmHg. Patients were randomly allocated to be treated either with (a) 1 mg terlipressin, (b) 1 mg terlipressin followed by incremental dobutamine doses to reverse the anticipated reductions in mixed-venous oxygen saturation, or (c) sole norepinephrine infusion (control; each $n = 20$).
Results Data from right heart catheterization, thermo-dye dilution catheter, gastric tonometry, as well as organ function and coagulation were obtained at baseline and after 2 and 4 hours. Terlipressin (with and without dobutamine) infusion preserved the mean arterial pressure at threshold values of 70 ± 5 mmHg, while allowing one to reduce norepinephrine doses to 0.18 ± 0.04 and 0.2 ± 0.05 μg/kg/min, respectively (vs 1.4 ± 0.07 μg/kg/min in controls at 4 hours; each $P < 0.01$). The terlipressin-linked decrease in mixed-venous oxygen saturation was reversed by dobutamine (at 4 hours: 59 ± 2 vs 69 ± 3%, $P = 0.023$). No statistically significant differences were found intra-group and between groups in terms of differences between gastric mucosal and arterial carbon dioxide partial pressure, blood clearance of indocyanine green, as well as the plasma disappearance rate of indocyanine green
Conclusions In catecholamine-dependent human septic shock, terlipressin (with and without concomitant dobutamine) stabilizes hemodynamics and reduces norepinephrine requirements. Dobutamine is a useful inotropic agent to reverse the depression in global oxygen transport resulting from sole terlipressin infusion without obvious side effects.

P34

Vasopressin substitution causes microcirculatory changes in patients with septic shock

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Introduction We tested the effects of arginine vasopressin on tissue oxygenation, microvascular reactivity and oral mucosa microcirculation in patients with septic shock.
Methods In 20 patients with septic shock, tissue microcirculation was determined before treatment with AVP (2 IU/hour), after 2 hours of treatment and 2 hours after treatment.

Table 1 (abstract P34)

	Base level	2 hours AVP	2 hours after AVP	*P* value step 1	*P* value step 2
SO_2 1 mm (%)	79; 40–99	72.5; 59–88	83; 45–93	<0.05	<0.05
SO_2 4 mm (%)	79; 48–97	68; 50–93	81; 24–99	<0.05	<0.01
Flow 1 mm	56; 11–390	33; 10–212	39; 10–249	<0.01	<0.01
Flow 4 mm	332.5; 149–517	280; 119–511	331; 150–581	<0.05	<0.05
Velocity 1 mm	22.5; 12–45	17.5; 11–33	20; 11–33	<0.01	<0.05

The thenar muscle StO_2 was measured by near-infrared spectroscopy (InSpectra; Hutchinson Technology, Hutchinson, MN, USA). Oral mucosal tissue oxygen saturation, microcirculatory blood flow and blood flow velocity were measured in depths of 1 and 4 mm with a laser Doppler flowmetry and remission spectroscopy system (O_2C).

Results See Table 1. Vasopressin infusion led to a significant decrease of oral mucosal oxygen saturation and blood flow, and a significant decrease of flow velocity in a depth of 1 mm. Changes in thenar tissue perfusion were not detectable.

Conclusion Vasopressin causes a deterioration of oral mucosal blood flow but not in thenar tissue perfusion.

P35

Rebound hypotension following terlipressin bolus infusion can be prevented by continuous low-dose infusion of terlipressin

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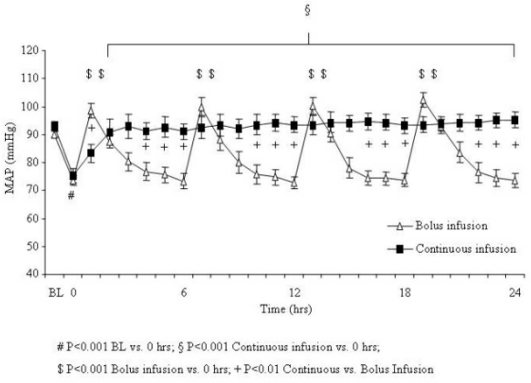
Introduction Bolus infusion of terlipressin, a vasopressin analog, increases the mean arterial pressure (MAP) in patients with sepsis-related arterial hypotension. However, bolus infusion of terlipressin may be associated with severe side effects like excessive systemic and pulmonary vasoconstriction. We hypothesized that continuous low-dose infusion of terlipressin may reverse arterial hypotension with reduced side effects.

Figure 1 (abstract P35)



Mean arterial pressure (MAP) during continuous and intermittent bolus infusion of terlipressin in endotexemic ewes.

Methods Sixteen ewes were chronically instrumented to determine the hemodynamics of the systemic and pulmonary circulation. After 16 hours of endotoxin infusion, all sheep exhibited a hypotensive–hyperdynamic circulation. Thereafter, the animals were randomized to be treated with either a continuous (2 mg over 24 hours) or bolus infusion (1 mg every 6 hours) of terlipressin.

Results Continuous infusion of terlipressin reversed the endotoxin-induced decrease in MAP during the entire 24-hour study period ($P < 0.001$). Intermittent bolus injections of terlipressin contributed to overshooting increases in MAP, as well as in systemic and pulmonary vascular resistance index (each $P < 0.001$), which were followed by sudden and strong rebound effects (Figure 1).

Conclusion A goal-directed continuous infusion of terlipressin may be superior to terlipressin bolus injection to treat patients with sepsis-related arterial hypotension.

P36

Apparent heterogenity in splanchnic vascular response to norepinephrine during sepsis

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Critical Care 2007, **11(Suppl 2):**P36 (doi: 10.1186/cc5196)

Introduction Sepsis alters vascular reactivity. We studied the impact of peritonitis and endotoxemia on hepatic and superior mesenteric arterial contractility.

Materials and methods We studied fecal peritonitis (P, $n = 7$), endotoxin-infusion (E, $n = 8$) and control (C, $n = 6$) for 24 hours after abdominal surgery and eight control pigs without surgery (SPA). Systemic and regional hemodynamics and *ex-vivo* splanchnic vascular reactivity to norepinephrine (NE; tissue bath) were measured and cumulative dose–response curves to NE were constructed. Tension was expressed in grams.

Results CO increased ($P < 0.05$) in P and E. SMA flow (median (range)) decreased in C from 24 (15–30) to 15 (11–21) ml/kg/min ($P = 0.022$) (Table 1).

Table 1 (abstract P36)

N of arterial rings	SMA (g)	HA (g)
C (17)	3 (2–4)	2 (1–3)
P (21)	3 (2–4)	3 (2–4)
E (17)	1 (0.3–2)*,‡	2 (1–3)
SPA (18)	10 (8–16)**,†	8 (7–10)**,†

Data presented as median (range). *$P = 0.002$ E vs P and C; **$P < 0.01$ vs C, P, and E; †$P < 0.001$ vs C, E and P; ‡$P = 0.008$ vs C.

Conclusions The splanchnic vascular response to NE is heterogenous in sepsis, and SMA is most affected. This may modify blood flow distribution if high NE doses are used.

P37

Effect of norepinephrine on cardiac output and preload in septic shock patients

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Critical Care 2007, **11(Suppl 2):**P37 (doi: 10.1186/cc5197)

Introduction Norepinephrine (NE) is a first-line vasopressor used in patients with septic shock. Because of its predominant α-agonist effect, it is assumed to increase vasomotor tone and hence the mean arterial pressure (MAP) without significant effect on the cardiac index (CI). However, a potential beneficial effect on CI can be expected from its venoconstrictor α-agonist-mediated effect combined with an inotropic β_1 agonist effect, provided that the increase in left ventricular afterload is not excessive (high levels of MAP). The aim of our study was to examine the cardiovascular effect of NE when it induces marked changes in MAP.
Methods In an observational study of patients ($n = 37$) resuscitated for septic shock, we analysed hemodynamic PiCCO data at two consecutive time points where the MAP changed by more than 15% in response to either initiation or to change of doses of NE. Two subgroups of patients were identified. The first subgroup (MAPincr) consisted of 21 patients in whom the MAP increased by more than 15% in response to either initiation of NE infusion ($n = 8$) or increase in NE dose (from 1.7 ± 1.7 to 2.2 ± 1.4 mg/hour; $n = 13$). The second subgroup (MAPdecr) consisted of 16 patients in whom the MAP decreased by more than 15% in response to the decrease in NE doses. For both subgroups, the time between the two consecutive sets of measurements did not exceed 2 hours and no other treatments that may alter hemodynamics were administered within this period (fluids, hemofiltration, diuretics or other catecholamines).
Results In the MAPincr subgroup, MAP increased from 56 ± 17 to 84 ± 12 mmHg ($P < 0.05$) while significant increases in CI (from 3.4 ± 1.0 to 3.7 ± 0.9 l/min/m^2), stroke volume index (SVi) (from 37 ± 12 to 41 ± 11 ml/m^2) and global end diastolic volume index (GEDVi) (from 706 ± 203 to 767 ± 225 ml/m^2) were observed. Neither the heart rate nor the global ejection fraction (GEF) significantly changed. In seven patients, the GEF markedly increased by >15% in parallel to the increase in SVi. In the MAPdecr subgroup, MAP decreased from 95 ± 12 to 70 ± 9 mmHg ($P < 0.05$). The CI (from 3.5 ± 1.4 to 3.0 ± 0.9 l/min/m^2) and GEDVi (from 815 ± 319 to 721 ± 253 ml/m^2) decreased significantly, while the heart rate, SVi ($P = 0.07$) and GEF did not change.
Conclusion In our septic shock patients, changes in MAP resulting from increases or decreases in the doses of NE, were associated with changes in CI related to changes in GEDVi (cardiac preload) and in some patients to changes in systolic left ventricular function evaluated by GEF. These findings suggest that administration of NE in septic shock is associated not only with an increase in MAP but also with an increase in systemic blood flow.

P38

Tissue Doppler imaging suggests an association between endotoxemia and impaired myocardial relaxation

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Critical Care 2007, **11(Suppl 2):**P38 (doi: 10.1186/cc5198)

Introduction Tissue Doppler imaging (TDI) is a novel technique that measures myocardial velocity. The peak early diastolic mitral annulus velocity (*E′*) offers a relatively preload-insensitive measure of LV relaxation. There are scant data regarding its use in sepsis or endotoxemia. This study sought to determine the effect of endotoxemia upon TDI variables.
Methods With ethics committee approval, 10 male Sprague–Dawley rats were studied. Anesthesia was induced with alfaxalone and maintained with isofluorane. Mechanical ventilation was performed via tracheostomy. All rats received 0.9% NaCl 3 ml/hour via a carotid line. Immediately after baseline assessment ($T = 0$), rats received 1 ml/kg i.v. infusion over 30 minutes (study group ($n = 5$), endotoxin 10 mg/ml (*Escherichia coli* O55:B5; Sigma, MO, USA); control group, 0.9% NaCl). Echocardiography was performed (15 MHz transducer, Vivid5; GE Healthcare) at $T = 0$, 60 minutes ($T = 60$) and 2.5 hours ($T = 150$). Measurements included the heart rate, mean arterial pressure (MAP), femoral venous pressure, LV outflow tract diameter and flow (peak velocity (V_{peak}), cardiac output (CO)), peak early diastolic mitral inflow (*E*), peak systolic mitral annulus velocity (*S′*) and *E′*.
Results There was no significant difference in mean ± SD weight (study 539 ± 88 g, control 504 ± 108 g, $P = 0.6$) or hemodynamic variables at $T = 0$. At $T = 60$, only V_{peak} was higher in the study group compared with controls (1.29 ± 0.24 vs 0.86 ± 0.21 m/s, $P = 0.03$). The study group demonstrated lower MAP, *E* and *E′* at $T = 150$ (Table 1).

Table 1 (abstract P38)

	Control	Study	*P*
MAP (mmHg)	118 ± 21	75 ± 35	0.05
CO (l/min)	0.156 ± 0.02	0.181 ± 0.07	0.5
E (m/s)	1.02 ± 0.2	0.76 ± 0.11	0.04
E′ (m/s)	0.095 ± 0.02	0.061 ± 0.02	0.03

Conclusion In this model, endotoxemia was associated with a decrease in *E* and *E′*. This decrease in E′ suggests a decreased rate of myocardial relaxation. This has not previously been reported.

P39

Hemodynamic and cardiac peptide in septic myocardial depression: the effects of calcium sensitizer

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Introduction The aim of this retrospective study is to evaluate hemodynamic and neurohormonal effects of levosimendan in cardiac patients with sepsis-induced cardiac dysfunction. Septic shock is characterized by profound cardiovascular alterations including myocardial depression. Levosimendan has recently been shown to improve cardiac function in septic shock.
Methods Fifteen patients with myocardial depression related to septic shock were enrolled. All patients had SIRS criteria, culture isolation of one or more pathogens, positive procalcitonin, SBP < 90 mmHg unresponsive to load challenge. We defined myocardial depression as a reduced SvO_2 in the presence of increased brain natriuretic peptide secretion and Troponin I release, and systolic and/or diastolic dysfunction by transoesophageal echo evaluation of ejection fraction and mitral annulus tissue Doppler imaging velocities. All patients received levosimendan infusion for 24 hours at 0.1 μg/kg/min combined with norepinephrine.
Results Data were obtained by evaluating the average of the percentage variation between T_0 (starting infusion) and T_1 (24 hours after infusion), T_2 (48 hours), T_3 (72 hours), T_4 (96 hours), T_5 (120 hours) and T_6 (144 hours). Levosimendan significantly increased SvO_2 and ejection fraction, and decreased

Troponin I and brain natriuretic peptide. Levosimendan improved diastolic function by increasing the *E′* velocity at tissue Doppler imaging at 48 hours. All data were analysed by the Fisher *F* test.

Table 1 (abstract P39)

	T_0	T_1	T_2	T_3	T_4	T_5	T_6
SvO_2 (%)	0	4	10	17	22	19	22
Trop I (ng/ml)	0	−65	−86	−82	−78	−62	−62
BNP (%)	0	−45	−41	−56	−50	−42	−44
E′ (cm/s)	<8	>8	>8	>8	>8	>8	>8
EF (%)	<30	>40	>40	>40	>40	>40	>40

Conclusions Levosimendan seems to improve systemic hemodynamics and neurohormonal cardiac function in patients with septic cardiac dysfunction.

P40

Neutrophil oxidative burst evaluation during acute normovolemic hemodilution: preliminary results

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Introduction In recent years there has been increasing evidence that a resuscitation strategy with different fluids can have widely divergent impacts on the immune response, neutrophil activation and tissue injury. This prospective study was undertaken to determine the neutrophil oxidative burst in the swine model during an acute normovolemic hemodilution (ANH) procedure with hydroxyethyl starch.
Methods Twelve pigs were anesthetized, instrumented and randomized into two groups: control and hemodilution (H). The control group was only anesthetized and instrumented while animals in the ANH group were submitted to acute normovolemic hemodilution to a target hematocrit of 15% with volume replacement performed with hydroxyethyl starch 130/0.4 at a 1:1 ratio. The withdrawn blood was returned to the animals 120 minutes after the end of hemodilution. Neutrophil oxidative burst was performed with blood samples collected at the femoral vein at the following time points: before ANH (baseline), after instrumentation (INST), immediately after ANH (H), 60 minutes after ANH (60H), 120 minutes after ANH (120H), 60 minutes after blood infusion (60BI) and 120 minutes after blood infusion (120BI), and determined with a flow cytometer. Spontaneous and stimulated oxidative burst activation of neutrophils were performed with dichlorofluorescein diacetate and phorbol myristate acetate. Statistical analyses were performed using one-way analysis of variance followed by a Dunnett test or *t* test. A *P* value of 0.05 was considered statistically significant.
Results Spontaneous oxidative burst activity in group H increased significantly from baseline (30.19 ± 4.79) to H (57.45 ± 9.86) and 60H (56.26 ± 14.64) ($P < 0.01$) while the control group did not present significant variation. Between groups there were significant differences at H (ANH = 57.45 ± 9.86; control = 23.18 ± 7.16; $P = 0.0007$), 60H (ANH = 56.26 ± 14.64; control = 34.53 ± 9.06; $P = 0.0225$), 120H (ANH = 43.59 ± 5.46; control = 28.65 ± 10.44; $P = 0.0220$) and 60BI (ANH = 38.60 ± 1.85; control = 25.59 ± 8.12; $P = 0.0082$).
Conclusion ANH with hydroxyethyl starch influences oxidative burst activity under experimental conditions.

P41

Relationship of IL-12 and thyroid indices in sepsis

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Critical Care 2007, **11(Suppl 2):**P41 (doi: 10.1186/cc5201)

Introduction Sickeuthroid syndrome is very frequent in critically ill patients. Cytokines may have a role in this syndrome. IL-12 is involved in the central regulation of the hypothalamic–pituitary–thyroid (HPT) axis during illness. The aim of this study is to evaluate the relationship of IL-12 and thyroid functions in septic patients.
Materials and methods Twenty-four septic patients and 18 healthy controls were enrolled into the study with the mean ages of 49.9 ± 20.6 and 45.8 ± 22.3 years, respectively. Hyperthyroid and hypothyroid patients were excluded. Free triiodothyronine (fT3), free thyroxine (fT4) and TSH were measured simultaneously with IL-12.
Results The mean IL-12, fT3, fT4 and TSH values of septic patients and the control group are presented in Table 1. IL-12 was significantly higher in septic patients (19.05 ± 10.7 pg/ml vs 4.8 ± 2.0 pg/ml, $P < 0.005$). fT3 and TSH values were significantly low in septic patients. There was a significantly strong correlation between IL-12 and fT4 in septic patients but not fT3 and TSH ($r = 0.88$, $P = 000$). There was no correlation between IL-12 and other thyroid indices in the control group.

Table 1 (abstract P41)

	IL-12 (pg/ml)	TSH (mIU/l)	fT3 (pg/ml)	fT4 (ng/dl)
Control group	4.8 ± 2.1	2.25 ± 2.1	2.93 ± 0.5	1.18 ± 0.14
Septic patients	19.05 ± 10.7	1.173 ± 1.85	1.56 ± 0.6	1.06 ± 0.3
P	<0.001	0.001	<0.001	0.118

Conclusion According to our findings, IL-12 has a role in HPT dysfunction in most critically ill patients.

P42

A network system for the treatment of pediatric septic shock

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Introduction We show the effect of a network system in the treatment of pediatric septic shock, especially for children with Waterhouse–Friderichsen syndrome. In 2003 we founded a pediatric intensive care network with 15 children's hospitals in Lower Saxony, Germany. The aims were the standardisation of clinical therapies, implementation of training programs and the installation of an emergency system in the region of lower Saxony.
Methods The first standard was implemented for the treatment of the Waterhouse–Friderichsen syndrome. At first, we started with the educational program. The program included different central symposia about septic shock in children. The second step was the standardisation of the diagnosis and the therapy, including the administration of human protein C concentrate (PC), and the clinical pathways. We implemented a round-the-clock emergency system with the possibility for transportation of critically ill patients, permanent consultation of the tertiary medical center and onsite treatment through the tertiary center staff if the patient could not be transferred. All patients were announced to the tertiary medical

center directly after admission into the network hospitals. The final step was the presentation of the project in the different hospitals.
Results We treated 10 children with Waterhouse–Friderichsen syndrome in the network. Three of them were attended on site and seven were transferred in the tertiary center. The announcement time in eight cases was 15 minutes–1 hour. Primarily, a consultation was accomplishing routinely. The transportation team of the tertiary center continued the treatment on site and afterwards in the center. All patients showed typical signs of Waterhouse–Friderichsen syndrome with purpura fulminans and severe multiorgan failure. No patient died and only one patient had necrosis of the skin, which existed already at admission. The others had a restitution ad integrum. No adverse effects were observed with the PC concentrate administration.
Conclusions The network system and the standard treatment with PC worked without severe problems. The survival rate and the outcome in our small study group were excellent. Our experience allows us to enlarge the system on other diseases.

P43

Intensive care unit outcome versus haemodynamic status on arrival at a general intensive care unit

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Introduction Goal-directed therapeutic protocols such as that described by Rivers and colleagues [1] have taken an important place in efforts to increase survival in septic patients. We looked at ICU outcomes for patients meeting the haemodynamic criteria of the Rivers trial on admission to our general ICU.
Methods We prospectively recorded haemodynamic parameters of 98 consecutive patients admitted to a mixed medical/surgical ICU and compared these with the ICU outcome. Patients who met systemic inflammatory response syndrome (SIRS) criteria [2] and had lactate ≥4 mmol/l or systolic blood pressure ≤90 mmHg met the Rivers criteria.
Results We included 98 patients admitted to the ICU (60 males) of mean age 61 ± 17 years. Fourteen patients (14%) died in the ICU, and the median length of stay was 3 (IQR 3) days. Overall 16 of the 98 patients met the Rivers criteria, four of whom died (25%). The median length of ICU stay for the Rivers patients was 5 (1.25) days (see Table 1).
Conclusions Sixteen out of 98 patients (16%) met Rivers criteria. Of medical and surgical emergency patients, this proportion rose to 16 of 55 patients (29%).
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P44

Optimization of antibacterial treatment in pediatric intensive care units using procalcitonin

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Introduction Neonates and infants in the ICU are at high risk of severe infections and sepsis. Often it is not easy to diagnose sepsis based only on clinical findings; reliable biomarkers are needed to prove the diagnosis.
Objective To study the value of procalcitonin (PCT) as a marker, verifying the diagnosis, which enables the start of de-escalating ABT in patients with clinical signs of sepsis.
Methods Three hundred and seventy-four patients on artificial lung ventilation from two pediatric ICUs of two Russian hospitals were enrolled. Blood samples for PCT testing (PCT LIA; BRAHMS AG, Germany) were taken under suspicion of sepsis or exacerbation of bacterial infection. In the first stage (January–December 2005), 50 neonates (age 6 (4–12) days) with various perinatal pathologies were studied (Group A), and routine ABT was prescribed, with blood samples taken and stored for further PCT assessment. In the second stage (January–November 2006), 324 infants (age 6 (1.5–9.4) months) after cardiac surgery were enrolled (Group B), and ABT was adjusted based on PCT-testing results. PCT > 2 ng/ml indicative of systemic bacterial inflammation in addition to clinical signs of sepsis was an indication for ABT with carbapenems. Data are shown as the median and interquartile range.
Results *Group A*. Sepsis was diagnosed in 16/50 (32%) patients. PCT > 2 ng/ml was observed in 23/50 (46%) cases, including 15/16 (94%) patients with clinically diagnosed sepsis. In patients with PCT > 2 ng/ml the mortality rate was 7.7% if carbapenems (meropenem or imipenem/cilastatin) were administered ($n = 13$), compared with 20% with different ABT ($n = 10$) – although in patients with PCT < 2 ng/ml ($n = 27$), ABT with carbapenems ($n = 12$) resulted in paradoxically higher mortality compared with other ABT schemes ($n = 15$): 17% vs 6.6%. *Group B*. Sepsis was defined in 24/324 (7.4%) patients. PCT > 2 ng/ml was in 53/324 (16%) cases, including all patients with clinically diagnosed sepsis. Early ABT with meropenem, combined with vancomycin or linezolid, allowed one to decrease sepsis-related mortality in these patients to 29%, which used to be as high as 74% before the introduction of this algorithm ($P = 0.0028$).
Conclusion Early verification of sepsis using PCT combined with carbapenems-based ABT enables decreasing sepsis-related mortality in critically ill infants and newborns staying in the ICU.

Table 1 (abstract P43)

	Patients			Patients reaching Rivers criteria		
	n	Mortality (*n* (%))	Median length of stay (days)	*n*	Mortality (*n* (%))	Median length of stay (days)
Total	98	14 (14%)	3 (IQR 3)	16	4 (25%)	5 (IQR 1.25)
Medical	33	9 (27%)	5 (IQR 2)	11	3 (27%)	5 (IQR 1.5)
Elective surgical	43	1 (2%)	2 (IQR 1)	0		
Emergency surgical	22	4 (18%)	3 (IQR 4.5)	5	1 (20%)	5 (IQR 1)

P45

Do they know what is sepsis time? Septic Patients Survey Enrolling Staffs study

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Introduction The aim of this study was evaluation of physicians' knowledge about SIRS, sepsis, severe sepsis and septic shock.
Methods A multicenter study in 21 ICUs in seven university, five public and seven private hospitals. A questionnaire with five clinical cases was first validated by five critical care boarded intensivists (INT) with 100% agreement. All interviewed physicians (Phys) received each question separately, in a predefined sequence, and no answer could be reviewed. After answering, the questionnaire was put in a sealed envelope with no identification. Statistical analysis was performed: chi-square, Kruskall–Wallis and linear correlation tests. $P < 0.05$ was considered statistically significant.
Results A total of 917 Phys (mean age 32.7 ± 7.21 years, 61.9% males, 38.1% females) were enrolled with 20.0% ($n = 55$) INT and 80.0% ($n = 220$) of nonintensivists (non-INT). Phys correctly recognized SIRS, infection, and septic shock in 80.4%, 92.4% and 85.1% of the cases, respectively. The lowest rate of recognition was observed in sepsis and severe sepsis cases (26.5% and 55.6%). Considering all questions, the overall percentage of correct answers was 68.1 ± 21.1%. INT performed better than non-INT (84.7 ± 17.2% and 64.0 ± 20.0%, $P < 0.00001$). Phys working at public and university hospitals performed better (70.2 ± 18.7% and 71.2 ± 19.5%) than those in private hospitals (59.7 ± 23.4%, $P = 0.001$).
Conclusion The recognition of sepsis and its severity are not satisfactory, mostly among non-INT and those working at private hospitals. Possibly, reviewing sepsis-related and organ dysfunction concepts are necessary for early identification of septic patients.

P46

Prevalence of endotoxemia in a population of patients admitted to an intensive care unit after elective surgery

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Critical Care 2007, **11(Suppl 2):**P46 (doi: 10.1186/cc5206)

Introduction The aim of this study was to investigate the prevalence of endotoxemia early after elective surgical procedures in patients admitted to an ICU of a university hospital.
Methods One hundred and four nonselect patients were recruited. Patients were excluded if they were admitted during the weekend or from another ICU and if they were on chronic dialysis. Within 4 hours of admission functional data were collected and severity scores (APACHE, SOFA) calculated. Arterial blood samples were also taken and processed according to Spectral Diagnostics' endotoxin activity (EA) assay [1]. The method allows one to express EA as a function of each patient's neutrophil chemiluminescence activity (on a scale from 0 to 1). An EA level of 0.4 is approximately equivalent to an endotoxin concentration of 25–50 pg/ml, and a level of 0.6 is approximately equivalent to a LPS concentration of 100–200 pg/ml. Data were analysed according to EA ranges: low ($EA < 0.4$), intermediate ($0.4 \leq EA < 0.6$), and high ($EA \geq 0.6$). Differences between ranges of EA were assessed by analysis of variance (Sigma Stat, SPSS), accepting $P < 0.05$ as significant. Data are expressed as the mean ± SD.
Results In our case mix, patients were 68 (65%) in the low group, 17 (17%) in the intermediate group and 19 (18%) in the high group. Age (61 ± 17 years) was not significantly different in the three groups ($P = 0.493$). Functional and severity scores were not significantly different between groups. Average values were as follows: WBC 11,093 ± 4605 *n*/mm^3 ($P = 0.385$), HR 76 ± 16 bpm ($P = 0.898$), MAP 88.8 ± 13.6 mmHg ($P = 0.576$), lactate 1.18 ± 0.77 mmol/l ($P = 0.370$), PaO_2/FiO_2 383 ± 109 mmHg ($P = 0.474$), APACHE II score 8.3 ± 3.7 ($P = 0.542$) and SOFA score 1.5 ± 1.4 ($P = 0.245$). Interestingly, those patients with higher levels of EA were characterized by longer length of stay in the ICU. The ICU length of stay was 1.9 ± 3.1 days in the low group, 8.7 ± 6.7 days in the intermediate group and 4.7 ± 7.7 days in the high group ($P = 0.038$).
Conclusions A rather high number of patients admitted to the ICU following elective surgery are characterized by intermediate-high levels of endotoxemia, as assessed by the EA assay, despite their relative low level of complexity on admission. High levels of EA were associated with a longer length of stay.
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P47

sTREM-1 is not suitable to discriminate survivors and nonsurvivors in surgical patients with severe sepsis or septic shock

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Objectives To evaluate in septic patients the plasma levels of sTREM-1, a soluble form of TREM-1, which seems to play an important role in inflammatory diseases, and to determine whether plasma sTREM-1 could be used as a diagnostic and prognostic marker in sepsis in the surgical ICU.
Design An observational clinical study.
Setting The surgical ICU of the University Hospital of Heidelberg, Germany.
Patients Patients admitted to the ICU over a 6-month period with clinical evidence of severe sepsis or septic shock.
Interventions None.
Measurements and results Sixty-six intensive care patients were enrolled in the study within the first 24 hours after the onset of severe sepsis or septic shock. Twenty-one healthy individuals served as controls. At day 0, day 1 and day 3 after diagnosis of severe sepsis or septic shock, plasma sTREM-1 was measured by ELISA. Plasma sTREM-1 concentrations of healthy controls did not differ from patients with severe sepsis or septic shock at day 0 (42.8 ± 44.9 pg/ml vs 40.8 ± 45.5 pg/ml, not significant), day 1 (42.8 ± 44.9 pg/ml vs 48.6 ± 57.2 pg/ml, not significant) nor at day 3 (42.8 ± 44.9 pg/ml vs 51.9 ± 52.8 pg/ml, not significant). Survivors were defined as patients surviving to at least day 28. There were no differences of plasma sTREM-1 between survivors and nonsurvivors at day 0, day 1 and day 3 (34.8 ± 44 52.4 pg/ml

vs 49.5 ± 35.9 pg/ml, 42.6 ± 61.1 pg/ml vs 59.6 ± 47.1 pg/ml, and 47.9 ± 60.2 pg/ml vs 58.2 ± 37.1 pg/ml, not significant).
Conclusion In this study including surgical patients with severe sepsis or septic shock, plasma sTREM-1 is not elevated compared with healthy controls. Furthermore, the measurement of plasma sTREM-1 did not allow one to differ between survivors and nonsurvivors. The suggested role of sTREM-1 as a diagnostic and prognostic marker in sepsis was not confirmed in this study.

P48

Can plasma-free DNA concentration be a diagnostic tool in critically ill septic patients?

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Recent evidence suggests that the plasma-free DNA concentration has potential use as a prognostic marker in many clinical situations including sepsis, trauma, and acute stroke [1]. However, its predictive value is arguable. We hypothesized that plasma DNA is increased in septic patients admitted to the ICU compared with nonseptic ICU patients, and it is correlated with disease severity and clinical outcome.
Forty-two consecutive patients (11 septic, 31 nonseptic) admitted to a mixed ICU and mechanically ventilated were recruited. Plasma-free DNA concentration was measured by real-time PCR assay for the β-globin gene, and the APACHE II score, SOFA score, serum C-reactive protein (CRP) concentrations, procalcitonin (PCT) concentrations, serum lipid concentrations, and clinical outcome (ICU/hospital days and mortality) were assessed on admission to the ICU. Assessments and samplings were repeated as the diagnosis of the patients changed (sepsis, severe sepsis and septic shock). Finally, 86 plasma samples were collected. Descriptive statistics, Mann–Whitney U, Kruskall–Wallis and Spearman's tests, and receiver operating characteristic analysis were used when appropriate.
Demographic data were similar. ICU and hospital mortalities were 26.2% and 33.3%, respectively. The mean DNA concentrations on admission were significantly higher in ICU patients compared with healthy subjects ($n = 11$) (13,405 GE/ml versus 390 GE/ml, $P < 0.05$) and septic patients compared with nonseptic patients (33,170 GE/ml versus 1,171 GE/ml, $P < 0.001$). Furthermore, during the overall ICU stay, increased DNA concentration associated with the increase of severity of illness was noted; however, this increase was statistically significant only between septic and septic shock samples (26,624 GE/ml versus 42,861 GE/ml, $P < 0.05$). The area under the curve obtained for the plasma-free DNA concentration in distinguishing between septic and nonseptic patients on admission was 0.9 (sensitivity 84%, specificity, 95%; cutoff 4,083 GE/ml). Also, the plasma-free DNA concentration was found to be higher in patients who died in the ICU compared with patients who survived, although not statistically significant. The DNA concentration demonstrated a significant correlation with CRP ($P = 0.037$, $r = 0.365$), PCT ($P = 0.007$, $r = 0.457$) and high-density lipoprotein ($P = 0.015$, $r = -0.415$) concentrations.
In conclusion, plasma DNA may be a potentially valuable tool to confirm the diagnosis of sepsis on admission to the ICU and to monitor disease severity.

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P49

Greater than the sum of its parts: C-reactive protein and the calculated ion gap together are superior in predicting mortality in critically ill surgical patients

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Introduction Inadequate tissue perfusion and an uncontrolled systemic inflammatory response are associated with poor outcome in critically ill surgical patients. An increased concentration of unmeasured anions, reflecting hypoperfusion, and the magnitude of the early inflammatory response both correlate strongly with mortality. Our aim was to assess the relationship between these factors, and their ability in combination to predict outcome.
Methods In a prospective study we evaluated 108 consecutive patients admitted to a surgical high dependency unit. Regional Ethics Committee approval was obtained. Serum electrolytes, albumin, phosphate, lactate and C-reactive protein (CRP) were measured on admission and on day 1. We derived the calculated ion gap (CIG) using a simplified modification of the Stewart–Figge equations.
Results Based on previous work, thresholds of 10 mmol/l for CIG and 100 mg/l for CRP were used to categorise patients. Of the patients with a CRP < 100 mg/l, 15.4% had an elevated CIG. Of the patients with a CRP > 100 mg/l, 36.7% had an elevated CIG ($P = 0.016$, chi-square test). Patients ($n = 63$) with a CIG < 10 mmol/l and CRP < 100 mg/l had a 1.5% mortality, whereas those ($n = 11$) with a CIG > 10 mmol/l and CRP > 100 mg/l had a 54.5% mortality ($P < 0.0001$, chi-square test) (Table 1).

Table 1 (abstract P49)

	CRP < 100 mg/l, CIG < 10 mmol/l	CRP > 100 mg/l, CIG > 10 mmol/l
Inhospital mortality	1.5% ($n = 63$)	54.5% ($n = 11$)

Conclusion Inflammation is a potent cause of oxidative stress, which in turn results in endothelial damage and increased concentrations of unmeasured anions. The combination of CRP and the CIG, as markers of inflammation and inadequate tissue perfusion, respectively, is a powerful predictor of mortality in the critically ill surgical patient.

P50

C-reactive protein predicts mortality on admission to a surgical high-dependency unit

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Critical Care 2007, **11(Suppl 2):**P50 (doi: 10.1186/cc5210)

Introduction C-reactive protein (CRP) is a non-specific marker that may be used to assess the magnitude of the inflammatory response in critically ill surgical patients. Our aim was to determine the temporal relationship between CRP measurement and mortality.
Methods In a prospective study conducted in a surgical high-dependency unit (HDU), 132 consecutive patients were evaluated. Regional Ethics Committee approval was obtained. Serum CRP

was measured on admission, day 1 and day 2 and was evaluated with respect to inhospital mortality.

Results CRP on admission to HDU discriminated survivors from nonsurvivors ($P < 0.0001$, analysis of variance). A CRP greater than 100 mg/l correlated very strongly with mortality. The mortality in patients with a CRP less than 100 mg/l ($n = 93$) was 2.2%. The mortality in patients with a CRP greater than 100 mg/l ($n = 39$) was 25.6% ($P < 0.0001$, chi-square test), (Table 1). However, there were no significant differences in CRP with respect to mortality on day 1 or day 2 ($P = 0.136$ and 0.236, respectively).

Table 1 (abstract P50)

	CRP <100 mg/l	CRP >100 mg/l	*P* value
Inhospital mortality	2.2% ($n = 93$)	25.6% ($n = 39$)	<0.0001 (chi-square)

Conclusion CRP on admission to the surgical HDU is a powerful predictor of mortality ($P < 0.0001$), but this correlation does not persist after the initial measurement. Our data suggest that early CRP measurement should be undertaken in all critically ill surgical patients in order to quantify the ultimate magnitude of the inflammatory response and the associated mortality.

P51

The biphasic aPTT waveform to diagnose sepsis in patients with systemic inflammatory response syndrome

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Introduction We tested the ability of the biphasic aPTT waveform to diagnosis sepsis in patients presenting to the Emergency Department (ED) with the systemic inflammatory response syndrome (SIRS). The biphasic aPTT waveform (BPW), which results from rapid complexing of VLDL and C-reactive protein during aPTT testing, has demonstrated promise as an early diagnostic test for sepsis.

Methods A prospective, observational study was designed in which all patients presenting to the ED of an urban university hospital were screened for SIRS. Patients with SIRS unrelated to trauma or myocardial infarction were eligible. Plasma for BPW testing was obtained at the time of enrollment and daily for 7 days in admitted subjects. The primary outcome was a diagnosis of sepsis related to the presence of a BPW at enrollment. Secondary measures were mortality related to the BPW, correlation of any positive BPW with sepsis, and of the BPW with statin therapy. Two criteria for a positive test, light transmittance at 18 seconds (TL18) and the initial slope of the waveform (slope) are used. Two independent experts made the final diagnosis.

Results We screened 5,400 consecutive admissions to the ED, identified 207 eligible subjects and enrolled 105 participants. The BPW was present at enrollment in 12 subjects by TL18 and in 28 subjects by slope. Forty-six out of 105 subjects eventually developed a BPW, 54 were diagnosed with sepsis. The sensitivity and specificity for sepsis were 17% (95% CI, 7–27.6) and 93.8% (95% CI, 87–100) by TL18 and 26.9% (95% CI, 14.9–38.9) and 71.4% (95% CI, 58.7–84.1) by slope. The positive predictive value of the test was 75 by TL18 and 50 by slope criteria. The AUC for ROC analysis of the BPW for diagnosis of sepsis is 0.469 by TL18 and 0.560 by slope. The odds ratio for developing sepsis related to any positive BPW was 2.977. The odds ratio for development of a BPW in patients on a statin at the time of presentation was 0.597. Five subjects died by 28 days, 4/5 having a BPW.

Conclusion The BPW has no utility in the ED to predict the development of sepsis in at-risk patients. The development of a BPW at any time during the hospital stay correlates with an increased risk of sepsis and mortality. Baseline statin therapy may reduce the chance of developing a BPW.

P52

Functional protein C levels in septic patients

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Objective To know whether functional protein C (FPC) levels in critical septic patients could be intended as an evolution marker correlated with prognosis and mortality.

Materials and methods A prospective study with determination of FPC levels in all septic patients admitted to the ICU. We used the IL test™ PC kit (Instrumentation Laboratory; synthetic chromogenic substrate). We considered an abnormal low FPC when levels were below 40%, normal FPC when levels were above 80% and low FPC when levels where between 40% and 80%. Data included patient age, diagnosis, SAPS II, SOFA score, OSF and mortality. The analytical data included serum lactate and FPC. Patients were divided into three groups: group I (FPC below 40%), group II (FPC 40–80%) and group III (FPC above 80%). The statistical study was performed with the Analyse-it® program. The severity was defined by the usual criteria of SAPS II score and lactate levels and then compared with the different FPC groups. Mortality was considered.

Results We included 65 patients. The total mortality rate was 16.9% (11 patients).

Table 1 (abstract P52)

$n = 65$	FPC	Lactate	*P*	Mortality (%)
Group I	30.9 ± 9	15.7 ± 5.8	<0.05	78
Group II	58.1 ± 13	1.8 ± 0.35		22
Group III	100.8 ± 12.8	1.3 ± 0.9	<0.05	0

Conclusions We found a direct and a progressive relation with statistical significance between the higher mortality rate and the lower protein C values. The results could mean that the level of protein C can be used as an evolution marker in septic patients.

P53

Severe protein C deficiency association with organ dysfunction and mortality in patients with severe sepsis

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Introduction We sought to determine whether severe protein C (PC) deficiency was associated with organ dysfunction (OD) and mortality in adult patients with severe sepsis.

Methods Retrospective examination of Lilly trials in adult patients with severe sepsis in which PC measurements were obtained at baseline. Severe PC deficiency was defined as ≤ 40% of normal. The Student *t* test was used to compare mean APACHE II and OD differences, while the chi-squared or Fisher's exact test was used for mortality.

Table 1 (abstract P53)

Study	EVAA			PROWESS			ENHANCE			ADDRESS		
Protein C	≤40%	>40%		≤40%	>40%		≤40%	>40%		≤40%	>40%	
n	65	60		615	959		795	1127		593	1154	
Mean APACHE II score	17.4	17.1	$P = 0.79$	25.9	24.1	$P < 0.001$	23.2	20.9	$P < 0.001$	18.5	18.1	$P = 0.14$
Mean OD	1.5	1.4	$P = 0.42$	2.8	2.2	$P < 0.001$	3.1	2.4	$P < 0.001$	1.6	1.4	$P < 0.001$
Placebo mortality	50.0%	20.0%	$P = 0.07$	41.8%	25.3%	$P < 0.001$				19.7%	12.0%	$P = 0.002$

Results Severe PC deficiency was associated with a statistically significant increase in the mean APACHE II score in two of four trials, a significant increase in the mean OD in three of four trials, and a significant increase in mortality in two of three trials (Table 1).
Conclusion Severe PC deficiency at baseline appears to be associated with a greater degree of organ dysfunction, and increased mortality in adult patients with severe sepsis.

P54

Human protein C concentrate in the treatment of hemolytic uremic syndrome

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Introduction Human protein C (PC) concentrate may anticipate thrombotic microangiopathy and facilitate fibrinolysis in the severe hemolytic uremic syndrome (HUS). We report the effects of PC in six HUS patients. HUS is characterized by a simultaneous occurrence of hemolytic anemia, thrombocytopenia and acute renal failure. Postdiarrheal HUS is often based on an infection with EHEC producing Shiga toxins. Our current pathogenetic understanding is that Shiga toxins cause endothelial injury, leading to thrombotic microangiopathy. There is still a 5% rate of mortality particularly caused by cerebral involvement.
Methods We treated six children with a severe cerebral manifestation, five of them suffered from a multiple organ dysfunction syndrome (MODS), of HUS with PC over 7–10 days. All patients suffered peritoneal dialysis, one patient a plasmapheresis. In addition to the treatment of the MODS, all of them received 100–200 U/day PC.
Results All of the patients showed signs of disseminated intravascular coagulation. We found typical hypodense lesions in basal ganglia and edema of the brain in CT. During the therapy with PC, MODS was remarkable improved and abnormal D-dimer and PAI-1 levels could be normalised. All of the patients recovered a nearly normal kidney function. Two patients persisted in a severe reduced neurological status. The others showed only slight or no neurological disabilities on discharge. No adverse effects were observed with the PC concentrate administration.
Conclusions There is no generally accepted therapy regimen to treat HUS in case of neurological involvement. Mortality in HUS accompanied with cerebral microangiopathy is high and difficult to alter. This is the first trial of human PC concentrate administration to anticipate thrombotic microangiopathy in HUS. All of our patients showed rapid clinical improvement under PC administration. Four of six patients were discharged in a healthy condition despite their severe disease. The containment of the severe neurological involvement and the lack of side effects in the treatment with human PC concentrate administration in our patients yield hope that PC treatment may be an effective therapy regimen in the treatment of severe HUS.

P55

Increasing microcirculation after drotrecogin alfa (activated)

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In severe sepsis, microcirculatory dysfunction caused by inflammation, endothelial activation and procoagulant response leads to mithocondrial dysfunction (termed microcirculatory and mitochondrial distress syndrome). If undetected, this condition can lead to parenchymal cellular distress and so to organ failure. As regional and microcirculatory distress are independent of systemic hemodynamic-derived and oxygen-derived variables, we recorded the course of microvascular parameters with a Microscan Video Microscope (Microvision, The Netherlands) in four patients with severe sepsis. We studied the sublingual region because of its embryologic correlation to splanchnic circulation, its thin mucosa. The instrument used a new improved imaging modality for observation of the microcirculation called sidestream dark-field imaging. We consider here four patients with severe sepsis related to esophagectomy, severe polytrauma with splanchnic organ damage and mediastinitis treated with drotrecogin alpha (activated) (DA) at 24 μg/kg/hour for 96 hours. The patients were admitted to the ICU, ventilated mechanically, monitored hemodynamically via a PICCO system and supported with dobutamine. Videomicroscopy was made before administration of DA and was repeated every 24 hours during the treatment with DA and at 24 hours after its suspension. We recorded values of blood pressure, cardiac function, lactate levels, acid–base balance, temperature and dobutamine dosage.
At admission the sublingual microcirculation showed a low capillary density, vessel heterogeneity with a qualitative low flow and flow–no flow. After the first 24 hours from the beginning of DA infusion, sublingual flow showed an increase of vessel density, particularly of the number of small vessels, and the number of continuously perfused vessels increased during and post therapy with DA. We analyzed the microvascular flow with a simple semiquantitative method dividing the images into four equal quadrants and quantificating flow (hyperdynamic, continuous, sluggish, flow–no flow, no flow) for each cohort of vessel diameter (small, medium, large). We analyzed the mean value of results of three images for each patient pre and post DA therapy. Data are presented as the median. Before starting therapy with DA, the microvascular flow index (MFI) was 2.06 for small vessels, 2.09 for medium vessels, and 2.37 for large vessels. After DA infusion, the MFI was 3, 3, and 3, respectively, for small, medium and large

vessels. Differences between groups were assessed using the Mann–Whitney U test. We showed a statistically significant difference with $P < 0.0001$ between MFI before and post DA therapy. We demonstrated a quantitative and qualitative improvement of sublingual microcirculation with an increase of capillary density distribution (area–width) and average velocity versus vessel width. The course of microvascular blood flow may play an important role in sepsis and septic shock because of its relation to the development of multiple organ failure and death. Several studies have demonstrated that changes in microvascular perfusion are an independent predictor of outcome. The improvement of the microcirculation and vascular tone in septic shock by DA is probably related to its anticoagulant/antithrombotic and antiinflammatory action, to the decrease of TNFα production and inhibition of iNOS induction, and to improvement of endothelial barrier function and inhibition of chemotaxis, but further investigations are required to elucidate the exact mechanisms. These observations could suggest that DA could have a particular interest in the early management of severe sepsis.

P56

Multicentre audit of the use of drotrecogin alfa (activated) in UK critical care units

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Background Following positive results from PROWESS, drotrecogin alfa (activated) (DrotAA) was approved for use in Europe in August 2002. At this time, ICNARC commenced an audit to monitor the diffusion of the drug into routine UK practice and to undertake a nonrandomised evaluation of its effectiveness.
Methods A data collection form was developed and tested to mirror the information collected in PROWESS. This form was completed for every admission that received DrotAA and a senior clinician confirmed completeness. Data were entered centrally and validated.
Analysis Admissions receiving DrotAA and with severe sepsis and two or more organ dysfunctions in the first 24 hours following admission to the unit were matched to controls on: source of admission; organ dysfunctions; ICNARC physiology score; and age. Four pools of control patients were used for matching: (a) historic admissions (January 2000–August 2002) from the same unit; (b) contemporaneous admissions from the same unit; (c) contemporaneous admissions from units that never used DrotAA; and (d) contemporaneous admissions from units prior to their first use of DrotAA. Analyses were undertaken using conditional, fixed-effects, Poisson regression.
Results One hundred and twelve units participated in the audit; 1,079 admissions (one in 16) with severe sepsis and two or more organ dysfunctions in the first 24 hours following admission to the unit received DrotAA. For the four control pools, matching was successful for: (a) 657 (61%); (b) 820 (76%); (c) 702 (65%); and (d) 965 (89%). Matched cases were older, more acutely ill and had higher hospital mortality than unmatched cases. The relative risks (95% confidence interval) associated with DrotAA were: (a) 0.84 (0.77–0.92); (b) 0.85 (0.78–0.93); (c) 0.75 (0.68–0.83); and (d) 0.80 (0.73–0.86). *A priori* subgroup analyses indicated greater effect for patients with three or more organ dysfunctions.
Interpretation All results were consistent with PROWESS, but need to be interpreted with caution due to their nonrandomised nature and the potential existence of important unknown confounders. In addition, the fact that only one in 16 potentially suitable admissions received DrotAA suggests a strong possibility for treatment bias.

P57

Surviving ratio of severe sepsis treated with activated protein C in one university intensive care unit during 2003–2006

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Introduction Treatment of severe sepsis with infusion of activated protein C (APC) (Xigris) in the ICU of Barlicki University Hospital was initiated in 2003. From 2003 the number of treated patients increased significantly. This is due to better recognition. The introduced program consists of education of working staff in all hospitals in the region. Barlicki Hospital is a reference hospital for treatment of sepsis, and patients with diagnosis of sepsis are transferred to this ICU. University ICU doctors are teaching workshops how to recognize and treat sepsis.
Methods The surviving ratio in patients treated with APC was estimated retrospectively. Analysis included the years from 2003 to 10 December 2006.
Results A total number of 61 patients, aged 18–65 years, were included in the analysis. The pathogens and infection location were different. Patients were diagnosed according to recommendations of the Polish Sepsis Group and treatment with APC was introduced. The increase in number was: in 2004 vs 2003, 200%; in 2005 vs 2004, 111%; in 2006 up to 10 December vs 2005, 57.8%. The surviving ratio increased every year but in 2006 it decreased compared with 2005.

Table 1 (abstract P57)

	2003	2004	2005	2006 (10 Dec)
Number of treated patients	3	9	19	30
Surviving ratio	33% (1/3)	43.5% (4/9)	62.7%	47%

Discussion During 4 years of treatment of severe sepsis in the ICU with APC, important changes were observed: faster recognition and diagnosis, transfer to the reference hospital, and introduction of adequate therapy. The decrease in the surviving ratio in 2006 is probably due to a more serious state of the admitted patients – more initial infection located in the abdomen after surgery.
Conclusion The education program is essential in increasing the number of fast recognitions, which influences the surviving ratio.

P58

A large, single-centre UK registry of drotrecogin alfa-activated use

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Introduction As one of the few treatment interventions to demonstrate mortality efficacy at a randomized controlled trial level [1], the prescription of drotrecogin alfa-activated (DrotAA) (Xigris™), where appropriate, plays an important role in the management of severe sepsis. However, concerns regarding the potential for serious bleeding events have helped sustain a degree of scepticism regarding the use of DrotAA [2]. As early adopters of evidence-based medicine, Cardiff Critical Care Unit has prescribed DrotAA since late 2002 and has considerable experience with

respect to its use. The aim of this study was to demonstrate the safety profile and efficacy of DrotAA treatment within a large, 29-bed university hospital critical care unit.

Methods Demographic data were obtained from the unit's daily updated Riyadh ICU programme database and clinical data were collected from patients' medical notes and observation charts. All data were prospectively entered into our DrotAA registry, the results of which are shown below.

Results Between October 2002 and November 2005, 133 patients with severe sepsis were treated with DrotAA. The mean age was 61 years (range: 20–87 years) and 54% were male. The mean admission APACHE II score was 22 (range: 11–48), and on day 1 of DrotAA infusion the median number of organs that failed was 2.0 (range: 0–4), 129/133 (97%) were mechanically ventilated and 131/133 (98.5%) were on vasopressors. The median time to start DrotAA after documented diagnosis of severe sepsis was 12.6 hours (range: 0–41 hours) and the median duration of DrotAA infusion was 89.5 hours (range: 10–105 hours). The incidence of serious (life-threatening) bleeding events was 2.3% ($n = 3$): gastrointestinal ($n = 1$), intraabdominal ($n = 1$) and intrathoracic ($n = 1$); all were nonfatal and there were no intracranial bleeds. The 28-day mortality was 31.6%, the ICU mortality was 33.1%, the hospital mortality was 36.8% and the 1-year mortality was 47%.

Conclusions This is one of the largest UK registries of DrotAA usage published to date. Our results demonstrate a very low incidence of serious bleeding events associated with DrotAA treatment (2.3% vs 3.5% in PROWESS); it is interesting to note that all three adverse events occurred prior to 2004. This detail, combined with our low median time to start DrotAA infusion (which has steadily decreased over the past 4 years), would suggest the presence of a learning curve for DrotAA usage on ICUs. It is also encouraging to note that our overall hospital mortality was lower than the predicted APACHE II hospital mortality for these patients (36.8% vs 42.4%). Finally, this is one of the first UK studies to describe long-term mortality outcome in patients receiving DrotAA therapy. Further studies are required to more formally assess the impact of DrotAA treatment on long-term survival from severe sepsis.

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P59

Audit of adherence to National Institute of Clinical Excellence guidelines for the use of drotrecogin alfa (activated)

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Introduction Activated protein C (APC) is an endogenous protein, which has fibrinolytic and anti-inflammatory properties. This is available as human recombinant APC and is used in the treatment of patients with severe sepsis [1]. The National Institute of Clinical Excellence (NICE) suggested guidelines for the use of APC [2]. We retrospectively audited the records of patients who received APC during their admission to our ICU between January 2003 and August 2006. We audited our practice against three parameters: compliance with the NICE guidelines, accuracy of data forms, and outcomes of treatment.

Materials and methods From January 2003 to August 2006 we used APC to treat 44 severely septic patients in our ICU. We obtained complete data for 37 patients. We collected data from the case notes, ICU charts and drotrecogin alfa (activated) data forms and recorded relevant data on an Excel spreadsheet proforma.

Results *NICE guidelines.* We were 100% compliant with patient selection criteria for APC administration, which included a known or suspected site of infection, SIRS criteria and organ dysfunction criteria. All prescriptions were made by intensive care consultants. We were not fully compliant in excluding patients who met exclusion criteria (2/37 patients), although these cases were justified clinically by the consultants prior to administration.

Data entry. In 90% of cases the patient selection fields were completed, but only 30% of the exclusion and outcome fields were completed. In 30% of patients where a lactate ≥1.5 times normal was listed as one of the inclusion criteria, it was not associated with a pH ≤ 7.30 or a base deficit ≥5.0; however, all these patients had ≥3 organ-dysfunction criteria and hence still met the inclusion criteria.

Outcomes. Seven patients (15.9%) died during or within 28 days of APC administration. The standardised mortality ratio (SMR) was lower in patients receiving APC when compared with the rest of patients admitted over the same period (SMR ~0.5 vs ~1.0). Twenty-eight patients had an APACHE II score <25 and the effective cost per survivor was ~€16,800. Patients with APACHE II scores ≥25 had an effective cost per survivor of ~€22,400. Nine patients (20.5%) had their drotrecogin alfa (activated) infusions interrupted or discontinued for various reasons (including seven patients who had hemorrhagic complications, three of which were serious).

Conclusions and recommendations We use APC in compliance with the NICE guidelines. APC is cost-effective in patients with an APACHE II score <25 in our ICU.

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P60

Retrospective observational outcomes for drotrecogin alfa (activated)

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Introduction Grand River Hospital (GRH) is a 495-bed non-teaching, acute care referral center in Southwestern Ontario, supporting regional programs including dialysis, oncology, surgery and stroke thrombolysis. Since the introduction of drotrecogin alfa (activated) (DAA) in 2003, GRH has treated 58 patients with this agent for severe sepsis and septic shock. We sought to compare, where possible, GRH ICU/hospital outcomes and bleeding complications with those from published literature.

Methods All charts for patients treated with DAA in our CAICU for severe sepsis and septic shock between February 2003 and June 2006 were reviewed retrospectively for infection source, ICU/hospital mortality, survival by age and incidence of hemorrhagic complications. Where possible, we compare our data with those from PROWESS, ENHANCE and a recent Ontario/Quebec-based multicenter usage evaluation. A two-organ system failure threshold for DAA consideration is used. Outcomes were categorized as ICU mortality and hospital mortality, as opposed to 28-day mortality used in PROWESS and ENHANCE.

Results All 58 patients who received DAA at GRH were included in our analysis. The mean age of patients treated with DAA was

59.4 years. Primary sources of infection were: intra-abdominal 36.2%, respiratory 27.6%, genitourinary 8.6%, and 27.6% from other sources. GRH ICU mortality was 44.8% and hospital mortality was 51.7%. Analysis by age revealed overall survival rates of 78.6% for patients ≤50 years, 54.5% for 51–60 years, 52.9% for 61–70 years, 20% for 71–80 years, and 0% for patients >80 years of age. Hemorrhagic complication rates were higher than in published reports. Of 58 treatments, we recorded a total of nine hemorrhages (15.5%). The mortality rate in this cohort was 33.3%.
Conclusions These data suggest that 'field performance' of DAA may not be replicating the favorable clinical endpoints as reported in PROWESS. The Ontario Ministry of Health should consider implementing a provincial registry system for patients with severe sepsis and septic shock, empowering ICUs to track relevant demographic, acuity, and outcome data with a view to optimizing DAA use through patient selection and risk stratification.

P61

Risk/benefit analysis of activated protein C in patients with intra-abdominal sepsis

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Introduction and objective To establish whether activated protein C (APC) is safe in surgical patients with intra-abdominal sepsis (IAS). APC has been used in the treatment of IAS in our hospital since 2003. Fears persist regarding the potential for clinically significant bleeding in this surgical subgroup of patients.
Methods Forty-four patients with IAS received APC as a standardized regime between March 2003 and August 2006. A retrospective medical and ICU chart review was undertaken. Data collected included clinically significant bleeding episodes and mortality. Descriptive subgroup analysis of unexpected non-survivors(died in the ICU with APACHE II (APII) predicted mortality < 50%) and unexpected survivors (survived to ICU discharge with APII predicted mortality > 50%) was performed as statistical analysis of such small patient numbers was inappropriate.
Results There was one episode of clinically significant bleeding (from a mucous fistula: self-limiting). There were no intracranial haemorrhagic events. ICU mortality was 38.6% with mean APII predicted mortality of 37.16% and inhospital mortality of 47.7%. These exceeded rates for APC-treated surgical cohorts in the literature [1]. Unexpected survivors (5/44) were more likely to have been admitted from theatre. They had a shorter mean time from hospital–ICU admission (10.5 vs 5.6 days), duration on a ventilator (10.8 vs 17.5 days), vasopressor (9 vs 17.7 days) and renal replacement therapy (10.5 vs 23.5 days) dependence. All unexpected nonsurvivors (11/44) had a diagnosis of fistula or perforation. They were more likely to have been transferred to the ICU from another hospital or ward than from theatre. Co-morbidities were more severe.
Conclusion 1. APC was very safe to use in this group of critically ill surgical patients. 2. Although patients may fulfil standard criteria for APC use, if there is no definitive surgical cure for the IAS, then APC is inappropriate. 3. Delay in commencement of APC in surgical patients due to bleeding concerns may be contributing to the high mortality. Earlier perioperative use of APC in selected cases may offer improved mortality benefit, and we are undertaking a prospective audit to investigate this.

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P62

Three years experience with drotrecogin alfa (activated) protein C in severe sepsis and septic shock at Salmaniya Medical Complex, Bahrain

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Objective To evaluate the role of activated protein C (APC) in severe sepsis and septic shock.
Method The data were collected in a prospective manner from July 2002 to November 2006 in the adult medical/surgical ICU at Salmaniya Medical Complex Bahrain. The number of demographic variables were collected from patients' files.
Results A total of 444 patients were admitted to the ICU with the diagnosis of sepsis or severe sepsis. One hundred and forty-nine severe septic patients were assessed for APC: 85 patients received APC, and 64 patients could not receive APC due to financial problems or due to bleeding, coagulation derangement or very recent surgeries. In the total 444 septic patients admitted to the ICU, 152 patients expired (mortality 34.2%) and 141 had positive blood culture; 233 patients received inotrops. The total average APACHE II score was 28.9 and for expired patients was 35.1.
Out of the total 444 septic patients 149 were assessed for APC; in the 85 patients fulfilling criteria for and receiving APC the mortality was 43.5%, and for the 64 patients not receiving APC the mortality was 64%. All suspected septic patients admitted to the ICU received appropriate antibiotic therapy within 4 hours of ICU admission and were upgraded/changed according to culture/sensitivity reports if necessary. In the nonreceiving group (i.e. 64 patients) 12 patients could not receive APC due to financial restriction because initially foreigners were not entitled to this drug in Bahrain, but later this restriction was removed, and the remaining 52 patients could not receive either due to bleeding or very recent surgeries. Some patients could not receive complete treatment either due to bleeding complications or because they died. The mortality was measured at 28 days.
Furthermore, as per our experience, if APC started in the early stage of sepsis and the course is completed the outcome is better – out of 85 patients who received APC, 45 patients received in the early stage and completed the dose and 32 of these patients survived at 28-day mortality. An average three (ventilator-free) organs failed in the survival group and two (ventilator-free) organs failed in the expired group. Seventeen patients started treatment in the early stage and could not complete the course due to bleeding or other complications, 11 patients expired; 13 patients started in the late stage and completed the course, five patients expiring; and 10 patients started in the late stage and eight of these patients expired.
Conclusion On the basis of our experience and the results of multiple trials, we recommend APC should be given to the patients who meet all the inclusion criteria.

P63

Drotrecogin alfa in patients with severe sepsis: experience from a tertiary care center in North India

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Introduction Drotrecogin alfa (DA) remains the only approved drug for the specific treatment of severe sepsis. Although it has been in wide clinical usage, there are no data on its use in Indian patients.

Methods Fifty-seven patients with severe sepsis (age 51 ± 15 years, range 20–77 years, male:female 32:25) admitted to the ICU were included. All patients had three or more signs of systemic inflammation with at least two major organ dysfunctions or the presence of ARDS. Demographic, clinical and laboratory profiles at baseline, and during the hospital stay, development of complications, duration of hospital/ICU stay and hospital survival were recorded. All management decisions including initiation of DA (24 μ/kg/hour), duration of treatment as well as its discontinuation were the prerogative of the ICU team.
Results The majority of patients had a confirmed infection ($n = 36$, 63.2%), with the commonest site of focus being the lung ($n = 25$, 43.9%) followed by the abdomen ($n = 13$, 22.8%). A significant number of patients had at least three major organ dysfunctions ($n = 37$, 64.9%). A large number of patients had an APACHE II score in the range 25–29 ($n = 22$, 38.6%). Whereas 44 patients (77.2%) were on some kind of vasopressor support, 51 needed ventilatory support (89.5%). A total of 20 patients (35.1%) survived to hospital discharge. Patients received DA for a mean duration of 74.8 ± 26.2 hours (range 25–96 hours) and only 32 patients could complete treatment (56.1%). The outcome was significantly better in patients who could complete therapy (53.1% vs 13.6%, $P = 0.001$). Major bleeding necessitating discontinuation was seen in four patients (7%) whereas the other 21 patients (36.9%) died before completing 96 hours of therapy. DA was initiated within 48 hours of development of organ dysfunction in the majority of patients ($n = 31$, 54.4%), and a trend towards better outcome in patients with early treatment was noted although the difference did not reach statistical significance (mortality rate 58% for early treatment vs 73.1% for delayed treatment, $P =$ not significant).
Conclusion Mortality of patients with severe sepsis remains high despite the introduction of DA. Early institution may be associated with better outcomes. Patients receiving a complete course of treatment have better survival.

P64

Severe sepsis and drotrecogin alfa (activated) use: results from the PROGRESS registry

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Introduction Since the launch of drotrecogin alfa (activated) (DAA) a number of institutions and countries have published data on its use in clinical practice, based on audit or registry data. Such publications have tended to report DAA use in higher disease severity populations together with higher mortality outcomes compared with clinical trials. We utilized the Global PROGRESS (Promoting Global Research Excellence in Severe Sepsis) database to examine the baseline characteristics and outcome of patients with and without DAA treatment.
Methods PROGRESS is a global, noninterventional, multicenter, prospective, observational study of severe sepsis patients treated in ICUs. Patients must have had a diagnosis of severe sepsis and have been treated in an ICU at a participating institution. All treatment modalities were as per standard of care at the participating institutions. We analyzed baseline characteristics and hospital mortality. We also performed an adjusted mortality analysis for DAA patients due to baseline imbalances in patients with and without DAA therapy.
Results Overall, 12,492 patients with severe sepsis from 37 countries were enrolled and 882 (7%) patients received DAA therapy. The highest rate of use of DAA was seen in the United States at 27% (206/760). Patients who received DAA versus those who did not receive DAA were younger (median age 59 versus 64 years), had greater organ dysfunction (cardiovascular dysfunction (90% versus 74%), respiratory dysfunction (90% versus 81%), renal dysfunction (60% versus 45%), metabolic abnormalities (63% versus 42%), three or more organ dysfunctions (84% versus 67%)) and higher median APACHE II scores (25.0 vs 23.0), all $P < 0.001$. The mortality rate for patients treated with DAA was 49.6% and for those not treated with DAA was 49.7%. Although imbalances in other baseline characteristics, not collected in PROGRESS, may have also been present, when adjusted for age and number of organ dysfunctions the odds ratio for hospital mortality associated with DAA use was 0.75 (0.63–0.90, $P = 0.002$).
Conclusion In a large global registry, patients receiving DAA therapy were younger with higher disease severity than patients not treated with DAA. When adjusted for age and number of organ dysfunctions, DAA was associated with a reduction in the odds of hospital mortality similar to that seen at day 28 in PROWESS. These data are supportive of the effectiveness of DAA in clinical practice.

P65

Epidemiology of severe sepsis in India

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Introduction A multicentre, prospective, observational study was conducted in 12 intensive therapy units (ITUs) in India from June 2006 to November 2006 to determine the incidence and outcome of severe sepsis among adult patients.
Methods All patients admitted to ITUs were screened daily for SIRS, organ dysfunction and severe sepsis. Patients with severe sepsis were further studied.
Results A total of 1,344 ITU admissions were studied. There were no SIRS in 31.3% and SIRS without organ dysfunction in 51.6%. SIRS with organ dysfunction was found in 230 (17.1%) patients, of which 54 (23.5%) were not due to sepsis and 176 (76.5%) were due to sepsis. The incidence of severe sepsis was 13.1% of all admissions. The mean age of the study population was 54.9 years (SD 17.6), of which 67% were male. The median APACHE II score was 22 (IQR 17–28) with predominant (88%) medical admission. ITU mortality of all admissions was 13.9% and that of

Figure 1 (abstract P65)

Parameter	Severe Sepsis
Infection characteristics	
Site of infection	Lung (46.2%), Blood (22%)
Gram positive	18
Gram negative	59
Fungal	05
Parasite & Virus	18
Culture positivity	48.6%
Time to antibiotic	5.95 hrs

severe sepsis was 54.1%. Hospital mortality and 28-day mortality of severe sepsis were 59.3% and 57.6%, respectively. The standardized mortality ratio of severe sepsis patients was 1.40. The median duration of stay in ITUs of the severe sepsis cohort who survived was 6 days (IQR 3–12). The number of episodes where infection was the primary reason for admission to the ITU was 89.8% and the rest of episodes were ITU acquired. See Figure 1 for infection characteristics.

Conclusion Sepsis was common in Indian ITUs and had predominant medical populations. ITU mortality was higher compared with western literature. Gram-positive infections were less common although the incidence of parasitic and viral infections were higher than in the West.

P66

PISA: the prevalence of infection in intensive care units in South Africa

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Introduction Sepsis in the ICU is a major cause of morbidity and mortality. In addition it increases the direct and indirect cost of care. Effective intervention to improve patient outcome and ensure optimal use of resources depends on the availability of data. No epidemiological data are available on the prevalence of sepsis in South Africa. This study was a 1-day sepsis prevalence study conducted in an attempt to address this lack of data.

Method Following appropriate institutional approval, 43 ICUs were selected using the proportional probability sampling technique. This was applied to a national database of ICUs. Every seventh bed was selected from all the serially placed units. Data collected identified the profile of the unit and the patient details for the day in question (15 August 2005). The primary endpoint was a peer-reviewed determination of the need for antibiotic prescription as determined by two independent reviewers. Sepsis was defined according to the ACCP/SCCM criteria. Secondary end-points included determination of diagnostic ability of attending clinicians, antibiotic prescribing patterns and appropriateness of modification of therapy based on microbiological data.

Results The mean age of patients was 55 years ($n = 248$) with a male:female ratio of 60:40. Sixty-eight per cent of patients were admitted post surgery. There was reasonable concordance for sepsis, severe sepsis and septic shock (Table 1). A total of 196/248 (79%) patients were deemed to require antibiotics by the attending clinician, compared with 69/248 (28%) who were deemed to have sepsis by independent review. Fifty-one per cent of patients were inappropriately diagnosed as having sepsis. The commonest site of sepsis (as determined by the assessors) was the lung (45%) followed by the abdomen (10%). In 42% of cases antimicrobial prescription was adjudged as being appropriate, while in 11% of cases antimicrobials were appropriately modified following microbiology results. The duration of therapy was appropriate in 26% of cases.

Conclusion The national prevalence of sepsis, the site of sepsis and the patient profile in South Africa is similar to that described in other studies [1]. Treating doctors are reasonably accurate in diagnosing sepsis but prescribe antiobiotics inappropriately in the vast majority of cases.

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Table 1 (abstract P66)

Diagnostic concordance

	Treating doctor	Assessors
None	169	54
SIRS	16	120
Sepsis	36	41
Severe sepsis	7	12
Septic shock	9	16

P67

Microbiology profile of sepsis in Brazil

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Introduction Sepsis occurs in 16.6% of the patients in the Brazilian ICU and is associated with a high mortality rate (46.6%). Several studies show different pathogenic agents among countries and increased antibiotic resistance. This study aims to describe the pathogen profile in Brazil's ICU septic patients.

Methods A prospective cohort study involving 75 ICUs all over Brazil was performed. All patients who were admitted or developed sepsis during a 1-month period were enrolled and followed until the 28th day and/or until their discharge.

Results A total of 521 patients filled the criteria of sepsis and were studied. The two main sources of infection were pneumonia and the abdominal tract. Gram-negative bacteria were isolated in 40.1%, followed by Gram-positive (38.8%) and fungus (5%). The most prevalent bacteria were *Staphylococcus aureus* (31.3%) and *Pseudomonas aeruginosa* (26.8%). Methicilin-resistant *Staphylococcus aureus* (MRSA) were present in 64.8%. Bacteria were isolated in blood samples in 19.57% and *S. aureus* was prevalent. The prevalence of antimicrobial-resistant bacteria was 26.6% and was associated with higher mortality at the 28th day (resistant bacteria 50.9% vs nonresistant bacteria 43.5%). Septic shock was related to the highest mortality, with rates ranging from 45.8%, 63.7% and 83.3% due to *S. aureus*, *P. aeruginosa* and *Acinetobacter* spp, respectively.

Conclusions Gram-negative bacteria were the most frequently isolated pathogens in the ICU in septic patients. MRSA represented the majority of *S.aureus* strains isolated. Antibiotic-resistant bacteria were associated with higher mortality. It is important to recognize the Brazilian ICU organisms' profile and their resistance pattern to guide rational administration of antimicrobial agents.

P68

Incidence of bacteraemia in a neurocritical care unit

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Introduction The incidence of bacteraemia and bloodstream infection, as defined by the CDC, in our neurosciences critical care

unit (NCCU) is at the moment unknown. It is known that being a patient in the intensive care environment is in itself a risk factor for the development of bacteraemia (3.2–4.1 per 100 admissions in several papers). The higher amount of invasive procedures and the severity of illness in this group of patients have been blamed. The aims of our study are: (1) to identify the incidence of bacteraemia in the NCCU, (2) to recognise the incidence of bloodstream infection (SIRS with bacteraemia), (3) to identify the most common pathogens associated with bacteraemia, and (4) to promote the continuous collection of data aiming to follow the behaviour of this problem in time.

Methods This is a prospective observational study looking at the presence of positive blood cultures in all the patients admitted to the NCCU during the period from 1 June to 31 August 2006. Blood cultures were taken from a peripheral site under aseptic conditions as per the NCCU guidelines. We tried to identify how many of the patients with positive blood cultures had evidence of concomitant SIRS/sepsis, as described by the modified Bone criteria, and the severity of this. An attempt was made to identify the most frequent microorganisms involved in this problem as well as their antibiotic susceptibility. As a secondary aim of our study we described the number of fatalities in the patients with bacteraemia. We tried to focus our approach to the fact that we serve a large neurological/surgical population as well as general patients and to see whether we could pinpoint differences in these two groups.

Results There were 201 patients admitted to the unit during the period of our study; 140 of these were neurosciences (NS) patients and the rest (61) were general (G) (either medical or surgical). Most of the patients were men and had a mean APACHE II score of 39 (NS group 33, G group 45).There were in total 64 episodes of positive blood cultures (BC); 39 of these episodes were accompanied by inflammatory signs (incidence of bloodstream infections of 19.4% of total admissions). Twenty-five of the episodes were not associated to clinical signs of infection. There were more patients with at least one episode of positive BC in the NS group (29 (20.7%)) than in the G group (10 (16.39%)). Out of 49 episodes in the NS group, 59.18% (29) were associated to some degree of inflammatory response (SIRS, severe sepsis, and MODS). Out of 15 episodes in the G group, 66.6% (10) developed inflammatory response. In 59% (25) of the positive BCs, the organism isolated was coagulase-negative staphylococcus (CNS). In the G group, 47% (7) grew CNS, 33% were diverse Gram-negatives and in 20% other Gram-positives. In the NS group, 64% (31) of isolates grew CNS, 21% were other Gram-positives and 15% were Gram-negatives. In 47 (73.4%) episodes of positive BC, the patients had either a central venous catheter or an arterial catheter. In 36 (56.2%) of the episodes the patients were already on antibiotics at the time of the sampling. The most frequent agent isolated was coagulase-negative *Staphylococcus aureus*, in 39 (59%) of the cases.

From the patients that had at least one positive BC, nine died; seven (78%) patients were in the G group, and two (22%) in the NS group. Twenty-five (68%) patients with at least one episode of positive BC had a systemic inflammatory response at the time of sampling. Seven (28%) of these died during the first 30 days in the NCCU. Nine (23%) patients had severe sepsis and four (44%) of these died. Four (10.2%) patients had MODS and three (75%) of these died.

Conclusions We had an incidence of positive blood cultures of almost 32% of the total admissions; 19.4% of admissions developed bloodstream infections. These numbers are very high if we consider the published data. Due to the specialist origin of our unit, we had more cases in the neurosciences group than in the general group. However, the incidence of sepsis and MOF in these patients was almost the same for both groups. We noted, as well, a larger number of deaths in the patients with sepsis and MOF. There needs to be more studies aiming to establish a casual relationship to explain this. CNS was the most frequently isolated organism and there was no difference among the groups. There is a potential for increased mortality in the patients that develop bloodstream infections in our unit, and we need to implement urgent measures to decrease them while further research is done in this area.

P69

Implementation of early goal-directed therapy in Finland

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Introduction The early recognition and rapid start of goal-directed treatment (EGDT) are important elements for better outcome in severe sepsis. These actions should take place in the emergency department (ED) before admission to the ICU. The aim of our study was to determine how the EGDT was performed and to evaluate the impact of EGDT principles on mortality in septic shock in Finland. Our study was conducted before national guidelines for severe sepsis were published.

Methods A prospective observational study of patients with severe sepsis and septic shock admitted to 21 ICUs in Finland from 1 November 2004 to 28 February 2005 (Finnsepsis). Only patients with community-acquired sepsis, who fulfilled the criteria of septic shock and were admitted directly from the ED to the ICU, were included. The following treatment targets were evaluated: (1) measurement of lactate during the first 6 hours from admission to the ED; (2) obtaining the blood cultures before antibiotics; (3) starting the antibiotics within 3 hours from admission; and reaching the (4) mean arterial pressure over 65 mmHg, (5) central venous pressure over 8 mmHg and (6) central venous oxygen saturation over 70% or mixed venous oxygen saturation over 65% during the first 6 hours with fluids and vasopressors.

Results Sixty-three patients were included. The median age was 57 years (IQR 18.5) and the median APACHE II score was 28 (IQR 10). The ICU, hospital and 1-year mortality rates were 25%, 38% and 52%, respectively. Only five (8%) patients reached all treatment targets and 24 patients (38%) reached four or more targets (group A).

The hospital mortality of group A was 29% (95% CI 15–49%) compared with 44% (95% CI 29–59%) of those who reached only three or less targets (group B) ($P = 0.3$). The median delay from ED arrival to ICU admission in group A and group B was 1.1 and 3.7 hours ($P < 0.001$), and the median SOFA score for the first day was 10 and 11 ($P = 0.4$), respectively. The median APACHE II score was 28 in both groups ($P = 0.9$). In multivariate analysis including all separate targets, delay for ICU admission and APACHE II score, the APACHE II value and measurement of lactate were independent predictors of mortality ($P = 0.001$ and 0.02). Only 18% of patients had serum lactate measured during the ED stay. The 1-year mortality of group A was 42% (95% CI 24–61%) and of group B was 59% (95% CI 43–73%) ($P = 0.2$).

Conclusions The adoption of EGDT protocol was poor in Finnish hospitals. The impaired early recognition of sepsis may lead to a delay in ICU admission. The rate of reached EGDT targets reflected mortality. In this study the most critical EGDT target was the measurement of lactate during first 6 hours after arrival in the ED. A forthcoming follow-up study will evaluate the impact of guidelines to treatment and outcome of septic shock in Finland.

P70

Impact of sepsis care bundles on hospital mortality in 135 consecutive patients with septic shock

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Introduction The purpose of the study was to describe the effectiveness of the Surviving Sepsis Campaign (SSC) bundles with regard to both implementation and outcome in patients with septic shock.
Methods This was a single-center prospective observational study of patients admitted to the medical–surgical ICU of an urban tertiary care teaching hospital meeting criteria for the international sepsis definitions. Patients were entered in the database from September 2005 to October 2006. After a widespread 2-month educational program, implementation of SSC Resuscitation Bundles (RB) and Management Bundles (MB) were accomplished. We determined the rate of compliance and the prognostic value of the RB, the MB and of each bundle element.
Results We analyzed 135 consecutive episodes of septic shock. The main sources of infection were: abdomen 39.5%, lung 29.9%, and urinary tract infection 11.1%. Global hospital mortality was 44.4%. Nonsurvivors were older (71 vs 64 years; $P = 0.01$), and had a higher APACHE II score (25 vs 20; $P = 0.000$), a higher SOFA score (10 vs 9; $P = 0.001$) and a higher number or organ dysfunctions at sepsis presentation (4 vs 3; $P = 0.007$). The rate of compliance with the RB was 38%. There were significant differences in mortality between compliant (C) and noncompliant (NC) groups despite the similar characteristics and the severity of septic shock. The NC group had a 58% mortality rate and the C group 22% (RR 2.6 (95% CI 1.49–4.5, $P = 0.001$)). The number needed to treat to save one life was 3. The compliance rate with MB was only 20%, and there were no differences in mortality between the C and NC groups (57.9% vs 52.6%). We only found differences in mortality between the C and NC groups in four bundle elements: serum lactate measured before 6 hours (35.2% vs 65.4%; $P = 0.007$), early broad-spectrum antibiotics (36.2.5% vs 56.1%; $P = 0.051$), $ScvO_2 > 70\%$ (35.7% vs 52.1%; $P = 0.057$) and activated protein C (65% vs 11% $P = 0.000$). In the multivariate analysis, activated protein C, early broad-spectrum antibiotics, $PaO_2/FiO_2 < 200$ and complete RB were associated independently with mortality.
Compliance rates with RB during three consecutive 4.6-month time periods were 28%, 41.4% and 33.3%, respectively. Compliance with MB was unchanged at 20%. The present dataset is underpowered to determine whether implementation of SSC bundles had some effect on mortality reduction.
Conclusions Implementation of SSC bundles was associated with less adherence than expected. However, septic shock patients receiving the complete resuscitation bundle had substantially lower mortality. Efforts to increase compliance with these interventions should be made. The poor adherence to management bundles probably shows the many uncertainties that remain within this group of interventions.

P71

Awareness of the Surviving Sepsis Campaign amongst emergency medicine and surgical trainees

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Introduction Data presented at the 2006 Barcelona conference of the European Society of Intensive Care Medicine showed that, where implemented, the Surviving Sepsis Campaign guidelines have improved mortality from sepsis. However, because of overall poor adherence to the guidelines, the stated aim of the campaign to reduce mortality from severe sepsis by 25% is unlikely to be met. In the United Kingdom, patients with sepsis of surgical origin will typically be seen by emergency medicine (EM) before being admitted to a surgical ward and are unlikely to be initially managed by the ICU. Both the EM and surgical juniors should therefore be aware of the guidelines. The aim of this study was to determine the level of awareness of the SSC guidelines in surgical and EM trainees.
Methods A questionnaire-based survey was undertaken of all EM and surgical trainees in the Eastern region of the United Kingdom. Participants were recruited by post, telephone, email and in person. The questionnaire assessed whether participants had experience in critical care, were aware of the campaign or its guidelines and assessed the level of familiarity of key concepts of the resuscitation bundle of the guidelines. In addition, participants were encouraged to comment on any aspect of sepsis management.
Results Summarised in Table 1. There are 29 EM and 52 surgical trainees in the Eastern region; responses were obtained from 22 and 34, respectively. The responses to the key concepts of the resuscitation bundle varied greatly, even between different participants from the same speciality in the same institution, suggesting a lack of clear direction. Free text responses included 'the only people that know about guidelines for sepsis are the ICU physicians' and 'the only time I have heard of early goal directed therapy was on ER'.
Conclusion Awareness is reasonable amongst EM trainees but poor amongst surgeons. If the aims of the SSC are to be met, consideration must be given to differences in healthcare systems in different countries. In the United Kingdom, educational activities should be directed towards EM and surgical trainees as well as those working in intensive care.

P72

Compliance with the surviving sepsis guidelines: a review of South African intensive care units

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Introduction Despite the availability of guidelines for practice in many clinical domains, it is common for clinicians to practice outwith these guidelines. As part of a 1-day sepsis prevalence study in ICUs in South Africa, a review was undertaken to determine the

Table 1 (abstract P71)

Trainees	Worked in ICU in past 2 years?	Claimed to be aware of campaign	Able to name SSC	Any training on sepsis in past 2 years?	Claim to be aware of research	Able to name piece of relevant research
Emergency medicine	8 (36%)	15 (68%)	10 (45%)	13 (59%)	13 (59%)	10 (45%)
Surgery	2 (6%)	6 (18%)	3 (8%)	9 (26%)	13 (38%)	8 (24%)

extent to which units comply with the surviving sepsis guidelines as promulgated by the International Sepsis Forum [1].

Method Following appropriate institutional approval, 43 ICUs were selected using the proportional probability sampling technique. This was applied to a national database of ICUs. Every seventh bed was selected from all the serially placed units. Data collected included the presence of an infection control policy (including guidelines for performance of blood cultures), recording of culture results, microbiological support structures, glucose control protocols and protocols for sedation analgesia and muscle relaxation.

Results Forty-three out of a total of 458 units were sampled. The mean age of patients was 55 years with a male:female ratio of 60:40. Sixty-eight per cent of patients were admitted post surgery. An infection control policy was present in 77% of units. A practice procedure for blood culture sampling was used in 51% of units, with records of culture results being documented in 56% of units. Microbiologists were available in 65% of units and they were involved in ward rounds in 26% of units. Physical consultation by a microbiologist in 47% of units and telephone consultations in 54% of units were possible. Sixty-one per cent of units had a glucose control policy. Sedation, analgesia and neuromuscular blockade protocols were present in 33%, 26% and 21% of units, respectively. See Table 1.

Table 1 (abstract P72)

Percentage of units utilizing protocols

Domain	Use (%)
Microbiologist available	65
Infection control policy	77
Glucose control protocol	61
Sedation protocol	33
Analgesia protocol	26
Neuromuscular blockade protocol	21

Conclusion The majority of units have an infection control policy, utilize glucose control regimens and have access to a microbiologist. Sedation, analgesia and neuromuscular blockade are infrequently utilized. Despite the availability of guidelines, it is common for many recommendations not to be implemented. Further work is required to determine the reasons for noncompliance with attention to educational programs and other strategies to improve practice.

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P73

The outcome of sepsis and septic shock presenting to the Emergency Department in Australia and New Zealand

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Introduction The outcome of sepsis and septic shock patients admitted to the ICU from the Emergency Department (ED) in Australia and New Zealand was investigated using prospectively collected data from the Australian and New Zealand Intensive Care Society Adult Patient Database.

Methods All adult patients with an APACHE III medical admission diagnosis of nonurinary or urinary sepsis, or nonurinary or urinary sepsis with shock, admitted directly to the ICU from the ED between 1 January 1997 and 31 December 2005 were identified. Predictor variables for hospital mortality were analysed using logistic regression with cross-validation (80% determination and 20% validation) and robust, cluster-specific (ICU site) standard errors.

Results A total of 7,649 patients (54% male) of mean (SD) age 60.2 (18.1) years and APACHE III score 74.0 (34.7) were identified. The number of patients admitted per year increased progressively (1997, $n = 368$ (7.7 admissions per contributing ICU); 2005, $n = 1,409$ (14.0 admissions per contributing ICU)). Nonurinary sepsis with shock was the most common admission diagnosis ($n = 3,394$, 44.4%) and urinary sepsis with shock the least common ($n = 607$, 7.9%). Overall ICU mortality and hospital mortality were 20.9% and 27.6%, respectively. Hospital mortality was predicted by hospital type (tertiary: 0.67 (0.51–0.90), $P = 0.007$; metropolitan: 0.63 (0.48–0.83), $P = 0.001$; private: 0.65 (0.47–0.91), $P = 0.011$; reference category rural), age (1.026 (1.019–1.034), $P = 0.0001$), APACHE III score (1.043 (1.038–1.048), $P = 0.0001$) and APACHE III score squared ($P = 0.032$), sepsis category (nonurinary shock versus the other three categories combined, 1.79 (1.48–2.16), $P = 0.001$), mechanical ventilation within 24 hours of ICU admission (1.38 (1.14–1.66), $P = 0.001$) and calendar year as a single main linear effect (0.94 (0.90–0.97), $P = 0.0001$). Significant interactions were demonstrated between (i) sepsis classification and calendar year (linear decrease in mortality, nonurinary shock x year 0.92 (0.86–0.99), $P = 0.019$), (ii) sepsis classification and age (nonurinary shock x age 0.986 (0.977–0.996), $P = 0.008$), and (iii) ventilation and time from hospital to ICU admission (<4.5 hours or ≥ 4.5 hours 1.38 (1.12–1.69), $P = 0.002$). The model ROC curve area and the P value for the Hosmer–Lemeshow C statistic were 0.86 and 0.37, respectively. Restricting the model to only those ICUs that contributed data for all 9 years of the study period yielded similar parameter estimates, including calendar year effect.

Conclusions The reported incidence of sepsis and septic shock in ICU patients presenting to the ED in Australia and New Zealand has increased since 1997; hospital mortality has decreased. These data require confirmation with a prospective study.

P74

Clinical simulation: caring for a critically ill patient with sepsis

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Introduction The purpose of this simulation research was to assess whether bedside nurses could better apply currently recommended therapeutic interventions for patients with sepsis by using a horizons trends clinical decision support tool, rather than just standard monitoring screen displays alone.

Methods Simulation research participants ($n = 75$) were first required to attend a didactic training session focusing on recognition and evidence-based treatment for critically ill patients with sepsis. Participants were then directed to apply these treatments in a simulated sepsis experience. Data were collected at two sites (AACN National Teaching Institute Critical Care Nursing Conference, New Orleans, May 2005 and Long Beach Memorial Medical Center's Health Skills Education Center). A METI HPS (human patient simulator) was connected to a Philips Medical Systems Intellivue MP 70 in a simulated critical care environment. Participants were given the patient history, and completed the rest of their assessment using the HPS and

Intellivue patient monitoring. Data were collected to compare the use of bedside monitor displays with and without horizon screen trends in the care of patients with sepsis. Group 1 ($n = 37$) completed the sepsis scenario using a standard screen display, and group 2 ($n = 38$) had the addition of horizon trends on the display.
Results The point that marked the onset of sepsis was when each of the physiologic parameters met the current evidence-based screening criteria (HR > 90, RR > 20, MAP < 65, temperature >38°C). Results of this study found statistically significant differences between the standard screen and horizons screen participant groups in the speed in which clinicians were able to reach each measured outcome. This was true in each of the five outcome measurements: onset of sepsis ($P < 0.001$), initiation of fluid bolus ($P < 0.001$), initiation of vasopressor ($P < 0.001$), blood culture order ($P = 0.012$), and antibiotic administration ($P = 0.020$).
Conclusions These results support the hypothesis that monitoring using horizons trending does indeed contribute to faster clinical decision-making in the simulated septic patient experience. Future research should concentrate on replicating these results in a real clinical environment.

P75

Medical microbiology ward rounds in critical care

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Background Direct microbiological input to critical care is essential for the management of the septic patient. Early broad-spectrum antimicrobial therapy with appropriate diagnostic studies to ascertain causative organisms is well established; there should be reassessment with the aim of using narrow-spectrum antibiotics to prevent the development of antimicrobial resistance, to reduce toxicity and to reduce costs [1]. In systematic analysis of ward rounds in ICUs the information most commonly missing from a patient's file concerned microbiology findings [2].
Methods We performed a telephone survey of all NHS critical care units in the North West of England ($n = 31$). Each unit was telephoned and the duty consultant was asked a series of questions relating to the type of microbiology input to their critical care unit.
Results We achieved a 100% response rate. The study looked at 11 teaching hospitals and 21 district general hospitals representing 12% of UK ICUs: 26 (83%) critical care units had live computerised access to microbiology data, 21 (68%) units had an antibiotic policy in place, and 19 (61%) units had a formal microbiology ward round. With the frequency ranging from once per week (one unit) to 7 days per week (four units), most units with a microbiology ward round had this service Monday–Friday (12 units). When asked to rate the value of this ward round, the mean score was 8.6 out of a possible 10 (range 10–5, mode 9). In those units without a microbiology ward round the desirability of such a service was scored on average at 8.5 out of 10 (range 10–3, mode 9).
Conclusion Direct microbiological advice at the bedside is highly valued by ICU consultants. Antibiotic prescribing is generally well controlled, with two-thirds of units having an agreed antibiotic policy in place. Work will continue to determine whether these results reflect the national picture in the United Kingdom.

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P76

Impact of a selective digestive decontamination and nasal mupirocin on the incidence of ventilatory-associated pneumonia and the emergence of bacterial resistance

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Introduction Selective digestive decontamination (SDD) can reduce the incidence of ventilatory-associated pneumonia (VAP). Some concerns have been raised about the risk of selection of resistant bacteria. We evaluated the impact of a SDD regimen on the incidence of VAP and the development of resistant pathogens.
Methods In a polyvalent eight-bed ICU, a retrospective analysis was performed of two periods of 8 months before (no-SDD, 178 patients, mean SAPS II 44.8) and after (SDD, 110 patients, mean SAPS II 48.9) the use of SDD with amphotericin, tobramycin and colistin for oropharyngeal and gastric decontamination and mupirocin for nasal decontamination. The results were analyzed with the chi-square test.
Results The incidence of VAP was reduced in the SDD group, even though it was not statistically significant (26.9% vs 16.3%, $P = 0.138$). The mortality of VAP and septic shock was reduced respectively from 39.6% to 16.7% ($P = 0.312$) and from 60% to 37.5% ($P = 0.835$). During the SDD period, Gram-positive infections increased while Gram-negative infections and Candida infections showed a reduction. The percentage of resistant species showed a reduction from 49.1% to 30.5% in all the categories of pathogens (Table 1).

Table 1 (abstract P76)

Percentages of pathogens

Infection	no-SDD total	no-SDD resistant	SDD total	SDD resistant
Gram-positive	32.5 (% of all VAP)	31% (% of all G+)	41.5 (% of all VAP)	20% (% of all G+)
Gram-negative	54 (% of all VAP)	69% (% of all G–)	50 (% of all VAP)	44% (% of all G–)
Candida	13.5 (% of all VAP)	12.5% (% of all candida)	8.5 (% of all VAP)	0% (% of all candida)

Conclusions SDD and mupirocin were correlated to a reduced incidence of VAP and mortality and to a reduction of resistant species.

P77

Comparison of bloodstream infections in intensive care unit patients, due to different Gram-negative bacteria

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Introduction To compare the incidence and risk factors of bloodstream infections (BSIs) due to *Acinetobacter baumannii*, *Pseudomonas aeruginosa* and *Klebsiella pneumoniae* and to

assess which of them is associated with higher mortality in ICU patients.

Patients and methods This study was conducted in the 28-bed multidisciplinary ICU of Evangelismos Hospital in Athens, during an 18-month period (August 2004–January 2006). All ICU patients with blood cultures due to *A. baumannii* or *P. aeruginosa* or *K. pneumoniae* bacteremia, obtained >48 hours after ICU admission, were studied. Patients with BSIs due to more than one of those three pathogens were excluded. Information included patients' age, gender, underlying disease, admission category, hospitalization before ICU admission, length of ICU stay, source of BSIs and ICU mortality were compared. The illness severity was assessed by APACHE II score on admission and on the day of BSI was calculated prospectively for all patients.

Results During the study period, among 855 consecutively admitted patients, with ICU stay longer than 48 hours, 197 patients developed BSIs due to *A. baumannii* (96 patients, incidence 11.23%), *P. aeruginosa* (44 patients, incidence 5.15%) and *K. pneumoniae* (57 patients, incidence 6.67%). Of these patients, 85 developed BSIs with two or more pathogens and were excluded. Thus, finally, 64 patients with *A. baumannii* BSI, 23 with *P. aeruginosa*, and 25 with *K. pneumoniae* were compared. Hospitalization before ICU was shorter for *K. pneumoniae* bacteremic patients compared with those with *A. baumannii* (1 vs 3 days, $P = 0.028$) and with those with *P. aeruginosa* (1 vs 6 days, $P = 0.005$). On ICU admission, patients with *A. baumannii* had a higher APACHE II score compared with those with *K. pneumoniae* (19.53 ± 7.6 vs 15.0 ± 5.4, respectively, $P = 0.017$) and lower hematocrit and hemoglobin values (29.8 ± 6.5 vs 35.4 ± 6.5, $P = 0.002$ and 9.9 ± 2.2 vs 11.9 ± 2.2, $P = 0.001$) respectively. Also on BSI day, hematocrit was lower in patients with *A. baumannii* and with *P. aeruginosa* bacteremia, compared with those with *K. pneumoniae* bacteremia (26.6 ± 4.5 vs 29.6 ± 4.5, $P = 0.016$ and 26.1 ± 3.8 vs 29.6 ± 4.5, $P = 0.021$). The respiratory tract was the most common source of BSIs due to *A. baumannii* compared with *P. aeruginosa* and *K. pneumoniae* (56.3% vs 26.1%, $P = 0.013$ and 56.3% vs 12.0%, $P = 0.001$). Mortality was higher in the presence of *P. aeruginosa* and *A. baumannii* BSIs, compared with *K. pneumoniae* (56.5% vs 24.0%, $P = 0.021$ and 48.4% vs 24.0%, $P = 0.036$, respectively).

Conclusion In ICU patients, the development of BSI due to *A. baumannii* is associated with a higher severity of illness on admission compared with those due to *P. aeruginosa* and *K. pneumoniae*. However, *P. aeruginosa* BSI is associated with the higher mortality.

P78

Maximal barrier precautions, intensivist supervision, and catheter-related bloodstream infections

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Introduction Catheter-related bloodstream infections (CR-BSI) have significant costs. Use of maximal barrier precautions (MBP) may reduce the incidence of CR-BSI. We studied MBP with/without intensivist supervision of residents on CR-BSI incidence.

Methods We prospectively studied CR-BSI incidence in an ICU following the implementation of MBP (hand washing before line placement, sterile site preparation, draping the entire patient in sterile fashion, use of hat, mask, gloves and gown, maintenance of a sterile field, assistants following the same precautions, and sterile dressing application). The Centers for Disease Control definition of CR-BSI was used. Data were compared with historical controls at the same ICU. Also, independent observers evaluated the procedure for technique break (omitting any conditions listed under MBP). Subsequently, in addition to MBP, all central venous catheters were placed under intensivist supervision. Data analysis included one-tailed *z* tests for proportions and *t* tests.

Results From 1 January 2000 to 31 December 2002 (control period) the CR-BSI incidence was 12.1/1,000 catheter-days. Following implementation of MBP (1 January 2003–31 October 2004) the CR-BSI incidence decreased to 3.5/1,000 catheter-days (19/5,499 catheter-days), $P < 0.02$; in 85 independently observed line placements using MBP, 7/85 patients had CR-BSI (8.2%). Technique breaks occurred in 34/85 procedures and were associated with six CR-BSI (17.6%); the 51/85 procedures without technique breaks had one infection (1.9%), $P < 0.01$. Intensivist supervision (11 January 2004 to 30 April 2006), in addition to MBP, further reduced the incidence to 1.5/1,000 catheter-days (7/4,667 catheter-days), $P < 0.04$.

Conclusion While MBP can reduce the incidence of CR-BSI, placement of central venous catheters by residents under intensivist supervision can further lower the incidence.

P79

Risk of catheter-related bloodstream infection: higher in more severe patients?

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Introduction Vascular devices are associated with the risk of catheter-related bloodstream infection (Cr-BSI). The aim of this study was to evaluate the risk of Cr-BSI in our ICU.

Methods A nonconcurrent cohort study at an adult, 11-bed medical/surgical unit, between 1 January and 31 December 2005. Data were retrospectively reviewed from clinical records and bacteriological data concerning the presence of central venous (CVC) or haemodialysis catheter (HDC) colonization and Cr-BSI (no data on arterial catheters) were collected. Catheter insertion and dressing of the insertion site were done according to CDC guidelines for Cr-BSI prevention. Diagnosis of Cr-BSI required microbial concordance between a culture of the removed catheter and a separate percutaneously drawn blood culture, and the exclusion of other overt source of bacteraemia. Intravascular devices were cultured for evidence of colonization whenever there was clinical suspicion of Cr-BSI. Severity scores (SOFA, SAPS II) were assessed and analysed facing Cr-BSI data.

Results During the study period, 378 patients were admitted to the ICU (59% male; mean age 58.3 ± 19.8 years), the mean SOFA score (admission) being 7.9 ± 4.0 and the mean SAPS II (at 24 hours) being 47.6 ± 19.7. In the 266 patients with CVC, the total duration of implantation was 3.190 days, with a mean duration of CVC placement/patient of 12 days. Positive cultures of CVC were found in 18 patients (6.8%). The incidence density of positive catheter cultures was 6.3/1,000 days of CVC use. CVC-related BSI was diagnosed in 5 patients, the risk of CVC-related BSI being 1.6/1,000 days of CVC use. Fifty-two patients also had a HDC. Positive cultures of HDC occurred in two of these patients (3.8%), none of them with Cr-BSI. The isolated microorganisms from CVC and HDC were typical skin bacteria, excluding two cases with catheter colonization in patients with other overt sources of bacteraemia. The mean SOFA score in patients with positive catheter cultures was 10.2 ± 3.1, the mean SAPS II was 63 ± 19.6 and the mean catheter placement duration in these patients was 32.1 ± 15.7 days. The overall ICU mortality rate was

20.1%, being 40% in the subgroup of patients in whom Cr-BSI was diagnosed.
Conclusions Preventing Cr-BSI is important, but special care is particularly relevant in patients with higher SAPS II scores and a longer duration of catheter placement. More studies are needed to confirm this possible higher risk of Cr-BSI in this more severe patient subgroup.

P80

Tunnelled central venous catheter-related infection in cardiothoracic critical care

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Introduction Tunnelled central venous cannulae (CVC) are used in cardiothoracic (CT) critical care for long-term inotrope, antibiotic and renal replacement therapy (RRT). The incidence of blood-stream-related infection (BSI) related to all types of CVC is between 2.9 and 11.3 per 1,000 catheter-days [1]. In CT or cardiology practice the incidence for all CVC-related infection is 2.9–4.5 per 1,000 catheter-days. The incidence of BSI is reduced using tunnelled CVC, although there are little published data on the incidence of BSI in tunnelled CVC in CT critical care. CVC-related infection has been recognised as a priority in the UK initiative 'Saving Lives' [2]. We reviewed tunnelled CVC-related infection in a tertiary UK CT centre with a significant transplant population.
Methods A retrospective analysis from November 2001 to 2006 of culture and sensitivity results of tunnelled CVC tips (Bard Groshong® cuffed catheter and HemoGlide®) and blood cultures from the same patients.
Results Ninety-three CT critical care patients received a tunnelled subclavian CVC. The indications were inotropes ($n = 40$ (43%)), antibiotic administration ($n = 27$ (29%)), RRT ($n = 14$ (15.1%)) and unknown ($n = 10$ (10.8%)). The mean duration of the catheter remaining *in situ* was 36 days (SD 44.0, range 1–164). Culture results are presented in Table 1. Twelve patients had an established CVC-related BSI. The mean infection rate/1,000 catheter-days was 3.6.

Table 1 (abstract P80)

	Positive CVC tip culture	Positive blood culture	Positive from both
Positive culture results (%)	36.6	18.3	12.9
Mean infection rate/ 1,000 catheter-days	10.2	5.1	3.6

Conclusion The incidence of tunnelled CVC colonisation and positive blood cultures in this group of CT critical care patients is in line with previously published data for all types of CVC. *Coagulase-negative staphylococcus* was the predominant isolate in both this audit and previously published data [1].
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P81

ANCCADI – Antibiotic Coated Catheter to Decrease Infection: a pilot trial

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Background Nosocomial catheter-related bloodstream infections (CR-BSI) have been associated with increased morbidity and possibly increased mortality in critically ill patients. Central venous catheters impregnated with rifampin and minocycline (RM) have been shown to decrease rates of colonization and CR-BSI when compared with controls and with the chlorhexidine/silver sulfadiazine catheter. However, recent randomized trials challenged the clinical impact of such catheters, showing decreased rates in colonization but not in CR-BSI. We designed this pilot trial to compare the rates of colonization and CR-BSI in RM catheters and controls in a Brazilian population of critically ill patients.
Methods A prospective, nonrandomized, controlled clinical trial was conducted in one medico-surgical 19-bed ICU. Adult patients needing a double or triple central venous catheter were sequentially assigned in permuted blocks of five to undergo insertion of a control or RM-impregnated catheter. After removal, all tips were cultured by the roll-plate method in association with one or two peripheral blood cultures. Rates of colonization and CR-BSI were recorded and compared.
Results Of 120 catheters inserted, 100 could be evaluated for colonization and CR-BSI. Forty-nine in the uncoated group and 51 in the coated group. Clinical characteristics of patients and risk for infection were similar in the two groups, use of propofol was more frequent in the uncoated group and the presence of a vascular device, other than the study catheter, was more frequent in the antibiotic-coated group. Three RM-coated catheters (5.9%) were colonized compared with nine (18.4%) control catheters (relative risk, 0,28; 95% confidence interval, 0.07–1.096; $P = 0.05$). Three cases of CR-BSI (5.9%) occurred in patients who received RM catheters compared with five in the control group (10.2%). There was no significant differences in the incidence of CR-BSI between RM-coated and uncoated catheters. Uncoated catheters were more frequently colonized but this difference just failed to show statistical significance. When the duration of catheter placement were taken into consideration, Kaplan–Meier analysis showed no significant differences in the risk of colonization or CR-BSI between RM-coated and uncoated catheters. Rates of CR-BSI were seven per 1,000 catheter-days in the RM-coated group compared with 11.4 per 1,000 catheter-days in the uncoated group ($P = 0.7$). Gram-positive and Gram-negative organisms were similarly responsible for colonizing catheters in our study; there was no difference in rates of colonization by *Candida* species.
Conclusion In this pilot study, we showed a trend toward lower rates of colonization in RM-coated catheters when compared with uncoated control catheters. The incidence and rates of CR-BSI were similar in the two groups, probably because of a small number of catheters studied. Development of a prospective randomized trial with a larger number of patients is underway to confirm or refute these results.

P82

Is the blood culture useful in febrile immunocompetent patients in the Emergency Department?

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Introduction Blood culture was commonly performed, without any specific indication, at the Emergency Department. However, the true positive rate was found to be very low (1.8–5%) and patients with true bacteremia usually had such risk factors as an indwelling catheter, severe underlying disease or an immunocompromised state. This study was performed to determine the usefulness of performing blood culture for managing febrile immunocompetent patients who present to the Emergency Department.
Method We prospectively analyzed the medical characteristic and the results of blood culture of febrile immunocompetent patients who were more than 18 years old and who presented to the Chonnam National University Hospital Emergency Center from April 2005 to October 2005. Fever was defined as a single axillary temperature higher than 38.0°C. The two sets of blood for culture were drawn at the antecubital area by the emergency physician who knew well how to obtain blood for culture. The bacteremia was classified as true bacteremia or contamination, based on the presence of clinical signs and symptoms and also on the criteria of MacGregor. For the true bacteremia group, we further investigated the changes that occurred with the previously administered antibiotic therapy according to the results of blood culture.
Results This study included 182 patients: of the 182 cultures, only 36 were positive with 10 contaminants (5.5%) and 26 true positives (14.3%). The most common disease that required blood culture in the Emergency Department was respiratory infection (57/182) and the most common disease with true bacteremia was urinary infection (41.9%). A low initial level of albumin was the characteristic associated with a positive blood culture result on multivariate analysis. Management of only five patients was influenced by the blood culture results (2.7%).
Conclusion The blood cultures, as were usually ordered for febrile immunocompetent patients in the Emergency Department, rarely altered patient management and the results had limited usefulness. The emergency physician who initially treats these patients has to consider this limitation of blood culture. Also, eliminating blood cultures for immunocompetent patients may hold down unnecessary medical expenses.

P83

Impact of early antibiotics on severe sepsis – are we doing a good job?

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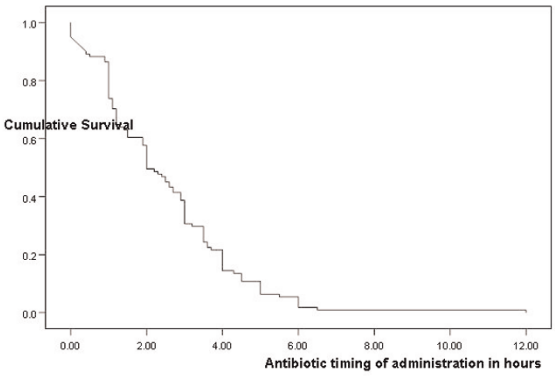
Introduction Despite improvements in technology and healthcare services, mortality rates from severe sepsis have remained unchanged over the past few decades. Exciting new data are emerging about the benefits of early, aggressive management in the Emergency Room (ER). We carried out this study to study the patterns of antibiotic administration in our ER and their effects on the length of hospitalization and survival.
Methods This was a prospective, observational cohort study that reviewed all adult patients presenting with systemic inflammatory response syndrome (SIRS) to the ER of the Aga Khan University Hospital, which is a 554-bed primary care/tertiary care referral facility, over a period from February to June 2006. SIRS was defined according to the criteria proscribed by the Society of Critical Care Medicine. A research officer stationed in the ER identified patients. Exclusion criteria were age < 18 years, patients transferred from other hospitals or chronic care facilities. Demographic and study-specific data were collected. The patient was followed until subsequent death or discharge. The primary outcome variable was survival to hospital discharge and the secondary outcome was length of hospitalization. An independent *t*-test analysis was carried out for the primary independent variable (timing of administration of antibiotics) and primary outcome (mortality) for significant differences between the groups. A two-sided *P* value <0.05 was considered as statistical significance. Logistic regression modeling was used to examine survival as a function of timing of antibiotic administration.

Figure 1 (abstract P83)



Results Patients enrolled in the study numbered 111. At presentation 36 patients (32.4%) had 1/4 criteria for SIRS, 67 (60.4%) had 2/4 criteria and only eight (7.2%) patients had 3/4 criteria. Sixteen patients (14.4%) were in shock. Sepsis was confirmed by cultures in 96 (86.5%) patients. One hundred (90.1%) patients received intravenous antibiotics in the ER; the average time from triage to actual administration was 2.8 (± 1.86) hours. The timing of administration of antibiotics was statistically significant in determining survival. Patients with sepsis and receiving antibiotics in <1 hour had a mean survival of 99% and a length of hospitalization of 3 days as compared with those receiving antibiotics in 1–4 hours (84.5% survival, LOS 5.25 days) and patients who received antibiotics in >4 hours (76% survival, LOS 7 days, $P < 0.003$). Using a Cox regression model, we were able to demonstrate that survival dropped acutely with an hourly delay in antibiotic administration. Overall mortality with sepsis was 34.2%.
Conclusions Administration of appropriate antibiotics within 4 hours of arrival in the ER has a significantly favorable impact on survival in patients with sepsis.

P84

Protective effect of antibiotic prophylaxis against early-onset nosocomial pneumonia in comatose patients

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Objective To study the impact of prophylactic antibiotics on the occurrence of early-onset nosocomial pneumonia in patients with medical coma.

Patients and methods An open, before and after, single-center trial, in the medical ICU of the University Hospital of Besancon, France. A first period (A, retrospective) extended during 18 months (April 2003–October 2004) without antibiotic prophylaxis and was followed by a second period (B, prospective) during 18 months (November 2004–April 2006). Patients received prophylaxis treatment by amoxicillin and clavulanic acid, shortly after intubation and during a 24-hour period. Inclusion criteria were medical loss of consciousness, Glasgow Coma Score < 8, and length of intubation > 48 hours.

Results A total of 101 patients were enrolled, 61 patients during period A and 40 patients during period B. No significant differences were found between mean age (48.6 years vs 50.4 years old), SAP II score (44.5 vs 46.5), aetiology of coma (mainly ischaemic stroke, cardiac arrest, refractory epilepsy, intoxication), and early-onset ($n = 12$ vs $n = 6$) or late-onset pneumonia ($n = 1$ vs $n = 2$). During period B, the time for onset of colonisation (6.6 days vs 3 days, $P = 0.008$) or pneumonia (8.4 days vs 4.2 days, $P = 0.03$) was increased compared with period A. We did not diagnose multidrug-resistant infection or colonisation. No difference was found with regard to mortality and morbidity: duration of mechanical ventilation (5.7 days vs 6.7 days) or total hospitalisation stay (26.6 days vs 16.9 days), total mortality ($n = 9$ vs $n = 10$ patients) or at day 28 ($n = 6$ vs $n = 7$ patients), respectively, in periods A and B. In multivariate analysis, tobacco, cardiac arrest and ischaemic stroke were independent risk factors of pneumonia.

Conclusion In our study, contrary to previous ones [1,2], antibioprophylaxy did not show a decrease in the incidence of nosocomial pneumonia in medical comatose patients with Glasgow Coma Score < 8 under mechanical ventilation. On the other hand, antibiotics induce a later onset of colonisation and lung infections. Despite a prevention of early-onset nosocomial pneumonia, our data do not support the use of regular prophylactic antibiotics.

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P85

Antibiotic prescribing practices in public and private-sector intensive care units in South Africa

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Introduction Considerable variability exists in antibiotic prescribing practices. A dichotomous health care system in South Africa has created the opportunity for vastly differing practices. As part of a national 1-day sepsis prevalence study (PISA), a review was undertaken of antibiotic prescribing practices in public and private-sector ICUs.

Method Following appropriate institutional approval, 43 ICUs were selected using the proportional probability sampling technique. This was applied to a national database of ICUs. Every seventh bed was selected from all the serially placed units. Antibiotic therapy was reviewed by two independent reviewers. Data collected included the appropriateness of pretherapy cultures, postculture modification of therapy, duration of therapy and, finally, impact of appropriate antibiotic choice on mortality.

Results See Table 1. Public-sector practice is better with respect to pretherapy sampling and duration of treatment. Better modification of treatment occurs in the private sector.

Overall mortality of both groups was 10/82 (12%) when antibiotic choice was appropriate compared with 28/90 (31%) ($P < 0.05$) when therapy was inappropriate.

Table 1 (abstract P85)

Appropriateness of antibiotic therapy

Intervention	Sector	Number	Percentage
Preculture sampling	Private	27/62	43*
	Public	73/120	61
Modification of antibiotics	Private	49/61	80
	Public	18/27	67
Duration of treatment	Private	25/134	19*
	Public	26/49	53

*$P < 0.05$.

Conclusion There are significant differences in antibiotic prescribing practices when public and private sectors are compared. Appropriate early antibiotic prescriptions reduce mortality. Attention to education and systems that address prescribing practices is indicated.

P86

Timing of admissions and outcome of pneumonia in intensive care units in the United Kingdom

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Critical Care 2007, **11(Suppl 2):**P86 (doi: 10.1186/cc5246)

Introduction This study aims to assess the association between the timing of admission and outcome in patients admitted with pneumonia to ICUs in the United Kingdom.

Methods All patients admitted to an ICU with a primary reason for admission of pneumonia were extracted from the Case Mix Programme Database. 'Early' admissions, admitted to the ICU on the day of admission to hospital (12,475), were compared with 'late' admissions, admitted to the ICU on a later date (21,948). The ICU and hospital mortality, number of organs failed, renal dysfunction, and length of stay in hospital were compared between the two groups. An association was sought between timing of admission and mortality. Patients were stratified by CURB 65 score on admission to the ICU. Mortality was compared between the two groups. Odds ratios were used to analyse data. $P < 0.05$ was considered significant.

Results There were small but statistically significant differences between the two groups in mean age, APACHE II score, CURB 65 score and number of organ failures, and the presence of

Table 1 (abstract P86)

CURB65	Odds ratio	95% CI	P value
1	1.02	0.9–1.16	0.8
2	1.23	1.13–1.34	<0.0001
3	1.25	1.16–1.35	<0.0001
4	1.46	1.29–1.65	<0.0001
5	1.41	1.03–1.91	0.03

respiratory organ failure. There was no difference in the presence of renal dysfunction. Late admissions with pneumonia had higher ICU and hospital mortality, and longer hospital stay. At each CURB 65 score the late admissions had higher hospital mortality, which was significant at scores of 2–5 (Table 1).

Conclusion Early admission may reduce mortality in patients admitted to ICUs with pneumonia. CURB 65 scores could facilitate triage of patients with pneumonia.

P87

Are routine endotracheal aspirates predictive of the etiology of ventilator-associated pneumonia?

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Introduction Most investigators discuss the predictive value of respiratory surveillance cultures in mechanically ventilated patients and doubt on the appropriate selection of the antibiotic therapy based on these findings, when pneumonia develops. The aim of our study was to evaluate whether microorganisms cultured from semiquantitative tracheal aspirates (SQTA) in the 48 hours prior to the clinical suspicion of ventilator-associated pneumonia (VAP) were predictive of the etiology, compared with the bronchoalveolar lavage (BAL) results performed on the same day that the clinical diagnosis was considered

Methods Routine SQTA were performed twice weekly in all intubated patients for over 72 hours according to the methodology described elsewhere [1]. Fiberoptic bronchoscopy with BAL was preformed the same day that VAP was suspected according to Johanson criteria (fever, leucocytosis, purulent secretions and infiltrate on radiograph) plus gas-exchange deterioration.

Results In our 22-bed ICU, during a 27-month period, 156 patients underwent BAL procedures due to clinical suspicion of VAP. Out of these, 118 patients (120 BAL) had semiquantitative tracheal aspirate (SQTA) performed 48 hours prior to the clinical diagnosis of VAP (males 71/118; mean age 47 ± 16 years; SAPS II 35 ± 10). See Table 1 for pathogen prediction by SQTA surveillance cultures. See Table 2 for concordance of SQTA–BAL when only multiresistant microorganisms are considered. Negative BAL cultures with SQTA growth were never found. Polymicrobial SQTA cultures: 13 concordant, seven only partial concordant, four not concordant. There was no incidence in our results related to previous antibiotic therapy: 33% of the concordant, 24% of the partial concordant and 29% of the no concordant were on antibiotics when SQTA was obtained.

Conclusions In our patient population, routine surveillance SQTA cultures accurately predict more than 60% of the etiologic agents of VAP. This prediction increases to 80% when multiresistant microorganisms are considered. Due to routine surveillance cultures, our antibiotic prescriptions can become more adequate.

Table 1 (abstract P87)

Concordance, 76/120 (63%)	a) Same microorganisms SQTA–BAL	66/76 (87%)
	b) No significant growth	10/76 (13%)
Partial concordance, 17/120 (14%)	a) 2 microorganisms SQTA–1 BAL	4/17 (24%)
	b) 1 microorganism SQTA–1 BAL	13/17 (76%)
No concordance, 27/120 (23%)	a) No significant growth SQTA–1 or 2 microorganisms BAL	14/127
	b) Different microorganisms SQTA–1 BAL	13/27

Table 2 (abstract P87)

Multiresistant microorganism	SQTA	BAL	Concordant	%
Ps. aeruginosa	22	22	20/24	83
Acinetobacter	14	11	10/15	67
MRSA	8	9	8/9	89
Klebsiella	2	2	2/2	100
Stenotrophomona	1	1	1/1	100
Total multiresistant microorganisms			41/51	80

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P88

Comparing a Brazilian guideline to treat nosocomial pneumonia with the ATS guideline in a tertiary hospital in Brazil

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Introduction The medical literature shows that the most important prognosis factor in nosocomial pneumonia is the correct empirical antimicrobial therapy. Recently the microorganisms have been becoming more resistant to the usual antibiotics and there are many reports of Gram-negative bacilli (GNB) only susceptible to Polimixyn b (PB). The ATS guideline does not suggest the use of PB as an empirical therapy, while the Brazilian Sepsis Guideline (BG) allows the use of this antibiotic in special circumstances. The aim of this study was to compare the efficacy of both guidelines, based on the microbiological data.

Methods This is a retrospective study with 93 cases of nosocomial pneumonia diagnosed according to the ATS criteria, managed in our ICU from 1 February 2005 to 16 September 2006. We analyzed the efficacy of both guidelines, using them during all the study period or stratifying the patients into two groups according to the research median period (24 November 2005).

Results There were 67 cases of ventilator-associated pneumonia (VAP) and 26 cases of non-VAP. The overall result shows that the ATS would be effective in 76% (CI 67–85%) and the BG in 87.9% (CI 81–94.7%) of the cases. This difference was statistically significant ($P = 0.035$). The most prevalent bacteria were *Acinetobacter* sp. and *Pseudomonas aeruginosa*. From February to August 2005 there were a burden of multiresistant (MR) GNB, only susceptible to PB. Using the ATS or the BG in this period, the guidelines would be effective in 64% (CI 51–77%) and 84.4% (CI 74.8–94%) respectively ($P = 0.017$). In the second half of the study we controlled the MR GNB, and the efficacy of both guidelines were similar between ATS and BG (97% vs 93.9%; $P = 1$).

Conclusions Our data show that the more restrictive ATS guideline can significantly lead to a wrong empirical therapy in MR GNB high-prevalence situations. The use of the BG can lead to a better empirical treatment in this situation. This information enhances the need for ICU flora knowledge, which are seasonal, so there is no 'all time and place perfect guideline', although the BG was a better option in our ICU than the ATS guideline.

P89

Outcomes from ventilator-associated pneumonia caused by multidrug-resistant organisms or *Pseudomonas*: results from 28 intensive care units

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Introduction Patients who develop ventilator-associated pneumonia (VAP) caused by either multidrug-resistant organisms (MDRO) or *Pseudomonas* may have poor clinical outcomes. We sought to further clarify this potential relationship using a database from a large multicenter trial of diagnostic and therapeutic strategies in patients who had suspected VAP.
Methods Patients receiving mechanical ventilation (MV) for ≥96 hours and who developed suspected VAP (new or worsening pulmonary opacities on CXR, and at least two of fever, leukocytosis, change in sputum purulence, increased O_2 needs, or isolation of potentially pathogenic bacteria from sputum) were eligible. At enrolment, all patients had cultures obtained from either BAL or endotracheal aspirates. MDRO were defined as those resistant to ≥2 classes of antibiotics. Patients were followed until 28 days after enrolment, death, or hospital discharge.
Results Seven hundred and thirty-nine patients from 28 ICUs in Canada and USA were enrolled. At enrolment, cultures from 10.0% (95% CI 7.9–12.4%) of the patients grew MDRO or *Pseudomonas*. The prevalence of MDRO at enrolment was 5.2% (3.6–6.8%). There were no differences in APACHE II, MODS, or PaO_2/FiO_2 at baseline between those whose specimens grew MDRO or *Pseudomonas* and those whose specimens did not. Patients with MDRO or *Pseudomonas* had higher 28-day mortality (RR 1.59, 95% CI 1.07–2.37, $P = 0.04$) and inhospital mortality (RR 1.48, 95% CI 1.05–2.07, $P = 0.05$) and a trend towards higher ICU mortality (RR 1.42, 95% CI 0.90–2.23, $P = 0.14$) than those whose specimens did not grow these organisms. Median duration of MV (12.6 vs 8.7 days), ICU length of stay (16.2 vs 12.0 days) and hospital length of stay (55.0 vs 41.8 days) was greater in patients with MDRO or *Pseudomonas* than in those whose specimens did not grow these pathogens ($P = 0.05$). Adequacy of initial empiric therapy was 68.5% in patients whose specimens grew MDRO or *Pseudomonas* compared with 93.9% in those without these organisms ($P < 0.001$).
Conclusion The isolation of MDRO or *Pseudomonas* from respiratory tract specimens of patients with suspected VAP is associated with prolonged MV, increased ICU and hospital stay, and increased risk of death. Inadequate initial empiric antibiotic treatment may be a contributing factor.

P90

Bacterial burden and bronchoalveolar cytokines in mechanically ventilated patients with suspected pneumonia

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Introduction Cytokines play an important role in pulmonary host defense. However, nonuniform findings have been reported about the correlation between bronchoalveolar bacterial burden and the lung inflammatory response.
Objective The aim of the present study was to evaluate the relationship between bronchoalveolar cytokine expression and bacterial burden in mechanically ventilated patients with suspected pneumonia.
Methods Mechanically ventilated patients with suspected pneumonia admitted to the ICU from November 2004 to January 2006 were prospectively enrolled. Fiberoptic bronchoalveolar lavage (BAL) was performed with 150 ml sterile isotonic saline in three aliquots of 50 ml; local anesthetic was not used. BAL samples for microbiologic quantitative cultures and BAL cytokines – IL-6, IL 8, TNFα, granulocyte colony-stimulating factor (G-CSF) and granulocyte–monocyte colony-stimulating factor (GM-CSF) – were measured.
Results Fifty-nine patients were included, and most of the patients (79.7%) had prior antibiotic therapy. Twenty-two patients (37.2%) had a positive bacterial culture defined as a diagnostic threshold >10,000 colony-forming units/ml. Only the concentration of TNFα was significantly higher in the group of patients with positive BAL (Table 1).
Conclusions (1) There is a significant correlation between TNFα in BAL fluid and the lung bacterial burden. (2) BAL TNFα is an early marker of pneumonia in mechanical ventilated patients despite prior antibiotic therapy.
Clinical implication Cytokine measurements in BAL may be a diagnostic tool to support the diagnosis of the initial phase of pneumonia.

Table 1 (abstract P90)

	BAL–	BAL +	*P*
IL-6 BAL (pg/ml)	180.3 ± 252	293.4 ± 421	0.410
IL-8 BAL (pg/ml)	1,301 ± 1,045	1,681 ± 1,315	0.442
TNF BAL (pg/ml)	48.9 ± 80.7	222.6 ± 308	0.022
G-CSF BAL (pg/ml)	444.8 ± 565	408.1 ± 491	0.713
GM-CSF BAL (pg/ml)	14.1 ± 23.4	9.35 ± 17.32	0.126

P91

Risk factors for treatment failure in patients with ventilator-associated pneumonia receiving appropriate antibiotic therapy

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Introduction Treatment failure (TF) can be anticipated in 30–40% of patients developing ventilator-associated pneumonia (VAP). Little information about lack of response of VAP to treatment is available. The aim of the study is to evaluate potential risk factors for TF in patients with VAP receiving appropriate antibiotic therapy.
Methods A prospective observational cohort study. Microbiologically confirmed ($>10^5$ colony-forming units/ml) clinical findings (CPIS > 6) were necessary for the diagnosis of VAP. TF was defined as a lack of clinical (in first 3 days of the therapy) and microbiological (in first 7 days of the therapy) response to therapy. All patients had surveillance cultures for endotracheal aspirate (every second day), urine and blood (weekly). Student's *t* tests, chi-square tests and logistic regression analyses were used for statistical analyses.
Results Eighty-one patients enrolled into the study; 40% of them were female and the mean age was 71 ± 14. Fifty-one of the

patients had TF. When the groups were compared (TF and treatment success), patients with TF were older, had more comorbidities, higher admission and VAP APACHE II scores, *Acinetobacter baumanni* pneumonia, higher initial bacterial load (colony-forming units/ml) and lower daily carbohydrate intake. Transfusions, bacteremia, infection with multidrug-resistant microorganismis and steroid therapy were similar across the groups. Among the significant parameters, age and comorbidity were not entered into the logistic regression since the APACHE II score covers these two parameters. VAP with *A. baumanni* (OR 4.4, 95% CI 1.2–16, $P = 0.027$), higher VAP APACHE II scores (OR 12, 95% CI, 3–45, $P = 0.0001$) and lower daily carbohydrate intake (OR 4.4, 95% CI 1.3–15, $P = 0.016$) were independent predictors for TF in logistic regression analyses.

Conclusion These results suggest that patients with higher VAP APACHE II scores and pneumonia with *A. baumanni* and lower carbohydrate intake were at risk for TF.

P92

Intensive care nurses' knowledge of evidence-based guidelines for the prevention of ventilator-associated pneumonia

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Introduction Nonadherence to evidence-based guidelines for the prevention of ventilator-associated pneumonia (VAP) has been reported. As a lack of knowledge may be a barrier for adherence, this study aimed to determine intensive care nurses' knowledge of evidence-based guidelines for VAP prevention.

Methods This study is a survey using a validated multiple-choice questionnaire, developed to evaluate nurses' knowledge of VAP prevention and based on a recently published review by Dodek and colleagues [1]. Knowledge of nine nursing-related strategies was evaluated. The questionnaire was distributed and collected during the Flemish Society for Intensive Care Nurses' annual congress (Ghent, 2005). Demographic data included were gender, intensive care experience, number of critical beds and whether nurses hold a special degree in emergency and intensive care.

Results We collected 638 questionnaires (response rate 75%). Nineteen per cent recognized the oral route as the recommended way for intubation. Forty-nine per cent knew that ventilator circuits are to be changed for each new patient only. Heat and moisture exchangers were checked as the recommended humidifier type by 55%, and 13% knew that it is recommended to change them once weekly. Closed suction systems were identified as recommended by 69%, and 20% knew that these must be changed for each new patient only. Respectively 60% and 49% recognized subglottic drainage systems and kinetic beds to reduce the incidence of VAP. Semirecumbent positioning is well known to prevent VAP (90%). The nurses' average score was 4.2/9, while nurses with >1 year experience and those holding a special degree both scored 4.5/9 ($P < 0.001$).

Conclusion Nurses lack knowledge of evidence-based guidelines for VAP prevention. Their schooling and continuing education should include support from current evidence-based guidelines.

Reference

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P93

Institution-specific guidelines for the management of ventilator-associated pneumonia

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Introduction ATS/IDSA [1] guidelines recommend consideration of local microbiologic data when selecting empiric treatment for ventilator-associated pneumonia (VAP) and broad-spectrum empiric therapy for patients with pneumonia caused by MDR pathogens. The purpose was to use local microbiologic data to develop institution-specific guidelines for VAP.

Methods We prospectively recorded local microbiologic and susceptibility data in our ICU. Respiratory specimens were tracheal aspirates in all cases and were evaluated by quantitative criteria.

Results We had 40 episodes (2,247 ventilator-days) of VAP (40/133 patients) and 45 isolates. In early-onset pneumonia (≤5 days, eight episodes, three with two isolates): six *Acinetobacter baumannii*: meropenem, colistin, gentamicin (five); three *Pseudomonas aeruginosa*: piperacillin, aztreonam, imipenem, ceftazidime, colistin, ciprofloxacin, cefepime, meropenem, aminoglycosides; one *Klebsiella pneumoniae*: meropenem, colistin, tetracycline; Fungi 1: no susceptibility results. In late-onset pneumonia (>5 days, 32 episodes, two with two isolates): 25 *A. baumannii*: four to amoxicillin-clavulanic, ceftazidime, piperacillin-tazobactam, aztreonam, imipenem, colistin, ciprofloxacin, cefepime, meropenem, aminoglycosides, 19 to meropenem, gentamicin, colistin, tetracycline and two to colistin; four *P. aeruginosa*: two to piperacillin-tazobactam, two to colistin; one *K. pneumoniae*: piperacillin-tazobactam, aztreonam, imipenem, ceftazidime, colistin, ciprofloxacin, cefepime, meropenem, aminoglycosides, amoxicillin-clavulanic; Fungi 1: no susceptibility results and three unspecified isolates.

Excluding fungi and unspecified isolates, we had 8/45 multisensitive isolates and 32/45 isolates sensitive to colistin (32), meropenem (26) and gentamicin (21). According to these data in early and late VAP the most adequate therapeutic combination to cover possible pathogens is meropenem + colistin. Using this combination we cover all possible pathogens and then de-escalate according to susceptibility results. Following the ATS/IDSA guidelines we would cover only 8/45 isolates.

Conclusions ATS/IDSA [1] guidelines may not be applicable in all institutions or countries and thus clinicians should incorporate local microbiologic data into institution-specific guidelines [2].

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P94

Administration of meropenem for the treatment of ventilator-associated pneumonia

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Introduction Ventilator-associated pneumonia (VAP) is associated with the greatest mortality among nosocomial infection. Death rates associated with Pseudomonas spp. or with late-onset VAP seem higher. Treatment of these infections is frequently complicated by antibiotic resistance, a problem that has been increasing in recent years.

Objective and methods The goal of the study was to evaluate the clinical efficacy of meropenem by continuous infusion administration (CIA) or by bolus intermittent infusion (BII) for the treatment of VAP caused by *Pseudomonas aeruginosa*. An historic control group with VAP caused by *P. aeruginosa* who received initial empiric antibiotic therapy with meropenem by BII ($n = 32$) was compared with a prospective cohort treated with meropenem by CIA ($n = 20$) in a 12-bed surgical ICU, at a 400-bed surgical complex of a district hospital. We looked for demography, APACHE II score, mortality, attributable mortality for VAP, days on mechanical ventilation (MV), and ICU length of stay. VAP was treated during 14 days with meropenem (1 g/6 hours intravenously). The antibiotic clinical effect was categorized as cure or failure. Difference between groups were tested by means of Student's *t* test end exact chi-square test, using the MedCalc program. We consider values of $P < 0.05$ as a significant difference.

Results Significant differences were not found between both groups of patients in sex, age, APACHE II score, and diagnosis. The CIA group showed significantly greater clinical cure than the BII group (CIA 18/20 (90%) vs BII 21/32 965.6%), $P = 0.041$) and smaller but not significant attributable mortality to VAP (2 of 20 (10%) vs 10 of 32 (31.3%), $P = 0.288$).

Conclusion Our results suggest that administration of meropenem by CIA may have more clinical efficacy than administration by BII for the treatment of VAP, but more studies are required to confirm this.

P95

A randomized trial of combination therapy versus monotherapy for the empiric treatment of suspected ventilator-associated pneumonia

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Introduction Delays in adequate antibiotic therapy for ventilator-associated pneumonia (VAP) are associated with poor outcomes, and early use of broad-spectrum antibiotics may improve clinical outcomes. However, indiscriminant use of broad-spectrum antibiotics is associated with the emergence of antibiotic-resistant bacteria, fungal infections, and increased healthcare costs. The purpose of this study was to determine optimal empiric treatment of VAP by comparing a strategy of combination therapy to monotherapy with broad-spectrum antibiotics.

Methods In a multicenter trial, we randomized mechanically ventilated adult patients with suspected VAP that developed after 96 hours in the ICU to receive either meropenem and ciprofloxacin or meropenem alone, as initial therapy. In addition, before starting antibiotics, diagnostic specimens were obtained using either bronchoalveolar lavage with quantitative cultures or standard endotracheal aspirates.

Results We randomized 740 patients in 28 ICUs in Canada and the United States. The baseline characteristics and etiologies of VAP were similar between groups. There was no difference in 28-day mortality between the combination and monotherapy groups (RR = 1.05, 95% confidence interval 0.78–1.42; $P = 0.74$). The duration of ICU and hospital stay, clinical and microbiological response to treatment, emergence of antibiotic-resistant bacteria, isolation of *Clostridium difficile*, and fungal colonization were similar between groups. Combination therapy resulted in a higher rate of adequate empiric therapy compared with monotherapy (93.1% vs 85.3%, $P = 0.01$). In a subgroup of patients with infection due to pseudomonas species, acinetobacter species and multidrug-resistant Gram-negative bacilli at enrollment ($n = 56$), the adequacy of initial antibiotics was 82.4% in the combination group versus 18.8% in the monotherapy group ($P < 0.001$); this difference was associated with an increase in the microbiological eradication of the infecting organisms (64.1% vs 29.4%, $P = 0.05$) but no differences in clinical outcomes.

Conclusion In patients who have suspected VAP, empiric treatment with combination therapy, as compared with monotherapy, is safe and is associated with a higher rate of adequate antimicrobial coverage but has no effect on clinical outcomes.

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P96

A canine model of *Pseudomonas aeruginosa* ventilator-associated pneumonia using a defined bacterial inoculum

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Introduction This prospective pilot study set out to develop an animal model of *Pseudomonas aeruginosa* that would be suitable for the application of molecular techniques to evaluate virulence in which instillation of a reference strain of *P. aeruginosa* results in a monoculture ventilator-associated pneumonia. For this purpose, male adult greyhounds were used in an animal research laboratory.

Methods The animals were anaesthetised, orally intubated and mechanically ventilated. An inoculum of *P. aeruginosa* (strain PA01) was instilled into the oropharynx at 1 hour and 8 hours post-intubation. The animals were terminated at 78 hours.

Results Pneumonia was evaluated based on macroscopic grading and microbiological (bacterial count) findings. We were able to maintain anaesthetic, haemodynamic and respiratory support for the study duration of 78 hours. A monobacterial pulmonary infection was established in four out of five animals. Administration of ceftriaxone 1 g daily effectively suppressed all other bacteria. This allowed proliferation of the single strain *P. aeruginosa* (PA01) we had inoculated with no culture of other organisms.

Conclusions Over a short period of time we were able to reproduce a monoculture ventilator-associated pneumonia in a significant percentage of animals. We successfully developed an animal ICU model that we were able to sustain for 78 hours. This canine model of *P. aeruginosa* (PA01) ventilator-associated pneumonia is suitable for the application of molecular techniques such as signature-tagged mutagenesis, differential fluorescence induction, and *in vivo* expression technology.

P97

Decrease in intravenous antibiotic use with adjunctive aerosolized amikacin treatment in intubated mechanically ventilated patients with Gram-negative pneumonia

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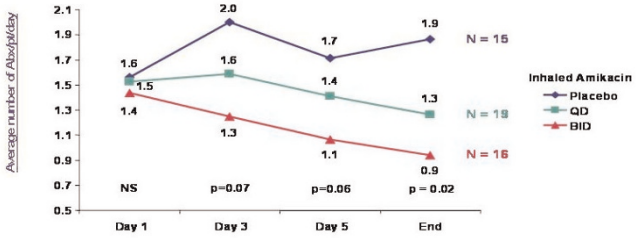
Introduction Aerosolized antibiotics may increase lung concentration, reducing the need for i.v. antibiotics. We evaluated

Figure 1 (abstract P97)



safety and i.v. antibiotic use with inhaled amikacin (AMK) during adjunctive treatment of intubated patients with Gram-negative pneumonia.

Methods A double-blind, placebo-controlled, study of aerosol AMK delivered via the Pulmonary Drug Delivery System (PDDS®; Nektar Therapeutics) in ventilated patients with Gram-negative pneumonia as an adjunctive to i.v. therapy per ATS guidelines. Patients were randomized to receive aerosol containing 400 mg AMK daily with placebo (normal saline) 12 hours later, 400 mg AMK twice daily or placebo twice daily. The i.v. antibiotics (agent and duration) were determined by the attending physician. The AMK peak serum concentration, trough concentrations and tracheal aspirates were drawn.

Results The mean number of i.v. antibiotics at the end of the study (mean 7 days) were two times greater with placebo than with twice-daily AMK ($P < 0.02$) (Figure 1). For daily and twice-daily AMK, the serum C_{max} were 1.3 and 1.8 μg/ml (respectively) on day 1, and 2.3 and 3.2 μg/ml on day 3. Mean trough levels were 0.87 and 1.49 μg/ml. Tracheal aspirate levels (mean) on day 3 were 6.9 mg/ml (daily) and 16.2 mg/ml (twice daily). Aerosol AMK was well tolerated with no difference in adverse events across treatment groups.

Conclusion Repeated doses of adjunctive inhaled AMK to mechanically ventilated patients with Gram-negative pneumonia was safe, well tolerated, and associated with less i.v. antibiotic use than placebo.

P98

Management of an outbreak of multiresistant *Acinetobacter baumanii* infection in a surgical intensive care unit

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The first report of multiresistant *Acinetobacter baumanii* (MRAB) was published in 1994. We report about an outbreak sensitive to Polimyxin only. In June 2006 a German holidaymaker (male, 70 years old; patient 1) in Greece felt dyspnea, thoracic pain and fever. He went to a hospital in Crete. CT indicated left-sided pleural empyema, mediastinal emphysema, pericardial effusion and pneumonia. Rapid deterioration lead to septic shock with need for mechanical ventilation. He came to our ICU (15 beds and six IMC beds) via air transport. Endoscopy showed esophagus perforation with need for operation and endoscopic stenting. Several BALs and a central venous catheter from the beginning showed MRAB with intermediate susceptibility to meropenem/aminoglycosides only. The patient received meropenem and gentamycin at first. Despite isolation, MRAB spread over and infected eight more patients in separate rooms and different sections of the ICU 32 days later. Further transmission occurred within a few days: three male patients with multiple trauma (42, 20, and 62 years old; patients 2, 3, and 4), cardia carcinoma (female, 66 years old; patient 5), necrotizing pancreatitis (female, 78 years old; patient 6), splenomegaly owing to polycythaemia vera (male, 74 years old; patient 7 – MRAB diagnosis postmortem), rectal carcinoma (female, 76 years old; patient 8 – isolation because of MRSA infection even before) and respiratory failure after gastric banding (female, 41 years; patient 9). All patients suffered from septic shock with high fever, needed high volume replacement and catecholamines several times and prolonged mechanical ventilation. MRAB was isolated in the tracheal secretion or BAL in all patients, in abdominal drainage (patient 6), and in central venous catheter (patient 5). Environmental investigations showed no problematic circumstances. Colistin i.v. is not available in Germany so it had to be procured from the USA, which caused a delay of treatment for a few days. Another delay occurred because of the rapid growing number of patients who needed Colistin. Patients were treated with an adjusted dosage for 16 days.

All patients of the ICU were isolated to avoid new infections as a precaution. After convalescence of two patients, all MRAB patients were moved to the IMC, which was converted to an ICU for this period, to isolate infected patients from uninfected. Three out of nine patients died.

All these laborious measures with a great expenditure of logistics worked well; no further transmissions were observed.

P99

Multidrug-resistant *Acinetobacter baumannii* susceptible only to colistin outbreak in a cardiac surgical intensive care unit

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Objectives Gram-negative bacilli including multidrug-resistant *Acinetobacter baumannii* (MDR-AB) are responsible for severe ICU-acquired infections, mainly pneumonia and bacteraemia. The aim of this study was to determine the incidence and mortality of this multiresistant strain of *Acinetobacter* in patients undergoing cardiac surgery, to elucidate the effectiveness of treatment with colistin and to identify whether additional measures were able to prevent and control the dissemination of MDR-AB isolates in our institution.

Methods A total of 1,451 patients attended the surgical ICU (SICU) after cardiovascular surgery from 1 September 2005 to 31 August 2006. We reviewed the prophylactic measures of the SICU and tried to identify epidemiological links between MDR-AB-infected patients. We implemented a two-scale multiple program. Scale 1 included classical infection control measures (that is, strict contact and droplet isolation, surveillance of throat, nasal and anal flora for MDR pathogens on all patients transferred from other hospitals, separate nursing staff for each infected or colonized case and strict antibiotic policy), while Scale 2 referred to geographic isolation of MDR-AB cases with exclusive medical and nursing personnel, use of separate supplies and facilities and intense environmental surveillance.

Results Fifteen patients were infected by MDR-AB, of which 13 presented respiratory tract infection, one suffered deep surgical site infection and bacteraemia and one from catheter-related infection. They were all treated with intravenous and aerolized colistin in combination with rifampicin or ampicillin and sulbactam.

Despite significant '*in vitro*' activity of colistin against this virulent organism and its acceptable safety profile, results were discouraging as only 13% survived. In fact, cure or clinical improvement was observed only in four patients (27%) while 11 patients (73%) developed sepsis and multiple organ failure.
Scale 1 measures were implemented for the whole 12-month period while Scale 2 for two separate 3-week periods. Following this infection control strategy we achieved intermittent eradication of the pathogen during a 12-month period with continuous function of the SICU.
Conclusions Increasing prevalence of MDR-AB in ICU patients demands installation of strict screening and contact precautions. Due to significant mortality of MDR-AB-infected patients, additional measurements like geographic isolation of all positive cases, exclusive medical and nursing personnel, use of separate supplies and facilities and intense environmental surveillance is highly recommended.

P100

Hypercalcaemia resulting from the use of tigecycline in the treatment of multidrug-resistant *Acinetobacter* in patients with multiorgan failure

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Introduction Tigecycline (Wyeth) is a new glycylcycline antimicrobial that has been used in the treatment of deep-seated multidrug-resistant *Acinetobacter* (MDRA) infections. Unexpected changes in routine hematology or serum chemistry have not been reported.
Methods All patients were managed within the liver ICU and received standard care. Laboratory data were collected daily and entered onto a specialist database. MDRA-positive cultures from blood, bronchoalveolar lavage, drain fluid or samples taken at laparotomy in the context of systemic inflammatory response syndrome resulted in the initiation of tigecycline 100 mg i.v. followed by 50 mg i.v. 12 hourly.
Results Eleven patients received tigecycline treatment for MDRA infections (seven male). Ten patients had a single course whilst one patient had three courses. Underlying disease states were necrotising pancreatitis (one), polytrauma (one), post hepatectomy (one), acute and acute on chronic liver failure (four), and post-orthotopic liver transplant (four). The median duration of treatment was 9 days (range 4–23 days); courses <7 days were because of patient death (2/11). The mean APACHE II score at initiation of therapy was 18 (range 13–26). Four out of 11 survived to ICU discharge and 3/11 to hospital discharge. Tigecycline was well tolerated but increases in corrected calcium were observed in 9/11 patients. The patient that received three courses of treatment had elevations in corrected calcium after each course. For the 11 patients, the mean corrected calcium before treatment with tigecycline was 2.41 mmol/l. The mean corrected calcium on finishing the course increased to 2.59 mmol/l ($P = 0.012$). There was no correlation between duration of treatment with tigecycline and degree of change in the corrected calcium level ($r = 0.08$). Hypercalcaemia resolved on discontinuation of the drug; 7/11 survived >7 days after treatment and had a mean corrected calcium of 2.46 mmol/l, which was not significantly different from pretreatment levels ($P = 0.94$).
Conclusion Tigecycline is well tolerated but appears to be associated with an elevated corrected calcium in critically ill patients. This returns to baseline values on discontinuation of the drug.

P101

A pharmacokinetic basis for improving therapeutic outcomes of aminoglycoside therapy during continuous venovenous haemodiafiltration

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Introduction The objective of this study was to quantify the impact of continuous venovenous haemodiafiltration (CVVHDF) on aminoglycoside pharmacokinetics and to suggest dosing strategies to improve therapeutic outcomes for these drugs in critically ill patients treated with CVVHDF. There has been limited published data on aminoglycoside pharmacokinetics during CRRT. This data deficit had led to subtherapeutic dosing, identified by a retrospective evaluation of amikacin and gentamicin serum concentrations, in patients treated with CVVHDF, undertaken as part of this research.
Methods A prospective pharmacokinetic evaluation of aminoglycoside pharmacokinetics during CVVHDF was undertaken. Pharmacokinetic profiles of once-daily doses of intravenous amikacin and gentamicin were obtained from blood and dialysate/ultrafiltrate samples for 12 critically ill patients treated with CVVHDF using varying flow rates (1 l/hour dialysate plus 2 l/hour filtration fluid or 2 l/hour dialysate plus 2 l/hour filtration fluid, extracorporeal blood flow 200 ml/min). Drug concentrations were measured using an immunoassay.
Results The mean clearance of gentamicin due to CVVHDF was 2.3 ± 0.3 l/hour (82.1 ± 11.3% of total body clearance (TBC)). The sieving coefficient (SC) was 0.85 ± 0.05. The CVVHDF clearance of amikacin was 2.8 ± 0.5 l/hour (93.0 ± 7.8% TBC). The SC for amikacin was 0.88 ± 0.06. The difference in gentamicin clearance versus amikacin clearance reflects differences in CVVHDF conditions. The mean effluent flow rate among the patient sample treated with gentamicin was 2.7 l/hour compared with 3.5 l/hour for amikacin. There was a strong correlation between creatinine clearance by the filter and measured drug clearance ($P < 0.001$). Individual patient estimates of aminoglycoside pharmacokinetic parameters (k, Vd) obtained during CVVHDF were used to allow appropriate dosage adjustment. Individualized pharmacokinetic–pharmacodynamic goals (e.g. Cpmax/MIC ratio) were used as indicators of adequate aminoglycoside dosing. The mean gentamicin and amikacin half-lives (approximately 8 hours) during CVVHDF therapy were far shorter than those previously reported in the literature for less efficient forms of renal replacement therapy. Failure to adjust for increased aminoglycoside clearance capacity due to CVVHDF carries a risk of subtherapeutic dosing and therapy failure.
Conclusion Dosing strategies on the basis of pharmacokinetic analysis of serum drug concentrations, effluent fluid drug concentrations and CVVHDF conditions improved therapeutic outcomes for aminoglycoside drug therapy.

P102

An *in vitro* study of elimination of oseltamivir carboxylate by haemofiltration

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Introduction Oseltamivir is the drug of choice for treatment of avian influenza A/H5N1 infection. One-quarter of patients with

influenza A/H5N1 develop acute renal failure. A proportion will require haemofiltration. There are no data to determine the elimination of oseltamivir carboxylate (the active metabolite) by haemofiltration. An *in vitro* study to determine elimination by measuring the adsorption and sieving coefficient of oseltamivir carboxylate using two haemofilter types was undertaken.

Methods An *in vitro* one-compartment model of continuous veno-venous haemofiltration was used. In phase 1 oseltamivir carboxylate adsorption to the haemofilter and circuit was studied by circulating a blood–crystalloid mixture containing clinically relevant concentrations of oseltamivir carboxylate through a haemofilter circuit and returning the ultrafiltrate to the mixing chamber. In phase 2 the ultrafiltrate was removed and replaced with a bicarbonate-based fluid to enable calculation of the sieving coefficient. The study was repeated 10 times with two haemofilter types: polyamide and polyacrylonitrile (PAN). Finally, oseltamivir carboxylate was added to the blood–crystalloid mixture without circulation through the circuit to determine its stability in solution. Blood samples collected were assayed by HPLC-MS/MS.

Results Oseltamivir carboxylate remained stable in solution (mean percentage change from baseline at 30 min: +3.97%, at 60 min: +1.91%, at 90 min: +2.36%). The mean ± SD initial oseltamivir carboxylate concentrations for the PAN (346 ± 85 μg/l) and polyamide (453 ± 185 μg/l) showed no significant difference. The mean ± SD adsorption at 90 min was 58.18 ± 17.84 μg for PAN and 75.22 ± 36.88 μg for polyamide haemofilters. There was no statistical difference in adsorption between the haemofilters. The initial drug concentration was a significant predictor of adsorption ($r^2 = 0.734$). The mean ± SD sieving coefficient of oseltamivir carboxylate for PAN (1.06 ± 0.04) and polyamide (1.03 ± 0.06) haemofilters showed no statistical difference between the haemofilters.

Conclusions Total adsorption is low and unlikely to be of clinical significance. Adsorption and the sieving coefficient are independent of the type of haemofilter membrane. The sieving coefficient of oseltamivir carboxylate is 1, therefore clearance during haemofiltration can be estimated from the ultrafiltration rate.

P103

A post-authorization survey to evaluate plasma concentrations of teicoplanin in adult hospitalized patients treated for sepsis in Gauteng, South Africa

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Objective This study measured and analyzed plasma concentrations of teicoplanin in patients >18 years in the first 4 days of administration.

Methods This was an open-label, multicentre, observational study in patients receiving teicoplanin for suspected or diagnosed Gram-positive infection. Data collection included demographics, method of administration, loading and maintenance doses, creatinine and adverse events. Trough and peak concentrations were determined 15 minutes prior to drug administration and 60 minutes after. Serum was separated and stored at −20°C until analysis. Levels were determined with an Abbott TDx®/FLx® analyzer and Seradyn Teicoplanin Innofluor assay kits. Seradyn internal teicoplanin controls were run within and between each batch. Mean trough and peak plasma levels were calculated for 4 days of therapy.

Results Seventy-four patients with complete records were analyzed and whilst all patients received an 800 mg loading dose on day 1, 40 received 400 mg twice daily thereafter (BD group) and 34 once daily (OD group), for nosocomial pneumonia ($n = 14$), skin and soft tissue infection (burn and nonburn including diabetic foot) ($n = 13$), bacteraemia ($n = 10$), intra-abdominal infection ($n = 8$), bone and joint infection ($n = 6$) and as pre-emptive therapy for severe trauma ($n = 13$). In the OD group, mean trough levels remained at 9.64 μg/ml from days 2 to 4 and peak levels remained at a mean of 24.84 μg/ml. In the BD group, mean trough levels increased by 5.65 μg/ml/24 hours to 21.8 μg/ml by day 4; the mean peak level increased by 5.06 μg/ml/24 hours to 43.89 μg/ml by day 4.

Conclusion Higher trough levels of glycopeptides (15–20 μg/ml) are targeted to improve efficacy and reduce resistance development. In the OD group the conventional target of 10 μg/ml was achieved, whilst in the BD arm 20 μg/ml was exceeded for 60% of the time by day 2 and 100% by day 4. BD dosing is recommended for most patients with severe infections, particularly those that are critically ill. No premature discontinuations or adverse events were reported during the study.

P104

Linezolid in the treatment of HIV-infected patients with complicated skin and soft tissue infections

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Introduction The incidence of HIV-infected patients with complicated skin and soft tissue infections has risen. Because of advanced immune suppression, slower responses to antibacterial treatment, and increased risk of bacteraemia relative to noninfected patients, the choice of initial appropriate empiric antibacterial therapy is an important aspect of care for HIV-infected patients. However, in recent years a dramatic increase of the resistance among Staphylococci to all classes of antimicrobial agents, including glycopeptides, has been reported.

Patients and methods We studied 146 patients with skin and soft tissue infections co-infected by HIV and 72 noninfected patients with soft tissue infections aged 18–45 years. All of the patients underwent operations aimed at surgical removal of the dead tissues and pus and received different combinations of antibacterial agents. Twenty-three patients after adequate surgery received Linezolid in doses of 600 mg twice a day intravenously during 3–4 days with oral follow-up of 600 mg twice a day.

Results The most frequent pathogens are Staphylococci in both groups of patients with soft tissue infections: 56% was noted among the noninfected patients and 61% among the HIV-infected patients. MRSA was identified in 30% of Staphylococci in HIV-infected patients. Among the patients receiving Linezolid, MRSA was identified in nine cases; in two cases vancomycin-intermediate *S. aureus* strains, and in one case vancomycin-resistant *S. aureus* strain. In three cases we revealed Staphylococcus bacteraemia, in one case MRSA bacteraemia in patient with retroperitoneal phlegmon.

A statistical difference was identified in duration of high temperature, purulence and wound healing in comparison with patients receiving different combinations of antibacterial agents. All patients receiving Linezolid were discharged from the hospital. The length of stay was 17 ± 1.67 days in comparison with patients receiving other antibacterial agents (from 19.52 ± 1.37 to 20.3 ± 1.46 days). The length of stay in hospital among the noninfected patients with soft tissue infection was 9.5 days. Modification of antibacterial treatment was not required in the group of patients

receiving Linezolid. No significant laboratory abnormalities and side effects were noted. We did not reveal statistical differences in the platelet count in group of patients receiving Linezolid (5 days after operation 213 ± 26.0/mm^3) in comparison with the group receiving other antibacterial agents (256 ± 32/mm^3). Thrompocytopenia is characterized to HIV-infected patients, but did not deteriorate in patients receiving Linezolid

Conclusion Linezolid in the complex treatment of HIV-infected patients with complicated skin and soft tissue infections may improve the results of therapy and may be used for initial empirical intravenous-to-oral antibacterial therapy.

P105

A clinico-microbiological study of extended spectrum β-lactamases in the intensive care unit

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Introduction Extended spectrum β-lactamase (ESBL) producing organisms are emerging as common nosocomial pathogens in the ICU worldwide. Early detection and prevention of spread is the primary measure to overcome the challenge posed by these difficult to treat ESBL infections. The aim of this study was to find the incidence, risk factors and microbiological and clinical outcome of patients infected with ESBL producing *Escherichia coli* and Klebsiellae in the ICU of a tertiary care cardiac center in India.

Methods A prospective, observational, case–control study of 150 patients was conducted from August 2004 to July 2005. ESBL testing was performed by the phenotypic confirmatory disc diffusion method. Clinical data and risk factors for ESBL acquisition were analysed as well as the antimicrobial therapy, and clinical and microbiological outcomes were studied.

Results A high incidence of ESBL producing *E. coli* and Klebsiellae was observed (85.8%). Meropenem (9.3%) and imipenem (2.8%) resistance in the ESBL producers was seen. On multivariate analysis with logistic regression, a central venous catheter was an independent risk factor for ESBL acquisition ($P = 0.01$, OR 3.55, 95% CI 1.4–9.02). The median ICU length of stay was 3.5 days and 3 days in the ESBL and non-ESBL groups, respectively. The overall mortality was 13.28% and 13.6% in the two groups, respectively. Microbiological outcomes were similar to clinical outcome, with 83.6% microbiologic success rate among ESBL producers.

Conclusion ESBL producing *E. coli* and Klebsiellae are problematic pathogens in our ICUs. Emergence of carbapenem resistance is of serious concern. Stringent infection control practices such as aseptic insertion and proper handling of central lines within the ICU should be followed by all.

P106

Impact of antibiotic utilization measures on acquisition rate of extended spectrum β-lactamase enzymes producing bacteria

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Introduction Antibiotic resistance patterns are continually changing; a new problem has been the emergence of Gram-negative bacteria, primarily *Escherichia coli* and *Klebsiellae pneumoniae*, producing extended spectrum β-lactamase enzymes (ESBL). Antibiotic use measures are presumably the most important intervention in preventing their clonal outbreak, and the risk factors for ESBL include intensive antibiotic exposure (especially third-generation cephalosporin monotherapy). The present study was performed to determine the impact of using piperacillin/tazobactum in reducing the acquisition rate of ESBL producing Gram-negative bacteria in the ICU.

Methods This open-label, prospective study was carried out in 140 adult patients admitted to the ICU over a period of 9 months, and was divided into two phases. Phase I (pre-intervention phase, 0–3 months): upon admission to the ICU, besides standard investigations, additional rectal swab cultures were taken for detection of ESBL within and after 48 hours of admission, and were repeated every 7 days of the stay in the ICU. Routinely prescribed antibiotics were allowed. Phase II (intervention phase, 4–9 months): this was subdivided into (a) first 3 months (4–6 months): piperacillin/tazobactum was the primary antibiotic used (more than 50% replacement of cephalosporins), and (b) last 3 months (7–9 months): here again, rectal swab cultures were taken and piperacillin/tazobactum was the primary antibiotic used. McNemar's test and Fisher's exact test were used for statistical analysis.

Results Eighty-five patients in phase I and 55 patients in phase II were enrolled. Third-generation cephalosporins were the primary antibiotic in 75.2% of cases in phase I and in 1.8% of cases in phase II ($P < 0.001$). The incidence of ESBL was 62.3% in phase I and it came down to 34.5% in intervention phase II ($P < 0.01$).

Conclusion Data from this intervention study support the concept that third-generation cephalosporins are of substantial importance in the emergence of ESBL; by decreasing the level of third-generation cephalosporin use and increasing the piperacillin/tazobactum use, their was a notable reduction in the acquisition rate of ESBL producing *E. coli*.

P107

The contamination by *Staphylococcus epidermidis* in the intensive care unit

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Introduction The most important way to prevent infections in the ICU is to respect asepsis during the numerous invasive procedures to which patients are exposed (central venous catheter, urinary catheter, orotracheal tube (OTT), fibrobronchoscopy (FOB), surgical drainages, patients nursing, surgical medications).

Methods The contaminations from *Staphylococcus epidermidis* have been valued in main infection centres on 951 patients admitted to our ICU for more than 72 hours from 1996 to 2005. From 2000, rigid asepsis protocols have been introduced for the cleansing of staff hands with the use of disinfectants such as Clorexidina and alcoholic gel.

Results From 1996 to 2005 the percentage of contamination from *S. epidermidis* has been 24.7% (22% in respiratory tracts, 8% in the urinary system, 41% in central venous catheter, 19% in the blood, 10% in other places). From 2000 to 2005 there has been a sensible reduction of 3%.

Conclusion The introduction in the last 5 years of strict protocols in order to control asepsis in our ICU, combined with the use of Clorexidina and alcoholic gel, have drastically reduced the contamination from *S. epidermidis*.

P108

Colonization and infection by MRSA in critically ill patients

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Objective To determine the incidence of colonization and infection by MRSA in critically ill patients.
Methods A prospective study during 30 months of the patients admitted to the ICU for 24 hours or more. Throat swab, tracheal aspirate and urine were taken on admission and twice weekly. The colonization and infection by MRSA were registered. The infections were diagnosed according to CDC criteria. The infections were classified based on throat flora as: primary endogenous (PE) when they were caused by germs that were already colonizing the throat on the ICU admission; secondary endogenous (SE) when they were caused by germs that were not colonizing the throat on the ICU admission but were acquired during the stay in ICU; or exogenous (EX) when they were caused by germs that were not colonizing the throat. The infections were classified based on the onset moment: early onset (EO) were those developed during the first 4 days of the ICU stay; and late onset (LO) were those developed 5 days after ICU admission.
Results Were admitted 1,582 patients, 953 males (60.24%). The mean age was 57.91 ± 18.83 years. The mean APACHE II score was 13.95 ± 8.93. Admission diagnoses were: 737 (46.59%) heart surgery, 189 cardiological (11.95%), 196 neurologic (12.29%), 185 trauma (11.69%), 120 respiratory (7.59%), 104 digestive (6.57%) and 51 intoxication (3.22%). Mortality was 14.79% (234 patients). A total of 36 patients had colonization by MRSA, two patients at ICU admission and 34 patients during the ICU stay. We documented 24 infections caused by MRSA (four EO and 20 LO; zero PE, 21 SE and three EX): 18 pneumonias (three EO and 15 LO; zero PE, 15 SE and three EX), three primary bacteremias (one EO and two LO; three SE), two surgical wound infections (two LO and SE) and one pressure sore infection (one LO and SE). Death occurred in 7/24 patients (29.17%) with infection caused by MRSA: 6/18 (33.33%) pneumonias, 1/3 (33.33%) primary bacteremias and 0/3 other infections.
Conclusions In our series, most of the infections caused by MRSA were pneumonias, had a late onset and were secondary endogenous.

P109

Impact of an MRSA search and destroy policy in a tertiary care emergency department

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Introduction An emergency department (ED) is a major hospital entrance and its case mix consists of patients at high risk of both introducing and acquiring infections. Alerted by the rise of hospital-acquired MRSA infections, the ED of a teaching hospital set up an ED infection control (IC) programme. The programme and its impact are discussed.
Methods The campaign consisted of the appliance of a proactive MRSA admission screening protocol, selective contact isolation (quarantine) and improving hand hygiene (HH). The MRSA admission screening strategy took into account past medical history or actual suspicion of MRSA carriage, transfers from other hospitals and long-term care facilities and admission of hospitalised patients to the ED for upgrading of care. According to their critical illness status, some patients were subject to quarantine. Improving HH was achieved by promoting alcohol-based hand disinfection, refraining all health care workers (HCW) from wearing hand jewellery or artificial fingernails, supplying HCW with clip watches and by developing promotional material. Education of HCW regarding principles and techniques of HH was provided by the IC department, supervised by link persons selected among medical, nursing and domestic staff. The number of new hospital-acquired MRSA infections per 1,000 admissions was recorded. Compliance to HH was measured by observation, microbiological analysis of total counts of colony-forming units on fingerprints, and by monitoring the consumption of hand-rub solutions (HH moments per patient-care day).
Results A selective MRSA admission screening policy increased the carrier detection rate up to 15%, compared with 1–2% in our preoperative outpatient clinic. The observed compliance to HH increased from 49% to 79% and consumption of hand-rub solution from 6 to 33 l per 1,000 patient-days. The number of HH moments increased from 19 to 47. Total counts of colony-forming units less than 50 improved from 39% of the analyses to 55%. Concomitantly, a decrease in MRSA attack rate from six to one new case per 1,000 patient-days was seen.
Conclusion An ED tailored selective MRSA screening and contact isolation protocol and a change in HH behaviour in the ED have mainly contributed to a decrease of the MRSA attack rates in our hospital far below the national rate.

P110

Candida airway colonization is associated with worse outcomes

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Introduction *Candida* airway colonization is common in mechanically ventilated ICU patients. Its significance and impact on outcomes are not well defined. We aimed to describe *Candida* airway colonization and assess clinical outcomes of patients with a clinical suspicion of ventilator-associated pneumonia (VAP) colonized with *Candida*.
Methods A retrospective post-hoc analysis of the prospective, multicentre VAP study, which enrolled patients with a clinical suspicion of VAP, admitted to an ICU for >96 hours and on mechanical ventilation (MV) for >48 hours. Airway cultures were done on randomization. Patients with positive *Candida* cultures from other sites were excluded. The remaining patients were divided into two groups according to their *Candida* airway culture status. Demographics, admission diagnosis, comorbidities, PaO_2/FiO_2 ratio and APACHE II score were recorded at randomization. The length of MV, ICU and hospital stay were compared, as well as hospital, ICU and 28-day mortality. Appropriate parametric statistical tests were applied according to data.
Results Of the 739 patients enrolled in the VAP study, 639 were included for analysis: 114 had *Candida* airway colonization (C) and 525 did not (NC). No significant differences were noted in demographics and APACHE II score (20 ± 6 vs 20 ± 6, $P = 0.37$) except more frequent admission for sepsis (7.0% vs 2.1%, $P = 0.005$) and respiratory conditions (21.9% vs 14.3%, $P = 0.04$) in group C. More colonized patients were on antibiotics at randomization (81.6% vs 56.7%, $P < 0.001$). A trend for increased

ICU (21.1% vs 13.9%, $P = 0.06$) and 28-day mortality (23.7% vs 16.4%, $P = 0.08$) and a significant difference in hospital mortality (34.2% vs 21.1%, $P = 0.003$) was observed in group C. A trend was found for increased median length of ICU stay (14.1 vs 11.6 days, $P = 0.07$) and duration of MV (10.9 vs 8.1, $P = 0.06$). Hospital stay was significantly longer (59.9 vs 38.6 days, $P = 0.006$) in group C.

Conclusion Respiratory tract *Candida* colonization in patients with clinical suspicion of VAP is associated with an increased burden of illness. Whether *Candida* colonization is responsible for worse outcomes remains to be established.

P111

Fungal infections in the intensive care unit? Another approach for defining a target group of patients who benefit from implementing preemptive antimycotic treatment

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Introduction *Candida* spp. is the third most common reason for sepsis in the ICU, not differentiating our results from the classic pattern of ICU-acquired infection. Prevention of sepsis development and identification of potentially modifiable risk factors are important goals in intensive care patents. Preemptive treatment of *Candida* sepsis accepted by some authors is defined as an early antifungal treatment given to patients with evidence of substantial colonization in the presence of multiple risk factors for *Candida* infection prior to establishing the diagnosis by cultures. Our aim was to form a focused group of patients with significant risk for *Candida* sepsis; to prove the feasibility and efficacy of our preemptive scheme for antimycotic treatment in order to reduce the risk of development of proved *Candida* sepsis.

Methods During a 2-year period (2005–2006), a study was performed in a 17-bed general ICU, divided into two phases: a case–control retrospective study in which controls comprising a representative subpopulation with severe bacterial sepsis were compared with cases (patients with *Candida* sepsis) with respect to multiple demographic and clinical factors in a univariate analysis; and a prospective phase creating a preemptive scheme based on results from the retrospective part followed by progressively implementing it among targeted patients.

Results Identified were 28 cases with *Candida* sepsis and 50 controls with severe bacterial sepsis with an all-cause mortality rate of 40.2%. The mortality rate for *Candida* sepsis was 46.4% with an attributable risk of 10/100 and was associated with a worse score of systemic injury (SAPS II = 51.7 ± 15.0), comparing with a mortality rate of 35.7% and SAPS II = 38.8 ± 13.3 for bacterial sepsis. *Candida* sepsis was always accompanied by concurrent bacterial sepsis (2.8 ± 1.1 microorganisms/patient isolated from blood cultures). Identified were risk factors with great significance in addition to already known ones: *Candida* colonization (OR = 3.4), diabetes (OR = 3.2), number of antibiotics used (OR = 2.9), a nothing per os regimen (OR = 2.63), ICU length of stay (OR = 1.97), length of antibiotic use (OR = 1.74), pancreatitis (OR = 1.7), shock at admission (OR = 1.54), ventilator days/ICU stay ratio (days)(OR = 1.4), multiple resistant bacterial strains (OR = 1.5). Patients with gastrointestinal surgery were at risk for development of early fungal sepsis – by the 10th day of admission – compared with the other clinical cases – by the 21st day of admission. The incidence rate of positive blood cultures for *Candida* in the group exposed to our scheme was calculated as 6.7% vs 18.5% in the control group.

Conclusions Based on our results, we accepted an algorithm for performing a preemptive therapy for which we observed clinical efficacy and which we considered indicated the following target groups of patients: with presence of clinical features of unresolving sepsis plus three defined risk factors (PPV > 70%) in a patient with length of ICU stay >20 days; lack of clinical improvement with combined antibiotic treatment against established bacterial strains; evidence of sepsis accompanied with multifocal *Candida* colonization of sterile body spaces. *Candida* colonization without risk factors requires continuous monitoring. The most important presumption to accept the preemptive strategy for a certain patient is to have a serious clinical conviction that there is an invasive fungal infection but it is still pending to be proved.

P112

Candida colonization and risk of candidemia in a cardiac surgical intensive care unit

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Introduction The aim of the study was to evaluate the incidence of *Candida* colonization in a cardiac surgical ICU, the predisposing risk factors and the impact of candidemia on outcome.

Methods In an effort to answer this question a prospective study was conducted among patients admitted to our 16-bed cardiac surgical intensive care unit ICU during 1 December 2004–30 October 2005. *Candida* colonization and candidemia were identified. Fungal colonization was defined as colonization index exceeding 0.20 (3 g, at least two samples of seven growing *Candida* spp.). Candidemia was defined as the isolation *Candida* spp. in at least one blood culture in a patient with temporally related clinical signs. The demographic characteristics of patients who developed candidemia, as well as the underlying disease and comorbidities, were recorded.

Results Over a 22-month period, 2,509 critically ill patients were evaluated. *Candida* spp. was isolated from any site in 141 patients (5.6%), while 10 patients (0.4%) presented ICU-acquired candidemia. They were all hospitalized for more than 7 days (range 7–34 days) in the ICU and had been exposed to broad-spectrum antibiotics (>3 agents). The mean age was 68 years (range 50–82 years) and the mean ICU stay 28 days. Candidemia appeared at a mean of 15.8 days after ICU admission. *Candida albicans* was the most common isolated pathogen. Candiduria in any count was detected in 12 patients but none of them experienced candidemia, while in seven patients *Candida* was isolated from urine and the respiratory tract. Six patients had major postoperative complications. Mortality due to candidemia was 60%. All patients received appropriate antifungal treatment. Prophylactic antifungal treatment was used in patients with multifocality colonization and in patients spending more than 7 days in the ICU after cardiac surgery.

Conclusion *C. albicans* is the most common fungal pathogen in our ICU. Seven percent of colonized patients developed candidemia. Major postoperative complications, excessive antibiotic exposure and acute renal failure seem to predispose to the development of candidemia. Patients with candidemia have high inhospital mortality, perhaps as a reflection of illness severity.

P113

Longitudinal evaluation of intensive care unit-related fluconazole use in Spain and Germany

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Objective To evaluate utilization patterns and outcomes associated with i.v. fluconazole therapy within ICUs in Spain and Germany.
Methods A prospective longitudinal observational study was conducted within 14 hospital ICUs in Spain and five in Germany. Patients on i.v. fluconazole therapy were included and were followed over one hospitalization period (admission until discharge). Data were collected during 2004, using electronic case report forms. Data included patient disease characteristics, patient risk status (APACHE scores), type of fluconazole therapy, drug-related adverse events, length of fluconazole therapy, and length of hospital stay. Switches in fluconazole therapy, dosing changes, additional concomitant antifungal therapy, overall mortality, and clinical outcomes were also evaluated. Logistic regression models determined univariate and multivariate associations with mortality.
Results A total of 303 patients were enrolled. Fluconazole was used initially as prophylaxis in 29 (9.6%) patients, preemptive therapy in 85 (28.1%) patients, empiric therapy in 140 (46.2%) patients and as definitive therapy in 49 (16.2%) patients. Thirty-six patients switched from fluconazole to a broader spectrum antifungal agent, and seven received a second concomitant antifungal drug. Reasons for switching therapies included lack of response due to suspected resistance, documented resistance or clinical reasons other than resistance. Thirty-two patients (10.6%) experienced fluconazole-related adverse events. The overall study mortality rate was 41.9% (127/303 patients). Mortality was significantly associated with switching i.v. treatment (odds ratio 5.0; 95% CI 2.3–11.1) and the presence of adverse events (odds ratio 4.1; 95% CI 1.8–9.2).
Conclusion The observational nature of this study precludes the establishment of any causality. This research merely documents the experiences of ICU patients who have been prescribed i.v. fluconazole therapy. Our results showed high mortality rates in the enrolled ICU patients. Patients developing adverse events and complications requiring a switch in fluconazole experienced worse outcomes

P114

Seropositivity incidence of anti-*Toxoplasma gondii* antibodies in critically ill intensive care unit patients

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Introduction *Toxoplasma gondii*, a worldwide-distributed parasite, could cause opportunistic infection with high mortality in immunosuppressive individuals. Its association with severe manifestations of immunosuppression has been known for several decades, and the occurrence of encephalitis and disseminated disease has since been observed in different clinical conditions such as lymphoreticular neoplasias, solid organ transplants, and mainly in patients with AIDS [1]. To our knowledge, the toxoplasmosis seropositivity rate in ICU patients who have critical illness induced immunosuppression is not yet investigated. We studied the seropositivity incidence of *T. gondii* in ICU patients by assessing IgG and IgM antibodies.
Materials and methods One hundred and three ICU patients with the mean age of 53.9 ± 13.9 years (51 men, 52 women) and 78 healthy volunteers with the mean age of 51.4 ± 9.2 years (39 men, 29 women) as a control group were included in the study. Anti-*T. gondii* IgG and IgM antibodies were determined by ELISA. Statistical analyses were done with the chi-square test and Kolmogorov–Smirnov one-sample test. $P < 0.05$ was considered as statistical significance.
Results *T. gondii* IgG antibodies were positive in 56.3% of ICU patients ($n = 58$) and in 24.3% of healthy volunteers ($n = 19$) ($P < 0.031$). IgM antibodies were positive in 13.8% of ICU patients ($n = 15$) and in 6.4% of healthy volunteers ($n = 5$); however, this difference could not reach statistical significance.
Conclusion The results of the study reveal that toxoplasma seropositivity is not uncommon in ICU patients. Therefore, to prevent the possibility of toxoplasmosis, seropositivity should be periodically assessed in critically ill immunocompromised ICU patients. It is clear that further studies are required to evaluate the effects of seropositivity on ICU outcome.
Reference
1. Ferreira MS, Borges AS: *Mem Inst Oswaldo Cruz* 2002, **97:**443-457.

P115

Consequences of cytomegalovirus reactivation in patients with severe sepsis

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Introduction Sepsis has been identified as a risk factor for cytomegalovirus (CMV) reactivation in nonimmunosuppressed patients in the ICU setting. Here we present a double-blinded prospective study assessing the consequences of CMV reactivation in non-immunosuppressed patients with severe sepsis.
Methods In three (two surgical, one medical) ICUs of a German university hospital, adult patients were screened for severe sepsis. Patients with recently occurring severe sepsis (<72 hours) were enrolled if their anti-CMV IgG titer was positive. The exclusion criterion was a manifest immunodeficiency. At enrollment the SAPS II was assessed. Patients were monitored for CMV reactivation weekly until death or hospital discharge by qualitative and quantitative PCR and virus culture. CMV reactivation was defined as CMV DNA detection or virus isolation. Patients with (CMV+) and without CMV reactivation (CMV–) were compared regarding inhospital mortality, duration of mechanical ventilation, length of stay (LOS) in the ICU and the hospital. Data were analysed using the Wilcoxon score rank sum test and chi-square test. The level of significance was set to 0.05.
Results CMV reactivation was observed in 38 out of 99 patients. Both groups (CMV+/CMV– patients) were quite similar in regard to gender and age at study enrollment. Interestingly, the median SAPS II was higher in CMV– patients (47 vs 42; $P < 0.013$). Accordingly, a lower mortality rate was anticipated for CMV+ patients compared with the CMV– group. Contrary to expectations, mortality did not differ between both groups (CMV+ 36.8% vs CMV– 42.6%; $P > 0.67$). This may point to a relatively

increased mortality in CMV+ patients, although CMV disease did not occur. There was a striking difference between the groups in respect to the period on ventilator: 21.5 days vs 8.0 days (median) in CMV+ and CMV– patients, respectively ($P < 0.005$). Similarly, CMV+ patients had a longer median LOS after enrollment either in the ICU (29.5 days vs 10 days, $P < 0.001$) and in the hospital (49 days vs 23 days, $P < 0.001$). This difference was assured when the analysis was restricted to survivors.
Conclusion Our data suggest that CMV reactivation leads to increased morbidity and treatment expenditure independently from CMV disease. Further analysis points at a crucial role of lung pathology due to CMV reactivation.

P116

The role of plasminogen activator inhibitor 1 measurement with endotoxin adsorption therapy (PMX-DHP) for postoperative septic shock patients

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Introduction A polymyxin B immobilized fiber column (PMX; Toray Industries Inc., Tokyo, Japan) was developed in Japan in 1994 and it has been used for treatment of endotoxemia or septic shock patients.
Materials and methods All patients received an urgent operation due to intra-abdominal infection. In 88 cases treated with a polymyxin B immobilized column through direct hemoperfusion (PMX-DHP), changes in hemodynamics, pulmonary oxygenation (PaO_2/FIO_2) and various mediators (IL-6, IL-8, IL-ra, plasminogen activator inhibitor 1 (PAI-1)) were examined before and after PMX-DHP, stratifying with the outcome (64 survivors and 24 who died). PMX-DHP was performed through a double lumen catheter (11.5 Fr), placed in the femoral vein or internal jugular vein, at a blood flow rate of 80 ml/min using nafamostat mesilate as an anticoagulant for 2 hours.
Results PMX-DHP significantly increased systemic arterial pressure and mean arterial pressure, with a greater increase in the survival group. Also, there appeared to be a trend for PaO_2/FIO_2 improvement as blood pressure increased. As the mechanism for improvement of pulmonary oxygenation by PMX-DHP has not been shown clearly, it remained to be examined further. PAI-1 values significantly decreased in the survivor group (from 436 ± 549 to 251 ± 283 ng/ml) immediately after PMX-DHP; also intracellular adhesion molecule-1 and endothelial leukocyte adhesion molecule-1 tended to decrease in both groups.
Discussion PAI-1 is elevated by endotoxin, thrombin and cytokines, and is an indicator of vascular endothelial cell activation. In septic dissminated intravascular coagulation from Gram-negative bacilli, a massive amount of PAI-1 is produced on vascular endothelial cells along with elevation of cytokine production and coagulation activity. In addition, PAI-1, one of the fibrinolysis inhibitory factors, plays an important role in regulating fibrinolysis by inhibiting tissue plasminogen activator, which converts plasminogen to active plasmin on fibrin, to block unnecessary fibrinolysis.
Conclusion The determination of PAI-1 may be a useful clinical parameter for predicting PMX-DHP efficacy.

P117

Mechanism and effectiveness of polymyxin B-immobilized fiber columns for removing mediators (HMBG-1, 2-arachidonoyl glycerol, anandamide, PAI-1, protein C and IL-6) in septic shock patients

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Introduction Septic shock remains a major cause of multiple organ failure with a high mortality rate. To remove an endotoxin in patient plasma, direct hemoperfusion (DHP) using a polymyxin B-immobilized fiber column (PMX; Toray Industries Inc., Tokyo Japan) was developed in Japan in 1994 and has since been used for the treatment of septic shock. The precise role of PMX is not clear.
Patients and methods We treated 27 septic shock patients using DHP-PMX. The patients were separated into two groups for analysis: those whose systolic blood pressure (SBP) increased by more than 30 mmHg immediately after DHP-PMX (15 cases), and those whose SBP did not increase by more than 30 mmHg after DHP-PMX (12 cases). Furthermore, the patients were separated into two other groups for analysis: those whose P/F ratio increased by more than 20% immediately after DHP-PMX (15 cases), and those whose P/F ratio did not increase by more 20% after DHP-PMX (12 cases). Mediators were measured at four points: before and after DHP-PMX, and 1 day and 3 days afterward.
Results The patient group consisted of 17 males and 10 females, 59.6 ± 12.7 years old. The average APACHE II score was 27.2 ± 9.1, and the average SOFA score was 11.7 ± 5.2 before DHP-PMX. Nineteen patients survived and eight died. When the changes in PAI-1, protein C, ATIII, IL-6 and high mobility group box protein 1 (HMGB-1) were compared between the groups, only the HMGB-1 levels had improved significantly in the SBP increased group ($P = 0.0125$). The SBP increased significantly after DHP-PMX in the HMGB-1-improved group ($P < 0.0001$). An improvement in the P/F ratio and a reduction in 2-arachidonoyl glycerol during DHP-PMX were significantly correlated ($P = 0.0184$).
Conclusion We showed that the circulation dynamics of septic shock patients can be improved by reducing HMGB-1 levels and that respiratory function can be improved by reducing 2-arachidonoyl glycerol levels using DHP-PMX.

P118

Characterization of the coupled plasma filtration–adsorption resin cartridge adsorptive capacity for cytokines and inflammatory mediators: adsorption profiles from septic patient plasma and *in vitro* endotoxin-stimulated whole blood

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Introduction Coupled plasma filtration–adsorption (CPFA) is an extracorporeal therapy that uses plasma filtration associated with an adsorbent cartridge and hemofiltration in postdilution to remove cytokines and inflammatory mediators associated with septic shock and severe sepsis. We evaluated the adsorptive capacity of the resin cartridge to remove various inflammatory mediators and cytokines *in vitro* and *ex vivo*.

Methods *In vitro* experiments included static and dynamic evaluations of resin binding. Whole human blood was stimulated with endotoxin for 4 hours at 37°C; or with the addition of added cytokines or toxins for evaluation. For static conditions, 4 ml plasma with 1 ml resin were incubated for up to 10 hours. Aliquots were withdrawn between 0 and 10 hours and cytokine inflammatory mediator and toxin adsorption were determined with standard ELISAs, multianalyte protein arrays, HPLC and diode array adsorption spectroscopy. Dynamic conditions involved defining the optimal linear velocity and evaluating the adsorption capacity under flow conditions. These experiments used a closed circuit consisting of a plasma filter and resin cartridge. Samples were taken from a blood port and immediately before and after the plasma cartridge. In addition, serum, pre-cartridge and post-cartridge plasma samples were also taken from septic patients undergoing CPFA.
Results Endotoxin-stimulated blood or samples from septic patients had high levels of cytokines and inflammatory mediators. The resin used in the CPFA adsorptive cartridge showed higher than 80% adsorption under both static and dynamic conditions for: IL-1α, IL-6, IL-8, MIP-1α and MIP-1β, TNFα, MCP, myoglobin. IL-6 appeared to be particularly adsorbed by the cartridge. Severe septic patients had great variability and often very high levels of IL-6 ranging from normal levels (50 pg/ml) up to 12,300 pg/ml. The mean of 10 patients treated before CPFA was 1,775 ± 3757 pg/ml, while post-session IL-6 was 995 ± 2178 pg/ml. The plasma levels before the cartridge ranged from 12 pg/ml to 1,750 pg/ml, while post-cartridge levels were below the level of detection.
Conclusions The resin in CPFA has a high adsorption capacity for several cytokines and mediators involved in severe sepsis and septic shock. Studies are currently ongoing to correlate cytokine reduction with clinically relevant improvements in these patients.

P119

Removing endocannabinoids and reducing oxidative stress with polymyxin-B-immobilized fibers in patients with septic shock

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Critical Care 2007, **11(Suppl 2):**P119 (doi: 10.1186/cc5279)

Introduction Arachidonylethanolamide (AEA) and 2-arachidonylglycerol (2-AG) are endocannabinoids involved in septic shock, and 8-epi prostaglandin F2α (F2-isoprostane) is a biomarker of oxidative stress. Because the antibiotic polymyxin-B binds to endotoxins and endocannabinoids, direct hemoperfusion therapy with polymyxin-B-immobilized fibers (PMX-DHP) decreases serum levels of endocannabinoids. To investigate the features of sepsis and to determine the proper usage of PMX-DHP, we compared perioperative changes in levels of endocannabinoids and F2-isoprostane in patients with septic shock
Methods Twenty-four patients with septic shock induced by peritonitis underwent laparotomy for drainage. Endocannabinoid absorption with PMX-DHP was examined in two groups of patients: patients in whom systolic arterial BP had increased more than 20 mmHg (BP elevation group; $n = 12$) and patients in whom BP did not increase or had increased no more than 20 mmHg (BP constant group; $n = 12$).
Results Levels of AEA did not change after PMX-DHP in the either the BP constant group or the BP elevation group, whereas levels of 2-AG decreased significantly after PMX-DHP in the BP elevation group but not in the BP constant group (Figure 1). F2-isoprostane gradually increased after PMX-DHP. On the other hand, levels of F2-isoprostane remained constant in the BP elevation group (Figure 2).

Figure 1 (abstract P119)

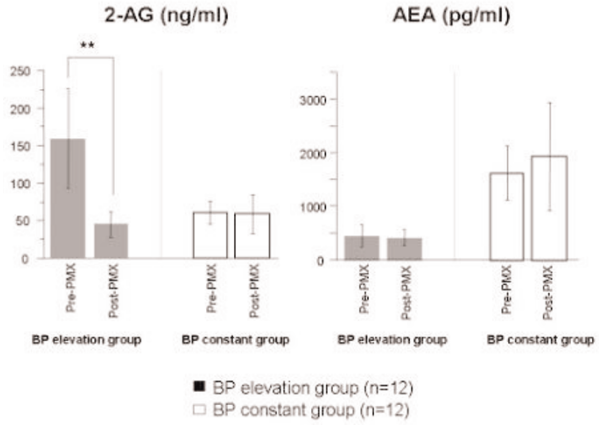
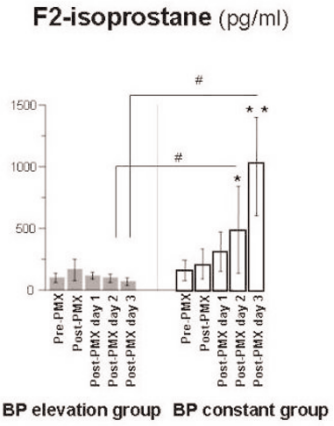


Figure 2 (abstract P119)



Conclusions Patients with septic shock are under considerable oxidative stress, and 2-AG plays an important role in the cardiovascular status of these patients. The removal of 2-AG by PMX-DHP benefits patients with septic shock by stabilizing cardiovascular status and decreasing long-term oxidative stress.

P120

Cytokines associated with insulin resistance in critically ill patients

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Introduction We examined the relationship between proinflammatory cytokines, adipocyte-derived adiponectin and hyperglycemia. Patients requiring long periods in the ICU have a relatively high mortality. Tight glucose control with insulin infusions has been shown to improve survival and prevent complications.
Methods A prospective, observational study at an academic ICU. A sequential sample was taken over a 2-month period. Ethics approval was obtained from the University Ethics Committee.

Baseline bloods for TNFα, IL-6, adiponectin (Adipo), total cholesterol (TC), triglycerides (TG), insulin, C-peptide (CPep) and cortisol (Cort) were collected on admission (D0). These were repeated on day 3 (D3), day 7 (D7) and discharge (D/C). Routine bloods ordered were also used. Data on the ICU charts were also used. No changes to ICU protocols were required. Of note, insulin infusions were started for blood glucose concentrations greater than 6 mmol/l. Exclusion criteria included all patients with diabetes mellitus, chronic renal failure and liver failure or cirrhosis.

Results Forty patients admitted to the ICU were enrolled and followed up to discharge. The median age was 35.5 years (minimum 18, maximum 66). The median APACHE II score was 10.5 (minimum 2, maximum 28) and the median duration was 6 days (minimum 1, maximum 43). D0, D3, D7 and D/C glucose concentrations did not differ (Kruskal–Wallis ANOVA, $P = 0.98$). TNFα peaked at D3 (4.9 pg/ml) and then started decreasing. Administered insulin (InsAd) accompanied the TNFα peak at D3 (32U) and then decreased. Adipo peaked at D7 (10,774 pg/ml) after the TNFα peak, which coincided with the TNFα decrease at D7 to 4.76 pg/ml. Endogenous insulin indicated by CPep peaked with Adipo at D7 (2.8 μg/l). TG levels increased in parallel with increasing TNFα from 0.7 mmol/l at D0 to 1.1 mmol/l at D3 and then declined. TC was lowest at D0 and increased up to D/C but remained relatively low. Table 1 shows several variables and their change over time from admission to discharge. Table 2 shows the correlations between these variables. Survivors had a lower median TNF than nonsurvivors (Mann–Whitney U test, $P = 0.066$).

Conclusion TNF contributes to increased insulin needs. TNF is known to cause insulin resistance. We have shown that TNF correlates inversely with Adipo. As Adipo increases, insulin needs are decreased (inverse correlation with InsAd). Also, TNF contributes to increase TG indicating increased free fatty acids (FFA) by lipolysis, which impairs glucose clearance. Adipo, an insulin sensitizing protein, is known to negatively regulate TNF levels as was indicated by our study. Adipo contributed to a decrease in TG indicating lower FFA and better glucose clearance. IL-6 at D/C also contributed to a higher glucose concentration at D/C. Increasing age contributed to lower Adipo levels at D/C, indicating lower insulin sensitivity. A higher BMI contributed to a higher glucose level at D0 and increased insulin needs at D0. Finally, a higher TNF level appears to be related to increased mortality

P121

The effectiveness of octreotide at different doses for sulfonylurea-induced hypoglycemia following overdose

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Objective The aim of the study was to investigate the effectiveness of octreotide at different doses in reducing the hypoglycemic attacks and the need for dextrose in treatment of refractory and recurrence hypoglycemia related to the toxicity of sulfonylurea.

Methods In the study, 40 New Zealand type of rabbits were used weighing between 2,500 and 3,000 g. The rabbits were randomly divided into four groups consisting of 10 animals. All the animals were given gliclazide 100 mg orally. For the treatment of hypoglycemic attacks in Group I, only 15 cm^3 50% dextrose (7.5 g) intravenously (i.v.) was used; in Group II, Group III and Group IV octreotide 25 μg, 50 μg and 100 μg single doses were used subcutaneously, respectively. Octreotide was given in Groups II and III and Group IV at the eighth hour (when hypoglycemic attacks onset). Groups II, III and IV were given an additional 15 cm^3 50% dextrose (7.5 g) i.v. infusion for each hypoglycemic attack developed. Following the toxic dose, animals were given the amount of dextrose used before and after octreotide administration and the number of hypoglycemic attacks were recorded.

Results There was a significant difference between Groups I, II, and IV in the number of hypoglycemic attacks and the number of dextrose requirement between 9 and 24 hours ($P = 0.001$). Groups receiving octreotide showed less hypoglycemic attacks and dextrose requirements than controls.

Conclusion Our experience suggests that octreotide may be used to reduce the number of refractory and recurrence hypoglycemic attacks developing due to overdose of sulfonylurea; large prospective studies would be needed to validate these findings.

Table 1 (abstract P120)

Changes in glucose, insulin, cytokines and lipids in the ICU over time

Day	Glucose	InsAd	TNF	Adipo	Cpep	TG	TC	IL-6
D0	6.13	8	3.49	4,413.82	1.8	0.7	2.15	337.01
D3	6.25	32	4.9	6,925.4	2.2	1.1	2.2	127.01
D7	6.79	20	4.76	10,774.25	2.8	1	2.5	32.17
D/C	5.87	0	4.11	8,288.6	2.5	1.3	2.8	46.95

Table 2 (abstract P120)

Relevant Spearman correlations between the parameters

A	B	*R*	*P*	A	B	*R*	*P*
TNF	Adipo	−0.59	0.000	TNF	Mortality	0.25	0.060
Adipo	InsAd	−0.46	0.005	ΔAdipo	LOS	0.45	0.004
TNF	TG	0.74	0.000	IL-6 D/C	Gluc D/C	0.34	0.042
Adipo	TG	−0.41	0.001	BMI	Gluc D0	0.39	0.012
TNF	Cortisol	−0.73	0.000	BMI	InsAd D0	0.31	0.053
Adipo	Cortisol	0.51	0.000	Adipo D/C	Age	−0.35	0.030
				Age	InsAd D/C	0.35	0.032

P122

Hyperglycemia and changes in osmolarity lead to an increase in IL-6 and IL-1β cytokine production of human peripheral blood mononuclear cells *in vitro*

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Introduction Acute hyperglycemia and insulin resistance are characteristics of metabolic and endocrine imbalances of critically ill patients and are subject to a substantial inflammatory response that is partly mediated by cytokines produced by peripheral blood mononuclear cells (PBMC). Treatment with intensive insulin therapy to keep patients normoglycemic has been shown to reduce inflammatory responses. It is unclear whether hyperglycemia, insulin or osmolarity changes exert direct effects on proinflammatory cytokines. We investigated the direct effects of these substances on cytokine production of PBMC *in vitro*.
Methods PBMC were isolated from peripheral blood of 10 healthy volunteers via Ficoll gradient. Cells were incubated for 3 hours at 37°C with/without low/high concentrations of glucose, mannitol, urea, insulin and stimulated with 0.5 ng/ml LPS. After 24 hours, concentrations of IL-6 and IL-1β were measured with an ELISA method.
Results Increasing concentrations of glucose, mannitol and urea resulted in a significant increase of IL-6 and IL-1β cytokine production. Insulin had no effect (Table 1).

Table 1 (abstract P122)

Substance	No supplementation	Low concentration	High concentration
Glucose	1,726	–	9,643
Insulin	609	555	636
Urea	2,056	3,421	3,835
Mannitol	367	–	3,269

Conclusion High concentrations of glucose, mannitol and urea lead to a significant increase in IL-6 and IL-1β cytokine production by PBMC *in vitro*. The most profound effect was seen with hyperglycemia. Besides hyperglycemia, also uremia and high osmolarity seem to augment inflammation. Insulin could not reverse the increase in inflammation. These findings may be relevant in explaining the beneficial effects of normoglycemia on the inflammatory response in critically ill patients.

P123

Insulin therapy inhibits poly(ADP-ribose)polymerase activation in endotoxin shock

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The nuclear enzyme poly(ADP-ribose) polymerase (PARP) is activated in various forms of circulatory shock. By triggering a cellular energetic dysfunction, and by promoting proinflammatory gene expression, PARP activation significantly contributes to the pathogenesis of shock. The activation of PARP is usually triggered by DNA strand breakage, which is typically the result of the overproduction of reactive oxidant species. In the present study we tested whether endotoxin-induced PARP activation and proinflammatory mediator production can be modified by insulin therapy. Rats subjected to bacterial lipopolysaccharide (LPS) with or without insulin pretreatment were studied. LPS-induced PARP activation in circulating leukocytes was measured by flow cytometry, and production of TNFα was measured by ELISA. LPS induced a significant hyperglycemic response, activated PARP in circulating leukocytes and induced the production of TNFα. Insulin treatment prevented the LPS-induced hyperglycemic response, blocked the activation of PARP and blunted the LPS-induced TNFα response. As hyperglycemia is known to induce the cellular formation of reactive species, we propose that PARP activation in endotoxin shock occurs as a result of hyperglycemia-induced reactive oxidant and free radical generation. The current findings may have significant implications in the context of the emerging concept of tight glycemic control for critically ill patients.

P124

Influence of diabetes and HbA1c on the course and outcome of sepsis in the intensive care unit

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Introduction It is an accepted opinion that patients with diabetes mellitus (DM) are at higher risk when treated for infections, although published data are lacking. Our recent research on non-ICU septic patients showed that admission HbA1c is in correlation with outcome. The aim was to evaluate the impact of DM on the course and outcome of patients with sepsis in ICU, as well as to evaluate the value of HbA1c as an outcome predictor in the ICU.
Methods In a prospective, 3-year observational study, patients with sepsis, severe sepsis and septic shock admitted to a medical ICU were included. Patients with DM were compared with nondiabetics in terms of course and outcome. HbA1c was measured for all patients with DM. Hospital mortality and length of stay (LOS) in the ICU and in hospital were the outcome measures. The incidence of organ failure, ARDS, hospital-acquired pneumonia (HAP) and ventilator-associated pneumonia (VAP) were used as indicators of the disease course. Nonparametric tests, multiple regression and logistic regression were used in statistical analyses.
Results Two hundred and twenty-nine patients with sepsis at admission (19.6% of all 1,169 ICU patients), 59 with DM, were included. Mortality in the ICU was 34.7%; the median ICU LOS was 8 (95% CI 7–9.3) days. Patient with DM, compared with nondiabetics, had higher mortality (38.9% vs 34.1%, $P = 0.60$) and longer ICU LOS (median 6 vs 10 days, $P < 0.001$), and higher incidence of renal failure, HAP, VAP. Surviving patients had significantly lower HbA1c levels (6.6 vs 9.6, $P = 0.001$). In a logistic regression, DM was found to be related to lethal outcome, together with APACHE II and SOFA scores. In multiple regression, DM related to LOS together with SOFA score and age. HbA1c was found to be independently related to ICU outcome together with SOFA score.
Conclusion The ratio of patients with DM among ICU patients with sepsis exceeds greatly the incidence of DM in the population. This emphasizes the risk they have. DM was associated with worse outcome, longer ICU and hospital LOS, and with higher incidence of complications. HbA1c was confirmed as an outcome predictor for ICU patients.

P125

Lipid metabolism and organ dysfunction in septic patients during intensive glycemic control

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Introduction Intensive glycemic control has been widely discussed in critical care patients. It remains unclear whether intensive insulin therapy also improves the prognosis of patients in a medical ICU, who often are more severely ill than are patients in a surgical ICU and have a higher risk of death. Recently, medical patients have been investigated, as a special group. We decided to study possible differences in lipid profile in septic shock patients during the first 72 hours and correlate it with different organ dysfunctions.
Methods A prospective, randomized, controlled study in a 12-bed medico-surgical ICU in a university hospital. Inclusion criteria: all consecutive patients admitted to the ICU with severe sepsis and or septic shock with onset in a maximum of 24 hours. Exclusion criteria: HIV patients, pregnancy, diagnosis of leptospirosis, age under 18, cancer patients. On admission, patients were randomly assigned to strict normalization of blood glucose levels (80–110 mg/dl) or to a conventional glycemic control (180–220 mg/dl) with the use of sealed envelopes. We collected laboratory tests at 0, 24, 48 and 72 hours after initiation. For statistical analysis we performed the Student *t* test.
Results We studied 58 patients with similar demographic data between the two groups. The increases in serum LDL ($P < 0.05$) and HDL (not significant) were different between groups. The mortality rate was the same but LDL and HDL had negative correlation with organ function among nonsurvivors.
Conclusions Targeting blood glucose levels to below 110 mg/dl with insulin therapy prevented morbidity, probably due to a better control of lipid metabolism, expressed as a more rapid serum LDL normalization and avoiding a greater decrease in serum HDL levels in the first 72 hours of septic shock.

Figure 1 (abstract P125)

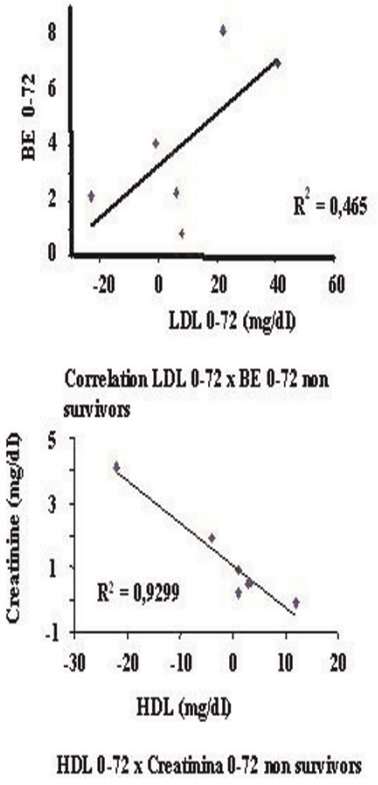
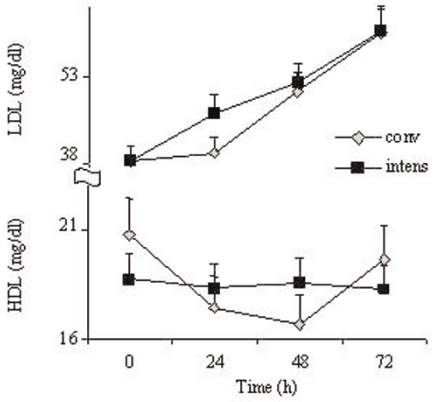


Figure 2 (abstract P125)



P126

Effect of intensive insulin therapy on coagulation and fibrinolysis of respiratory critically ill patients

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Critical Care 2007, **11(Suppl 2):**P126 (doi: 10.1186/cc5286)

Most intensive care deaths beyond the first few days of critical illness are attributable to nonresolving multiple organ failure (MOF), either due to or coinciding with sepsis. One of the mechanisms that is thought to contribute to the pathogenesis of MOF is microvascular thrombosis. Recently, we reported improved survival and prevention of MOF of critically ill patients with the use of intensive insulin therapy to maintain normoglycemia for at least several days [1,2]. We hypothesize that intensive insulin therapy also prevents severe coagulation abnormalities, thereby contributing to less organ failure and better survival.
We studied a subgroup of long-stay critically ill patients with a respiratory disease upon ICU admission, who had been enrolled in a randomized controlled trial evaluating the impact of intensive insulin therapy in medical ICU patients [2]. Plasma samples were analyzed for a panel of coagulation markers (prothrombin time, activated partial thromboplastin time, fibrinogen and D-dimer levels) that were used to assign points towards the International Society of Thrombosis and Haemostasis overt disseminate intravascular coagulation (DIC) score. Circulating plasma thrombin–antithrombin complexes and plasminogen inhibitor type 1 levels were also determined. As markers of inflammation, we measured circulating serum levels of several cytokines and CRP.

Mortality of intensive insulin-treated patients was lower than of conventionally treated patients for all classes of upon-admission DIC score, except for those patients with a DIC score of 6 or higher. There was no effect of insulin therapy on any of the fibrinolytic, coagulation or inflammatory parameters tested. The accuracy of the DIC score to predict mortality in this patient sample was only moderate and comparable with that of CRP and the SOFA score. Also, circulating plasminogen inhibitor type 1 or thrombin–antithrombin complexes levels did not correlate well with mortality or DIC score.

These findings indicate that the coagulation system did not play a key role in mediating the survival benefit of intensive insulin therapy.

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P127

Variable adsorption of insulin at catheter materials used in intensive care units: polyethylene vs polyurethane – possible cause for hypoglycemia during intensive insulin treatment?

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Critical Care 2007, **11(Suppl 2):**P127 (doi: 10.1186/cc5287)

Introduction Intensive insulin therapy reduces morbidity and mortality in postoperative critical care; however, this treatment also increases the risk of hypoglycemia. A possible cause for unstable blood glucose (BG) levels could be a variable adsorption of insulin at plastic material of infusion tubings. We evaluated *in vitro* and *in vivo* the adsorption of insulin at standard tubing materials (polyethylene (PE) and polyurethane (PU)) and the effects of this adsorption process on blood glucose levels.

Methods (1) *In vitro*, a standard perfusor syringe (Perfusor®; BBraun, Germany) was filled with 50 IE normal insulin (Actrapid®; NovoNordisk, Germany) dissolved in 50 ml saline 0.9%. The syringe was connected to PE or PU tubings (BBraun) and, at an infusion rate of 1 ml/hour, the insulin concentration in the syringe and at the end of the tubings was measured at hourly intervals for 5 hours and again after 24 hours by the Bradford protein assay. Insulin concentrations were compared using the Student *t* test. (2) In a prospective, double-blinded, cross-over study, approved by the ethics committee, 10 patients on the surgical ICU received insulin via PE or PU tubing each for 24 hours in random sequence. All blood BG values, total infused insulin solution volume, and critical care scores were documented and statistically analysed by the Wilcoxon test.

Results (1) The insulin concentration in all syringes was always >97% of the estimated value. The initial concentrations of insulin at the end of PE and PU tubings were lower than expected (23 ± 4% of anticipated concentration in the first 6 min). In PE, the concentration rose to 37 ± 2% and in PU to 78 ± 4% after 24 hours ($P < 0.0001$). (2) *In vivo* the mean BG values did not differ between PE and PU (PE 141 ± 17 mg/dl; PU 132 ± 23 mg/dl (not significant)). Severity of illness was not different between the groups: TISS 37 ± 5 (PE) vs 39 ± 5 (PU), SAPS 43 ± 13 (PE) vs 41 ± 15 (PU) on both days; neither were catecholamine doses and 24-hour fluid balance. However, significantly more insulin solution was infused in PE (66 ± 18 ml/24 hours) compared with PU (44 ± 15 ml/24 hours) ($P = 0.0015$).

Conclusion Infusion of insulin using PE and PU tubings leads to a relevant adsorption of the drug in both materials. Adsorption to PE is significantly higher compared with PU. Thus, a large variation of insulin application to the patient is possible if different tubing materials are used. Furthermore, variability of adsorption, a competitive adsorption with other drugs if insulin is not infused via a single line as well as changes of effective insulin application following routine change of tubings, may be one cause of unexpected hypoglycemia that can be deleterious to the patient.

P128

Hyperglycemia upon onset of nosocomial bloodstream infection adversely affects outcome in a mixed intensive care unit population

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Introduction Hyperglycemia in critically ill patients is frequently related to a hypermetabolic stress-response and has been associated with increased morbidity and mortality. The aim of this study was to assess the relationship between blood glucose levels and clinical outcome in a mixed cohort of critically ill patients with a nosocomial bloodstream infection (BSI).

Methods A retrospective observational cohort study was conducted including 130 adult patients with a microbiologically documented BSI admitted over a 2-year period (2003–2004) to the ICU. Blood glucose levels were evaluated from 1 day prior to onset of BSI (d–1) until 5 days after onset of BSI (d+5). The contribution of hyperglycemia, divided into three subgroups (≥150 mg/dl, ≥175 mg/dl, and ≥200 mg/dl, respectively), to in-hospital mortality was estimated by logistic regression.

Results The mean age of the study population was 54.7 ± 19.0 years. Inhospital mortality was 36.2%. Hyperglycemia (≥175 mg/dl and ≥200 mg/dl) was observed more often among the non-survivors. Over the seven study days, no differences were found in daily morning blood glucose levels between survivors ($n = 83$) and nonsurvivors ($n = 47$) (all $P > 0.05$). Although in the nonsurvivors the evolution of glycemia tended to be higher, this trend was not statistically significant compared with the survivors. Multivariate logistic regression revealed that age ($P = 0.022$), APACHE II score ($P = 0.003$), antibiotic resistance ($P = 0.001$), and hyperglycemia (≥200 mg/dl) upon onset of BSI ($P = 0.001$) were independently associated with inhospital mortality, whereas appropriate antimicrobial therapy ≤24 hours ($P = 0.016$) and previous history of diabetes ($P = 0.022$) were associated with better outcome.

Conclusion Trends of blood glucose levels were higher among nonsurvivors. Hyperglycemia (≥200 mg/dl) upon onset of nosocomial BSI adversely affects outcome in a heterogeneous ICU population.

P129

System for automated discontinuous venous blood withdrawal for glucose determination of patients in the intensive care unit

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Introduction Intensive insulin therapy to establish normoglycaemia reduces mortality and morbidity in critically ill patients. Frequent glucose monitoring is restricted in critically ill patients due to the

high workload that has to be performed by the staff. Hence the usage of an automated discontinuous venous blood sampling system might be an alternative to improve the adjustment of the insulin therapy. The primary aim of the study was to investigate whether the glucose concentration in manually withdrawn blood samples correlates with automated withdrawn blood samples.

Methods In a 12-hour trial, six volunteers were investigated (male/female 5/1; age 28.2 ± 2.2 years, BMI 22.5 ± 1.3, nondiabetics). A 75 g OGTT was performed to enable a better dynamic range of the glucose values. Two venous cannulae were inserted into the dorsal hands for reference measurement and for connection to the automated blood sampling system. To reduce the volunteer's health risk, pressure, air bubble sensor and flushing fluid monitoring were integrated into the system. Blood samples were obtained frequently in 15/30-minute intervals. Roche Microsamplers and the OMNI S6 glucose analyser were used for determination of the blood readings.

Results The automated blood sampling system performed its operation in all volunteers over the whole trial period. The median Pearson coefficient of correlation between manual and automated withdrawn blood was 0.983 (0.862–0.995). Furthermore, the results (173 data pairs) were analysed via the recently published 'Insulin Titration Error Grid Analysis' and 99.4% were suggesting an acceptable treatment. The results of the traditional 'Error Grid Analysis' showed that 96% of the data were in zone A and 4% in zone B.

Conclusion The automated discontinuous blood withdrawing system provides reproducible blood samples from peripheral venous blood. In combination with a glucose sensor and an algorithm it might be used in future as a closed loop system for insulin and glucose infusion at the ICU.

P130

Evaluation of the clinical effectiveness of a computerised decision-supported intensive insulin therapy regimen

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Introduction It has been proposed that intensive insulin therapy (IIT) aiming for a blood glucose (BG) of 4.4–6.1 mmol/l reduces mortality in critically ill patients when compared with conventional insulin therapy (CIT) targeting BG at 10.0–11.1 mmol/l. Difficulties with IIT include inadvertent hypoglycaemia and low efficacy at achieving the target BG. We proposed that computerised decision support may mitigate these problems.

Objective To comprehensively describe BG and outcome from decision-supported IIT.

Methods A clinical information system at each bedspace guided staff through the IIT algorithm. The time spent within glucose ranges was calculated assuming a linear trend between successive measurements.

Results Patient characteristics are shown in Table 1. The IIT group had more frequent BG evaluation (7,007 over 8,944 patient-hours, 0.78 tests/hour) than the CIT group (3,609 over 8,617 hours, 0.42 tests/hour). The median (interquartile range (IQR)) proportion of time spent in the target range 4.4–6.1 mmol/l was similar in the IIT and CIT groups (23.21% (15.4–29.8) vs 17.9% (9.8–29.3), respectively; $P = 0.17$). Similarly, time spent with a BG between 6.2 and 7.99 mmol/l was no different for the two groups (48.5% (IQR 36.9–59.3) for IIT and 43.9% (IQR 34.7–60.9), $P = 0.72$). In the IIT and CIT groups, five and six patients experienced a BG below 2.2 mmol/l, respectively.

Table 1 (abstract P130)

	IIT ($n = 50$)	CIT ($n = 50$)	P value
LOS, median (IQR)	7 (3–21)	6 (3–11)	0.05
Survivors	34 (64.2%)	24 (48.0%)	0.07
APACHE II, mean	23.2	25.4	0.17
Medical	31 (62%)	35 (70%)	0.53
Surgical	19 (38%)	15 (30%)	0.53

Discussion Computerised decision-support and more intensive monitoring did not improve BG control or reduce the incidence of hypoglycaemia.

P131

Glargine insulin: an alternative to regular insulin for glycemic control in critically ill patients

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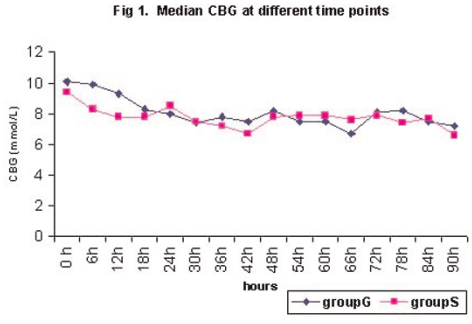
Critical Care 2007, **11(Suppl 2):**P131 (doi: 10.1186/cc5291)

Introduction The objective of this study was to determine the efficacy and safety of subcutaneous (s.c.) once-daily (OD) glargine insulin, a long-acting insulin, in comparison with a s.c. regular insulin, based on a protocolized sliding scale regimen for achieving glycemic control in patients admitted to the ICU.

Methods One hundred patients admitted to the ICU with an admission capillary blood glucose (CBG) >150 mg/dl (8.3 mmol/l) were involved in this prospective, randomized study. Patients with age <18 years, pregnancy, shock, requiring continuous intravenous insulin infusion, renal failure were excluded. Patients were randomly assigned to receive either s.c. glargine insulin 10 U (CBG ≤ 9.9 mmol/l) or 18 U (CBG ≥ 10.1 mmol/l) s.c. OD (Group G, $n = 50$), or s.c. regular insulin based on a 6-hourly sliding scale (Group R, $n = 50$). CBGs were recorded at 6-hour intervals up to 96 hours or until ICU discharge, whichever was earlier. The target CBG in both groups was <150 mg/dl (8.3 mmol/l). Patients in group G received rescue doses of regular insulin, as required. Demographic characteristics, mean and median CBG, and episodes of hypoglycemia were studied.

Results Demographic profiles were comparable between the two groups. There was no significant difference in mean CBG in both groups (Group G 152.1 mg/dl (8.4 mmol/l), Group R 149.9 mg/dl (8.3 mmol/l), $P = 0.66$). Median CBGs were comparable at 6-hourly time points in both the groups except at 0 and 6 hours in the glargine arm (CBG at 0 and 6 hours, Group G 10.0 mmol/l and

Figure 1 (abstract P131)



Median capillary blood glucose (CBG) at different time points.

9.9 mmol/l, Group R 9.4 mmol/l and 8.3 mmol/l, $P = 0.04$ and 0.02, respectively) (Figure 1). There were three episodes of hypoglycemia in Group G and one in Group R, which were corrected.

Conclusion OD s.c. glargine insulin is a safe and effective alternative to regular insulin for glycemic control in critically ill patients.

P132

Investigation of insulin clearance in severely acutely ill patients with glucose intolerance evaluated by means of bedside-type artificial pancreas

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Background and purpose Glucose intolerance in acutely ill patients is one of the risk factors of their morbidity and mortality, and glucose control with insulin therapy improves the outcome. We investigated relationships among insulin clearance (IC), which is considered to be one of the factors related to effectiveness of insulin therapy, and glucose tolerance, glucose intolerance, and severity of the diseases, in order to clarify the significance of IC on the severity of the diseases including glucose intolerance and on the therapies.

Materials and methods Twenty-three ICU patients with glucose intolerance in whom strict blood glucose control was performed by means of a bedside-type artificial pancreas (NIKKISO Corp., Japan) were investigated. The diabetics were excluded. The items investigated were IC (ml/kg/min) measured by the glucose clamp method, daily mean blood glucose level as a parameter of glucose intolerance (BGm, mg/dl), proportion of septic patients (%), SOFA score and mortality (%) as indicators of the severity of the diseases, and blood concentration of free fatty acid (FFA) and stress hormones (glucagon, growth hormone, cortisol, adrenalin, noradrenalin) as factors that might affect glucose intolerance. The method of investigation involved patients being classified into four groups according to IC, and those groups were compared with each other; low IC group (group L: IC < 9, $n = 2$), normal IC group (group N: 9 < IC < 15, $n = 13$), high IC group (group H: 15 < IC, $n = 8$), and severely high IC group (group S: 19 < IC, $n = 5$) (group S was a subgroup of group H).

Results (1) FFA values were low or normal in all groups. (2) There were no significant differences in stress hormones among group N, group H, and group S. Those hormones in group L were significantly higher than, or had a tendency to be higher than, those in group N, group H, and group S. (3) The mean values of BGm in the groups had a tendency to be higher in the order of group S (179 ± 30), group H (172 ± 25), group N (162 ± 26), and group L (153 ± 8). (4) The severities of the diseases (sepsis (%)/SOFA score/mortality (%)) in the groups were significantly higher in the order group L (100%/20.0 ± 1.4/100%), group S (100%/9.6 ± 7.0/40%), group H (88%/7.0 ± 6.5/25%), and group N (54%/5.8 ± 5.2/15%).

Interpretation and conclusions The increase of IC was related to glucose intolerance. IC increased and glucose intolerance became severe as the severity of the diseases progressed. In the most severe state, or in a near-terminal state, however, IC decreased and glucose intolerance improved, although stress hormones increased significantly. Therapies focused on the improvement of IC were considered important in acutely ill severe patients with glucose intolerance as well as blood glucose control by insulin therapy.

P133

Diurnal and other variations in blood glucose in intensive care unit patients receiving insulin infusions

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Critical Care 2007, **11(Suppl 2):**P133 (doi: 10.1186/cc5293)

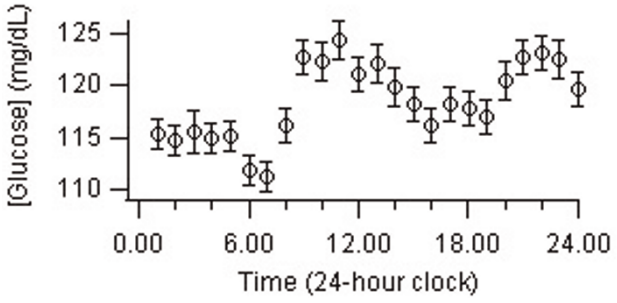
Introduction Treatment of hyperglycemia in ICU patients using an insulin infusion protocol was shown by van den Berghe and colleagues to reduce mortality and morbidity in ICU patients. Consequently, many healthcare bodies proposed guidelines for the control of hyperglycemia in the ICU. However, the patchy evidence underpinning these guidelines and a high rate of complications lead to controversy about the optimal glucose target range. Studies showing insulin infusions are effective have reported average glucose values at single time points. However, single time points are difficult to interpret as they do not provide information about the proportion of glucose measurements that need to be in range for benefit. We hypothesized that blood glucose variance was greater if all glucose measurements were considered and asked whether there was a diurnal pattern that accounted for some of the variance.

Methods Prospective collection of all glucose measurements for ICU patients receiving an insulin infusion protocol between 20 May 2006 and 6 August 2006 in 64 ICU beds at a teaching hospital. We report glucose values from all ICU patients, ≥8 hours after infusion initiation.

Results We compared the 6:00 a.m. glucose value with those collected at all other times in 149 consecutive patients. The 6:00 a.m. values were lower than the remaining values (mean ± SD: 112 ± 30 mg/dl ($n = 477$) vs 119 ± 35 mg/dl ($n = 10,364$); $P < 0.0001$) and as hypothesized had a smaller variance by F test ($P < 0.0001$). Inspection of the time-averaged data (±SE) revealed a diurnal variation in the blood glucose with peaks occurring at 11:00 a.m. and 10:00 p.m. (Figure 1). This diurnal pattern may account for some of the observed variation in insulin requirements and contribute to episodes of hypoglycemia in the critically ill.

Conclusion Glucose variance is increased if all time values are considered rather than a single time point and there is a diurnal pattern to glucose in ICU patients receiving insulin. Consideration of this diurnal variation when treating hyperglycemia in the ICU may avoid hypoglycemia and so facilitate better glucose control with insulin infusions.

Figure 1 (abstract P133)



P134

Severe hypoglycaemia during intensive insulin therapy: a rare event in critically ill patients

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Introduction Tight glycemic control reduces mortality in surgical intensive care patients and in long-term medical intensive care patients. The incidence of severe hypoglycaemia (glucose ≤2.2 mmol/l) in the intensive treatment group has been 3.1–5.1%. Recently, a large study on intensive insulin therapy was prematurely discontinued due to safety issues. The incidence of hypoglycaemia was 9.8% in intensive treatment group and the mortality among patients experiencing hypoglycaemia was 18.6%. As the safety of intensive insulin therapy has been questioned, we screened all patients during a 17-month period to see the incidence of hypoglycaemia and its effects on the prognosis of the patients.
Methods A retrospective study was performed in two ICUs, one eight-bed general ICU and one 10-bed surgical ICU. All patients treated between 7 February 2005 and 30 June 2006 were included in the study. A nurse-driven intensive insulin protocol with a target blood glucose level of 4–6.1 mmol/l had been introduced in 2004. All blood glucose measurements performed during the ICU treatment were analysed. The patients were divided into two groups according to the lowest detected blood glucose value (≤2.2 or ≥2.3 mmol/l).
Results A total of 1,024 patients (1,124 treatment periods) were included in the study. Thirty patients were excluded due to incompleteness of the data. During the study period 61,203 blood glucose measurements were performed, 1,578 (2.6%) of which were below the target value of 4 mmol/l. Severe hypoglycaemia (≤2.2 mmol/l) occurred in 25 patients (36 measurements). The incidence was 0.059% of the measurements and 2.3% of the patients. The median age, sex, APACHE II score, SAPS II or diagnosis category did not differ between the groups. The median (IQR) ICU and hospital length of stay was 4.3 (1.8–10.6) and 18 (8.5–39.5) days in patients with lowest blood glucose ≤2.2, and 2.7 (1.2–5.7) and 13 (7–23) days in patients with lowest blood glucose ≥2.3 ($P = 0.058$ and $P = 0.077$, respectively). The hospital mortalities were 25% and 15%, respectively; the difference was not statistically significant.
Conclusions Severe hypoglycaemia during intensive insulin therapy is rare in protocol-driven ICU treatment compared with previous clinical trials. When present, hypoglycaemia may have an impact on the outcome of the patients

P135

Intensive insulin therapy and indications for intensive care admission

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Introduction Insulin resistance and hyperglycemia are common in critically ill patients, and are associated with higher morbidity and mortality in these patients if not controlled. Intensive insulin therapy has been shown to reduce morbidity and mortality. It is not clear, however, whether the patients' indication for admission into the ICU is related to the time to achieve glycaemic control or the total dose of insulin required. This study was designed to audit the efficacy of an intensive insulin therapy protocol in achieving glycaemic control in patients presenting with different conditions.
Methods A prospective observational study was performed over 8 weeks on patients admitted to an adult ICU who received nutrition support for up to 48 hours. Intensive insulin therapy was administered to those patients who developed hyperglycemia. The demographics, blood glucose and insulin doses were documented. Haemoglobin, white cell count, neutrophil count, antioxidants, CRP and prealbumin were measured. Outcome measures were the mean and total insulin dose and the time to achieve glycaemic control.
Results Forty patients, 22 (55%) males and 18 (45%) females, who received nutritional support for 48 hours or more were studied. The mean (SD) age was 59.4 (14.7) years. Enteral feeding was given in 32 (80%) and parenteral feeding in 14 (35%) patients, while six (15%) patients received both enteral and parenteral feeding. The mean (SD) energy in 48 hours was 3,307.4 (527.0) kcal, mean (SD) insulin was 1.37 (1.23) IU, mean (SD) blood glucose was 7.76 (0.9) mmol/dl and total insulin to achieve glycaemic control was 65.51 (58.6) IU. The time taken (SD) to achieve glycaemic control was 15.16 (12.65) hours. As expected, there was a relationship between the total insulin dose and the time to achieve three consecutive glycaemic controls ($r = -0.43$, $P = 0.023$). Also, between the total insulin dose and mean blood glucose $r = 0.508$, $P = 0.001$. There was no significant relationship between the total insulin dose and indication for ICU admission, and the total insulin dose and body mass index.
Conclusion Findings from this study showed that the indication for admission did not affect either the total dose of insulin required to achieve glycaemic control or the time it takes to achieve three consecutive glycaemic controls.

P136

Implementation of glycemic control – problems and solutions

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Introduction Glycaemic control is another example of protocol-driven therapy in intensive care medicine to improve outcome in critically ill patients. While the advantage of this approach seems to be obvious, little is known about the problems of implementing such a protocol. The intention of this study was to evaluate problems of implementation and to develop strategies to overcome them.
Setting A 16-bed surgical ICU of a university teaching hospital with 50 critical care nurses, about 30% in part-time employment.
Method Over a 7-month period all patients staying longer than 48 hours in the ICU with hyperglycaemia (>150 mg%) on three consecutive measurements were included in the study. These patients were treated according to a protocol at the discretion of the attending nurse. On daily rounds and every 4–5 weeks supervision was performed, and the protocol was modified three times during this period according to staff comments. Further on, medical as well as nonmedical problems of implementation were analysed and discussed. Attitudes and perceived impeding aspects of the implementation process were recorded by means of a questionnaire.
Results Since insulin sensitivity showed enormous variability, glycaemic control required a high nursing effort. Impeding aspects to titrate blood glucose into the target range were the absence of a nutritional protocol (high carbohydrate intake, despite inflammation/infection leading to hyperglycaemia that was difficult to

control) and fear of hypoglycaemia (<60 mg%) leading to low-dose insulin with consecutive hyperglycaemia. Lack of communication (and therefore a loss of information) between critical care nurses and the intensivists and poor acceptance from physicians to leave this field of intensive care medicine to the nurses were additional factors that slowed the implementation process.
Conclusion Implementation of protocol-driven medicine requires a high quality of information flow. The lack of linearity between blood glucose and insulin dose (variability of insulin sensitivity) required a sometimes intuitive (experienced) decision to titrate the insulin dose. The conflict of physicians with this new role of critical care nurses might be due to the lack of understanding of the evolution of the nursing profession.

P137

Computer-advised insulin infusion in critically ill patients – a randomized controlled trial

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Critical Care 2007, **11(Suppl 2):**P137 (doi: 10.1186/cc5297)

Introduction Tight blood glucose (BG) control has been shown to decrease morbidity and mortality in patients in the surgical ICU [1] but is difficult to achieve using standard insulin infusion protocols. We previously evaluated a software model predictive control (MPC) insulin administration algorithm in postcardiac surgery patients [2]. This study investigated the use of an enhanced MPC algorithm (eMPC) in more severely ill patients over 72 hours.
Methods Fourteen (seven male) critically ill ventilated medical and surgical patients, mean age 65 years, with an arterial BG > 6.7 mmol/l within 24 hours of ICU admission (RBH) or already receiving insulin infusion, and expected to require mechanical ventilation for more than 72 hours, were treated either with BG control by the standard ICU insulin intravenous infusion protocol [2] or eMPC-advised insulin infusion ($n = 6$) for 72 hours. The eMPC algorithm, installed on a bedside computer, requires input of current insulin requirements, bodyweight, carbohydrate intake and BG concentration. The algorithm advises the time to next BG sample (up to 4 hours) and the insulin infusion rate, targeted to maintain BG at 4.4–6.1 mmol/l. Patients in the eMPC group had BG measured hourly (for safety) but values were only entered if requested by the algorithm.
Results The mean (SD) glucose concentration was significantly lower in the eMPC group (6.0 (0.34) vs 7.1 (0.54) mmol/l, $P < 0.001$). The mean insulin infusion rate was not significantly different (4.1 (2.7) vs 3.1 (1.8) IU/hour, eMPC vs standard care). BG sampling occurred more frequently in the eMPC group, with a mean of every 1.1 vs 1.9 hours ($P < 0.05$). No patients in either group had any BG measurements <2.2 mmol/l.
Conclusion The eMPC algorithm was effective in maintaining tight BG control in this more severely ill patient group without any episodes of hypoglycaemia (BG < 2.2 mmol/l), but required more frequent BG measurement.
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P138

Evaluation of a model predictive control algorithm using time-variant sampling to establish tight glycaemic control in clinical practice

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Critical Care 2007, **11(Suppl 2):**P138 (doi: 10.1186/cc5298)

Introduction Tight glycaemic control (TGC) in critically ill patients significantly improves clinical outcome. Even with increased workload for ICU nursing staff, targets for TGC are often not achieved. The aim of the present study was to evaluate in clinical practice a model predictive control algorithm (MPC) using time-variant sampling, which will be used in a fully automated insulin titration system (CLINICIP system).
Methods This was an open randomized controlled clinical study. Fifty mechanically ventilated medical ICU patients were included for a study period of 72 hours. Patients were randomized either to a control group, treated by an insulin algorithm as routinely used in the ICU, or to the MPC group, using a laptop-based fully automated MPC algorithm. The target range for blood glucose (BG) was 4.4–6.1 mM for both groups. Efficacy was assessed by calculating the median BG, hyperglycaemic index (HGI) and BG sampling interval. Safety was assessed by the number of hypoglycaemic BG measurements < 2.2 mM.
Results Patients were included for 72 (69–73) hours (median (IQR)) in the control group and 71 (70–73) hours in the MPC group. The median BG and HGI were significantly lower in MPC vs control patients (see Table 1). A single BG measurement < 2.2 mM was detected in the MPC group vs 0 in the control group. The sampling frequency was significantly higher in the MPC group.

Table 1 (abstract P138)

	MPC group ($n = 25$)	Control group ($n = 25$)	*P*
BG (mM)	5.9 (5.5–6.3)	7.4 (6.9–8.6)	<0.001
HGI (mM)	0.37 (0.17–0.91)	1.56 (1.06–2.45)	<0.001
Interval (min)	105 (94–139)	173 (160–194)	<0.001

Data presented as the median (IQR).

Conclusion The use of MPC improved BG and the HGI. This improvement was accompanied by an increased sampling frequency. MPC with time-variant sampling is a reliable tool for the implementation of TGC in patients in the medical ICU.

P139

The effect of tighter glucose control on outcome

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Critical Care 2007, **11(Suppl 2):**P139 (doi: 10.1186/cc5299)

Introduction Evidence is accumulating that tight glucose control improves outcome in critically ill patients. This study was performed to evaluate the effect of lower blood glucose levels in critically ill patients on outcome.
Patients and methods The unit is a 10-bed closed-format medical–surgical ICU in a general hospital. Starting in 2003 insulin was prescribed to ICU patients using several nurse-driven

computerised protocols, each subsequent protocol aiming for lower glucose levels. From February 2004 until May 2005 protocol 1 was used, aiming for glucose between 5.0 and 9.0 mmol/l; from July 2005 until December 2005 protocol 2 was used, aiming for glucose between 4.5 and 7.5 mmol/l. Serum glucose was measured at 6:00 a.m. in all patients from blood derived from arterial lines or venous puncture. The rest of the day blood glucose was measured either using the Glucotouch (protocol 1) or the AccuCheck (protocol 2) devices. To eliminate differences due to these different methods of measurement, only the 6:00 a.m. glucose measurements done by the central laboratory were studied here. Data were derived from ICU and laboratory databases.

Results See Table 1. The median morning glucose was reduced from 7.5 mmol/l with protocol 1 to 6.8 mmol/l with protocol 2, resulting in small but nonsignificant improvement in outcome. Subgroup analysis focusing on medical or surgical patients or on patients with specific length of stay in the ICU also revealed nonsignificant differences in outcome.

Table 1 (abstract P139)

	Protocol 1	Protocol 2	*P*
Number of patients	601	413	
Number of morning glucose measurements	1,558	1,378	
Morning glucose (mean/median)	8.23/7.5	7.48/6.8	<0.001
APACHE II score at ICU admission (mean/median)	13.6/12	13.9/12	Not significant
Age (years, mean/median)	66.4/70.3	67.1/70.6	Not significant
ICU mortality all patients (%)	10.6	9.0	Not significant
Hospital mortality all patients (%)	17.6	15.0	Not significant
Mean ICU length of stay (days, mean/median)	3.04/1.1	2.47/1.1	Not significant
Mean hospital length of stay (days, mean/median)	17.00/10.0	13.62/9.1	Not significant

Conclusions A small but significant decrease in serum glucose probably results in a small but statistically nonsignificant decrease in mortality and length of stay.

P140

Reliability of arterial, capillary and venous point-of-care glucose measurements in the intensive care unit setting: evaluation of two glucometers

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Critical Care 2007, **11(Suppl 2):**P140 (doi: 10.1186/cc5300)

Introduction Increased risk of hypoglycemia is the major drawback of strict glycemic control, which has been extensively used in critically ill patients. Fast and precise glucose measurements are therefore mandatory. Our aim was to evaluate the accuracy of two methods of bedside point-of-care testing for glucose measurements using arterial, capillary and venous blood samples in ICU patients.

Methods A cross-sectional study with prospective data collection included 86 patients admitted to a 40-bed clinical-surgical ICU of a tertiary care hospital. Results from two different methods of glucose measurement were compared with central laboratory arterial blood measurements: Accu-chek Advantage® (Roche) arterial, venous and capillary samples; and Precision PCx® (Abbott) arterial samples. All samples were collected simultaneously. Agreement between measurements was tested with the Bland–Altman method.

Figure 1 (abstract P140)

Arterial central lab minus:	Mean difference – mg/dl	95% limits of agreement – mg/dl
Arterial Precision PCx	-17.8	-50.0, 14.2
Arterial AccuChek	-6.7	-35.3, 22.0
Fingerstick AccuChek	- 6.4	- 44.1, 31.2
Venous AccuChek	-8.2	- 56.4, 41.0

Results Comparisons between pairs of measurements are shown in Figure 1.

Conclusions The two glucose meters evaluated might not be sufficiently reliable to be used in the ICU setting, especially for patients under strict blood glucose control. Moreover, there are marked differences between the equipment and a decrease in precision if capillary or venous samples are used.

P141

Implementing tight glycaemic control: performance of bedside glucometers

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Critical Care 2007, **11(Suppl 2):**P141 (doi: 10.1186/cc5301)

Introduction Implementing tight glycaemic control (TGC) in the ICU requires accurate blood glucose (BG) monitoring. We evaluated the performance of two bedside glucometers (GM) in ICU patients.

Methods Four hundred and fifty-two arterial blood samples were prospectively analysed in 37 adult ICU patients subjected to TGC. Arterial BG was simultaneously determined using a reference test (ABL®) and two GM (Accu-Chek® and HemoCue®). Data were

Figure 1 (abstract P141)

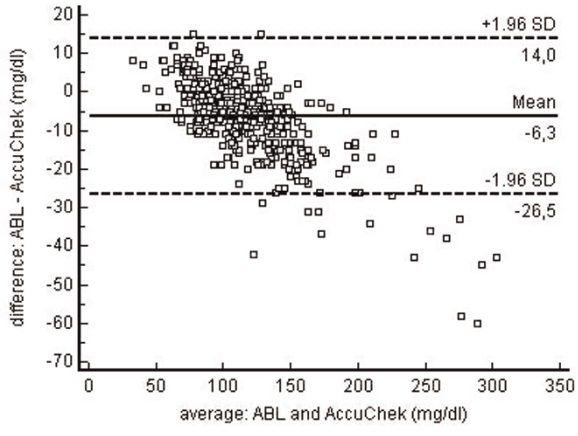
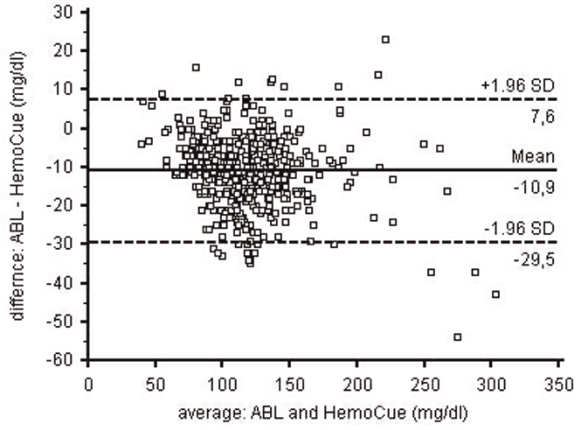


Figure 2 (abstract P141)



analysed using linear regression and the Bland–Altman (BA) method.

Results Correlation between the reference method and both GM in the overall BG range was reasonable, but not perfect ($r^2 \geq 0.93$). This was further underlined by BA analysis (Figures 1 and 2), showing a bias to overestimate BG with GM. In the TGC range (80–110 mg/dl) correlation was low for both GM ($r^2 \leq 0.66$). This was confirmed by BA analysis, demonstrating broad limits of agreement: +14.2 and −26.6 mg/dl for Accu-Chek® and +5.5 and −31.1 mg/dl for HemoCue®.

Conclusions The accuracy of the tested GM in our ICU patients was insufficient for safe clinical practice. Therefore, to avoid potentially harmful hypoglycaemia, caution is warranted when TGC is implemented exclusively based on BG results obtained by GM.

P142

Comparison of accuracy of glucose-oxidase-based and glucose-dehydrogenase-based point-of-care glucometers

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Critical Care 2007, **11(Suppl 2):**P142 (doi: 10.1186/cc5302)

Introduction Bedside capillary or arterial blood glucose monitoring is mandatory for ICU patients under tight glycemic control. Point-of-care methods are based on glucose-oxidase (GO) or glucose-dehydrogenase (GD) enzymatic methods whereas the laboratory reference method is hexokinase for measuring the plasma glucose levels.

Methods In this prospective observational study, blood glucose was simultaneously measured on the Glucocard Arkray (GO, capillary), on the Accu-chek Inform Roche (GD, capillary and arterial) and on the Rapid-Lab 1265 Bayer (GO, arterial), and each value was compared with the reference laboratory result.

Results A total of 262 matched analyses were done in 60 patients. Biases are defined as the glucose laboratory value minus point-of-care value. The bias, 95% limits of agreement, and numbers of observed discrepancy (*d*) paired results >20% and >10% are reported in Table 1.

Conclusions GO methods underestimate while GD methods overestimate all blood glucose levels as compared with plasma glucose levels measured by the reference method of hexokinase. Capillary methods have wider 95% limits of agreement than measures carried out on arterial blood.

P143

Continuous glucose monitoring for intensive care patients using whole blood microdialysis

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Critical Care 2007, **11(Suppl 2):**P143 (doi: 10.1186/cc5303)

Introduction The objective of this study was to investigate whether continuous glucose monitoring for intensive care patients could be implemented using blood microdialysis (MD) as tight glycaemic control reduces mortality and morbidity of critically ill patients. Currently investigated is whether the subcutaneous tissue is an adequate and representative site for glucose monitoring. We have designed and tested a novel system that allows continuous measurement of glucose concentration in whole blood based on MD.

Methods Na-heparin is pumped to the tip of a double lumen catheter and the blood–heparin mixture is withdrawn continuously at a mixing ratio of 1:1 at a flow of 4 ml/hour. The blood–heparin mixture is microdialysed in a planar flow-through MD unit and is discarded thereafter. The dialysate is collected and analysed for glucose concentration via Beckman analysis and referred to venous blood samples taken from the reference arm. Eight healthy volunteers underwent a 12-hour investigation including an OGTT. Glucose readings from dialysate and venous blood were obtained in a 15–30 minute interval.

Results All eight subjects successfully completed the 12-hour trial. The coefficient of correlation between continuously withdrawn microdialysed blood and venously taken reference blood samples was $r = 0.9834$ (0.9753–0.9958). The Clark Error Grid Analysis (EGA) revealed that 99.5% of all data pairs are in the A range (220 of 221). Applying the novel Insulin Titration EGA yielded in 100% of data pairs the 'acceptable treatment' area.

Conclusions Blood MD based on continuous blood withdrawal and extracorporeal MD is a promising approach to obtain dialysate reliably, safely and continuously for long-term determination of blood glucose concentration with online sensors. The correlation between glucose concentration of dialysate and reference venous blood samples is excellent. The patency of the double lumen catheter in the current form could be improved by introducing

Table 1 (abstract P142)

Point-of care method	Number of comparisons	Bias (mg/dl)	Agreement (mg/dl)	Number >20% *d* (%)	Number >10% *d* (%)
Glucocard, GO capillary	262	+8.5	±36	32 (12)	103 (39)
Accu-chek, GD capillary	262	−6.3	±37	40 (15)	123 (45)
Rapid-Lab, GO arterial	262	+5.3	±11	(0)	21 (8)
Accu-chek, GD arterial	234	−7.9	±17	17 (7)	67 (29)

adequate flushing sequences or by using it with central lines. Further long-term studies are necessary to test the system together with online sensors.

P144

Subcutaneous glucose monitoring in patients with severe sepsis

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Critical Care 2007, **11(Suppl 2):**P144 (doi: 10.1186/cc5304)

Introduction Tight glycemic control (TGC) to improve mortality and morbidity in ICU patients requires frequent blood glucose measurements and thus increases the workload for medical staff. TGC could be simplified by subcutaneous glucose monitoring as suggested for diabetes care. Due to altered tissue perfusion as often seen in critically ill patients, it remains unclear whether subcutaneous adipose tissue (SAT) is a reliable measurement site. In this study we evaluated clinically whether SAT can be used as safe, alternative site to establish TGC in patients with severe sepsis.
Methods For 26 hours, arterial blood and SAT microdialysis samples were taken from 10 patients with severe sepsis. Hourly SAT glucose concentrations were calibrated to arterial blood glucose (Bg) by one-point calibration either 1 hour (BgSAT1h) or 6 hours (BgSAT6h) after catheter insertion. The relation between Bg and calibrated SAT glucose readings was clinically evaluated applying a well-established insulin titration error grid analysis.
Results Arterial and SAT glucose readings were comparable (Bg: 143 (122–167) mg/dl; BgSAT1h: 147 (130–177) mg/dl; BgSAT6h: 146 (117–181) mg/dl; median (IQR)). Relative differences between Bg vs BgSAT1h and BgSAT6h indicated −2 (−193 to 30)% and −4 (−42 to 25)%; median (5th and 95th percentiles)), respectively. Clinical evaluation of the data indicated that 86% (BgSAT1h) and 95% (BgSAT6h) of the glucose readings from SAT would allow correct treatment according to an insulin-titration guideline. Fourteen percent of the data for BgSAT1h and 5% of the data for BgSAT6h would cause a violation of the guideline and thus unwanted glucose excursions and a possible risk for the patient.
Conclusions Clinical evaluation of subcutaneous glucose monitoring to establish TGC indicated that only 86% of the readings would allow acceptable treatment according to a titration guideline. Although this result could be substantially improved by introducing a 6-hour stabilisation period for the trauma caused by catheter insertion, the clinical applicability of subcutaneous glucose monitoring for patients with sepsis has to be considered with care.
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P145

Nutritional support in critically ill patients

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Critical Care 2007, **11(Suppl 2):**P145 (doi: 10.1186/cc5305)

Introduction Early adequate nutritional support (NS) in critically ill patients can improve clinical outcome [1]. Although enteral nutrition is considered the best method, it carries a risk for developing ventilator-associated pneumonia, particularly if patients are nursed horizontally [1]. The aim of this prospective audit is to assess the compliance of nutritional practise in our ICU with some aspects of recommendations of Canadian Clinical Guidelines.
Method Demographic data, head elevation (HE) from the horizontal position, daily nitrogen and calorie intake were recorded. Daily recommended calorie requirements were calculated according to body weights on admission. The nasogastric tube size and the gastric residual volume threshold (GRVT) before abandoning enteral feeds were also recorded.
Results During 2 months 55 patients (male 47%, female 53%) were admitted, including 47 (85%) emergency admissions. Thirty-three (60%) patients stayed in the unit for >48 hours with an average stay of 7.1 days. Thirty-two (58%) patients received NS, and 26 (81%) of these were within 48 hours of admission. Enteral and parenteral routes were used in 26 (81%) and six (18%) patients, respectively. In five (15%) patients both methods were used during the change of route of administration. The daily calorie intake expressed as a percentage of the recommended intake is presented in Table 1. HE was more than 300 in 70% of the 570 measurements. Blood sugar was between 6.3 and 6.9 mmol/l. Gastro Prokinetics was used in 80%. There was no feeding protocol in the unit and low GRVTs were used before abandonment of the enteral regime.

Table 1 (abstract P145)

	Total days (%)	Calories (%)	Nitrogen (%)
Nasogastric feeds	155 (71.5)	80.21	63.5
Total parenteral nutrition	48 (22.22)	151.52	118.1
Nasogastric feeds + total parenteral nutrition	13 (6.06)	158.01	126.9

Conclusion We found that there was overfeeding in the parenteral and combined routes. HE was satisfactory in 70% and more patients could receive enteral feeds if a high GRVT was used. Small-bore tubes are easy to implement and were not practised.
Reference
1. Dhaliwal R, Heyland DK: **Nutrition and infection in the intensive care unit: what does the evidence show?** *Curr Opin Crit Care* 2005, **11:**461-467.

P146

Prokinetics effect on gastric emptying in critically ill ventilated patients measured by the C13 breath test with a novel device

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Introduction Gastroparesis in critically ill ventilated patients is relieved by prokinetics. The best prokinetic combination is not known and may be identified by BreathID measurement of gastric emptying (GE).
Methods A prospective crossover study in stable ventilated ICU patients without upper gastrointestinal pathology. GE measurement: 4-hours expiratory $^{13}CO_2$ recording following intragastric administration of C^{13} sodium acetate in 100 ml Osmolite. Baseline measurement (BM) and following 24 hours i.v. therapy with: metoclopramide (10 mg every 6 hours), metoclopramide with continuous erythromycin (10 mg/hour), continuous erythromycin and bolus erythromycin (200 mg every 12 hours) were done in each patient. The BM and drug administration order was altered in a subgroup of patients. GE was assessed by calculating the

Figure 1 (abstract P146)

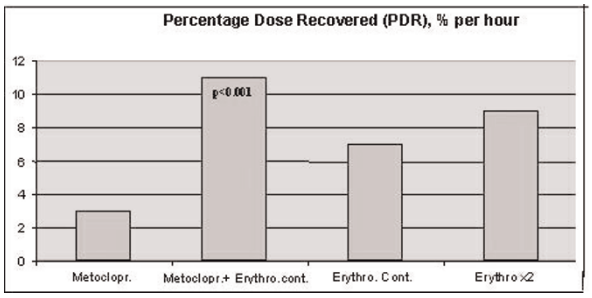

Table 1 (abstract P146)

Metoclopramide	13.7%
Metoclopramide + erythromycin continuous	50.5%
Erythromycin continuous	33.3%
Erythromycin x 2	38.7%
Best individual	85.2%

percentage dose recovered (PDR), a measure of delta over baseline reflecting the rate of substrate metabolized. The $^{13}CO_2$ measurements and calculations were done by our BreathID Computerized system (BreathID Ltd, Jerusalem, Israel) with its sensor attached to the expiratory ventilator tubing.

Results Thirty-one patients were included. Figure 1 shows the PDR of all patients under the different prokinetic drugs. Table 1 presents the average percentage of GE improvement over BM with different therapies, and the average improvement of individuals' best combination. Comparing 20 patients, BM first, with 11 at different timings, revealed no difference of baseline or best combination ($P = 0.1$, $P = 0.2$, respectively).

Conclusions In this population: 1. Metoclopramide is poor in improving GE. 2. The combination of metoclopramide and continuous erythromycin is the most effective. 3. The BreathID is a convenient and novel way to monitor GE in order to study and individually tailor the most effective (up to 85% over BM) prokinetic combination.

P147

A study of enteral tube feeding in critically ill patients

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Critical Care 2007, **11(Suppl 2):**P147 (doi: 10.1186/cc5307)

Introduction For critically ill patients unable to eat, enteral tube feeding (ETF) is the preferred mode of feeding. The study aimed to investigate the amount of enteral feed obtained by patients on ICU in a busy London Teaching Hospital, the efficiency of initiation of feeding, and possible reasons for the failure of the above.

Methods A prospective observational study was carried out over 1 month on patients admitted to a general and cardiothoracic ICU, who received ETF. Baseline data including age, reason for admission and illness severity score (SOFA) were documented. Length of time from admission to start of feeding was noted, and the volume of feed delivered to patients was recorded. The quantity of calories delivered to the patient was compared with the patient's ideal nutritional requirement (determined by the ICU ETF protocol). Feeding interruptions were also recorded.

Results Fifty-two patients receiving ETF were observed for a total of 7,349 hours: 67.3% of patients were surgical and 32.7% medical. Patients received a median of 75% of their ideal calorific requirement. Feeding was started a median of 15 hours after admission, and a median of 5% of feeding time was interrupted after ETF had been started. Reasons for interruption included high gastric aspirates, starvation for procedures and displacement/blockage of feeding tube. The time to start ETF was significantly different according to admission categories ($P = 0.033$), with abdominal and cardiothoracic surgical patients having the greatest delays. Abdominal surgical patients also had a higher proportion of feeding interruptions due to high gastric aspirates and starvation for procedures. The SOFA score on day 1 significantly correlated with the time taken to start feeding ($P = 0.008$), length of total feeding interruption ($P = 0.012$), length of feeding interruption due to high gastric aspirates ($P = 0.043$), and length of feeding interruption due to starvation for procedures ($P = 0.026$).

Conclusion The majority of patients received a high proportion of their ideal calorific requirement and began feeding within 24 hours. The data indicate that patients having had abdominal surgery or the sickest patients may be may be more likely to experience delays in initiation and interruptions to feeding.

P148

Proton pump inhibitors and the incidence of *Clostridium difficile* on the intensive care unit

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Critical Care 2007, **11(Suppl 2):**P148 (doi: 10.1186/cc5308)

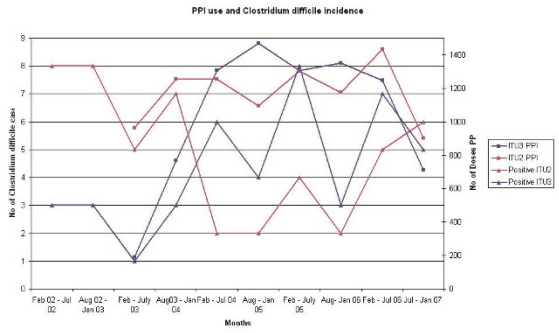
Introduction *Clostridium difficile* associated disease (CDAD) is recognized as a major cause of morbidity and mortality among patients in hospital. There have been reported associations between the use of proton pump inhibitors (PPIs) and CDAD in community and hospital settings [1,2]. The aim of this study was to investigate the effect of introducing PPI prophylaxis in critically ill patients on the incidence of CDAD.

Methods Retrospective analysis of microbiology results of patients admitted to general and neurotrauma ICUs between February 2002 and September 2006. Prior to March 2004 the general ITU used PPIs for all patients as gastric acid prophylaxis, and the neurotrauma ITU used PPIs for only patients at high risk of GI ulceration. Following instigation of ventilator care bundles in March 2004 both units gave PPIs to all ventilated patients. The incidence of *C. difficile* toxin-positive samples and the number of doses of PPI used each month were compared for before and after this time period. The use of antibiotics was also compared between the two units over the time period to exclude this as a confounding variable.

Results We identified 92 *C. difficile*-positive faecal samples during the 57-month period from February 2002 to September 2006. This averaged 1.61 cases per month. The general ITU (ITU2) presented 49 cases (53.2%), and the neurotrauma ITU (ITU3) 43 cases (46.8%). In February 2002, PPI usage was infrequent in the ITU3, but more common in ITU2. The *C. difficile* rates were also higher in ITU2 than in ITU3. PPI usage increased in ITU3 until, on the instigation of the ventilator care bundle, PPIs were used for all patients from March 2004. Our preliminary data demonstrate an increase in *C. difficile* rates in ITU3, to meet the rates of ITU2, at the same time as PPI usage was increased (Figure 1). The ITUs back onto each other and share the same medical and nursing staff. Antibiotic usage was similar across both units with regards to cephalosporins, meropenem and pipracillin/tazobactam.

Conclusion *C. difficile* rates have remained relatively stable on the general ITU (ITU2) but showed a significant increase on the

Figure 1 (abstract P148)



neurotrauma ITU (ITU3), concurrent with increased PPI usage. We believe this worthy of further investigation.

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P149

Retrospective study of dysphagia following hospital discharge of intensive care patients

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Critical Care 2007, **11(Suppl 2):**P149 (doi: 10.1186/cc5309)

Objective A retrospective study to assess the incidence and causal factors associated with long-term dysphagia following intensive care discharge.

Methods A questionnaire was sent out 4 months post ICU discharge to 193 intensive care patients (Level 3 care with a stay of over 48 hours). We reviewed the case notes of those patients who reported swallowing difficulties to establish whether they had undergone, had any characteristics of or received therapies potentially associated with dysphagia.

Results We had a 50% response rate to our questionnaire. An overall dysphagia post ICU stay rate of 19.5% was observed. Fever and age over 65 were both common findings as one may expect and showed the highest association with subsequent dysphagia. We did not find any suggestion of a relationship between changing tracheostomy (suggesting repeat procedures) and subsequent difficulty swallowing. One patient within this group subsequently developed a tracheal stenosis. See Table 1.

Table 1 (abstract P149)

Factor	Number	Percentage
Fever	14	82
Age > 65 years	11	58
Percutaneous tracheostomy	10	50
Sterds	7	37
Cardiopulmonary resuscitation	3	15
Shiley fenestrated low-pressure cuffed tracheostomy tube	2	10
Mini-Trach II – Seldinger (Portex Minitracheotomy Kit)	1	5
Neuromuscular Blockade	0	0

Conclusion We found the percentage of patients reporting swallowing difficulties post percutaneous tracheostomy (PCT) (Portex Blue Line Ultra tracheostomy tube) to be higher than one would expect. This may be confounded by neurological injury necessitating the need for a PCT, but we feel this may be an area of concern meriting further investigation given frequent PCT in ICU practice.

P150

Intestinal corticotropin-releasing factor is decreased in shocked trauma patients and may affect gut function

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Critical Care 2007, **11(Suppl 2):**P150 (doi: 10.1186/cc5310)

Introduction The reasons for the typical bowel dysfunction following traumatic injury are unclear. Corticotropin-releasing factor (CRF) in peripheral blood/tissue may induce intestinal barrier dysfunction via receptor-mediated mechanisms independently of the hypothalamic–pituitary–adrenal axis. This mechanism seems to involve interactions of CRF with enteric nerves and mast cells, which results in increased gut intercellular tight junction permeability to macromolecules, as well as increased epithelial cell apoptosis leading to loss of mucosal integrity. We investigated whether blood and intestinal tissue CRF is associated with postoperative gut dysfunction in shock.

Methods CRF analysis was performed on full-thickness bowel specimens obtained from shocked trauma patients requiring emergency abdominal surgery for penetrating injury, and from patients undergoing small bowel resection during elective bowel surgery. Venous blood was taken before anaesthesia, intra-operatively and on postoperative day 1. CRF extracted from tissue and blood was quantified using radioimmunoassay. On day 1 postoperatively, intestinal permeability was tested by urinary lactulose:mannitol (L:M) measurement. Institutional ethical approval was granted and patients gave written informed consent.

Results Trauma patients ($n = 6$, male/female = 6/0, age 27 ± 10.2 years, ISS 23 ± 6.8) were younger than elective patients ($n = 6$, male/female = 4/2, age 52.8 ± 7.7 years, $P < 0.0006$), and had significantly lower mean tissue [CRF] (0.034 ± 0.015 x 10^{-3}% total protein (TP)) than elective patients (0.117 ± 0.075 x 10^{-3}%TP, $P = 0.023$). The median (IQR) intraoperative blood CRF level was higher in trauma patients (86.7 (5.5) pg/ml vs 59.8 (9.6) pg/ml, $P = 0.03$) than elective patients. In trauma patients this correlated negatively with postoperative L:M ($r = -0.9$, $P = 0.037$), although intestinal permeability was greatly and equally increased in both groups (combined mean ± SD L:M, 0.58 ± 0.55).

Conclusions CRF is detectable in bowel tissue following trauma and is significantly lower in trauma vs elective surgery patients, while CRF in blood may be a factor associated with gut barrier changes following shock and emergency laparotomy.

P151

Using the Cortrak magnetic device to facilitate early enteral nutrition in critically ill patients

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Critical Care 2007, **11(Suppl 2):**P151 (doi: 10.1186/cc5311)

Introduction Confirmation of correct nasogastric tube (NGT) positioning is required before commencement of enteral nutrition

(EN). In the ICU, however, the use of sedation, 24-hour feeding and proton pump inhibitors can make the standard confirmatory methods recommended by the UK National Patient Safety Agency (UKNPSA) [1] unreliable, and result in the need for multiple chest X-rays (CXR), increased cost and feeding delay. We studied the role of the Cortrak® (Viasys MedSystems, USA) against standard practice, and assessed the following outcomes: time required to confirm correct NGT position, time to starting feeding, and potential cost savings.

Methods We enrolled patients admitted to our ICU who required NGT insertion for EN. A Corflow NGT with Cortrak stylet was inserted, and the position monitored using the Cortrak magnetic sensor. The Cortrak system tracks the trail of the stylet tip as it progresses towards the stomach and provides a visual representation of the NGT position on a video screen, allowing rapid determination of insertion success. The position of the NGT was also assessed using pH paper and/or CXR, as appropriate, according to the standard UKNPSA guidelines. Data were analysed using a paired *t* test and time-to-event analysis.

Results Fifty-two patients were recruited and 57 insertions were analysed: 32 first insertions, and 25 reinsertions. Gastric content was successfully aspirated in 40% (23/57) of insertions, and 14% (8/57) had pH 6 or above. Forty-six CXRs were requested, with three patients requiring multiple CXRs. The Cortrak correctly confirmed the position of NGT in all 57 insertions. The time required to confirm the NGT position was significantly less with the Cortrak than with conventional methods (mean ± SE Cortrak: 9.6 ± 1.7 min; pH paper: 11.6 ± 1.7 min; CXR: 122 ± 23 min; $P < 0.0001$). There was a 1.5-hour delay in starting EN in the standard practice group compared with the Cortrak group (mean ± SE 3.98 ± 0.5 hours vs 2.58 ± 0.4 hours, $P = 0.049$). If the Cortrak results had been acted upon, 46 CXRs could have been avoided, which equates to a saving of £2,300 (€3,220).

Conclusions The Cortrak demonstrated 100% accuracy in confirming the position of NGT in this patient series. It exposes patients to less radiation, facilitates earlier EN and is cost-effective. Consideration should therefore be given to including it into the standard UKNPSA guideline.

Reference

1. **UK National Patient Safety Agency** [http://www.npsa.nhs.uk]

P152

Propranolol attenuates factors affecting hypermetabolism in pediatric burn patients

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Background The aim of this study was to determine the effect of propranolol on infections and clinical parameters during the acute phase postburn. Severe thermal injury is followed by a period of hypermetabolism that is directly proportional to the size of insult sustained. Infection and multiorgan failure are now the leading cause of death from severe thermal injuries. Propranolol, an anticatabolic agent, improves hypermetabolism postburn. However, there is evidence that propranolol worsens immune function and increases the incidence of infection in critically ill patients.

Methods Sixty-six patients with burns >40% total body surface area were enrolled into the study and randomized to receive standard burn care (controls, $n = 33$) or standard burn plus propranolol for more than 21 days (propranolol, 0.5–1.5 mg/kg every 6 hours, $n = 33$). Biopsies were taken three times a week for microbiological determination. Clinical parameters were collected and blood was drawn at regular intervals throughout the hospital course and analyzed for IGF-1, IGFBP-3, and HGH. Patients underwent weekly resting energy-expenditure measurements. Statistical analysis was performed using analysis of variance with Bonferoni's correction and Student's *t* test where applicable.

Results Propranolol treatment reduced heart rates by 10% and significantly improved stroke volume throughout the acute hospital stay compared with controls ($P < 0.05$). Resting energy expenditure was significantly decreased in the propranolol group when compared with controls at discharge ($P < 0.05$). Infection rates on admission were the same for both groups (17% propranolol vs 22% control). The incidence of infection throughout hospital course was significantly lower in the propranolol group (60%) compared with controls (87%) ($P < 0.05$). Propranolol significantly increased IGF-I, IGFBP-3, GH, and prealbumin, while it significantly decreased CRP and fatty acids ($P < 0.05$).

Conclusions Following a severe burn, propranolol attenuates infections, inflammatory markers and fatty acid levels while improving cardiac work and endogenous anabolic hormone levels. We suggest that propranolol is a safe and efficacious modulator of the postburn response.

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Early enteral immunonutrition following gastric and oesophageal surgery

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Introduction The study investigates the effect of early enteral immunonutrition on patient recovery after extensive elective surgery in the upper abdomen [1,2]. It investigates the speed of patient recovery administering early enteral immunonutrition combined with total parenteral nutrition [3].

Materials and methods The total of 40 patients who had undergone this type of surgery were involved in this study. Near the end of the surgery procedure a percutaneous jejunostomy was performed in 20 patients (G1), and enteral nutrition started on the first postoperative day with small doses of immunonutrient (Reconvan) 10 ml/hour. After every 12 hours the tolerance was estimated (abdominal distension, diarrhoea, vomiting). After every 24 hours the immunonutrient dose was increased by 20 ml/hour until we reached the maximum of 80 ml/hour. In the first three postoperative days the patients were also administered total parenteral nutrition, and after that only enteral nutrition. The other group of 20 patients (G2) was administered only parenteral nutrition from the first postoperative day. Preoperatively, every patient was measured for body weight, body height and body mass index, and using laboratory tests we established the levels of albumin, transferine, blood urea nitrogen and creatinine. On the third and ninth postoperative days we repeated the same laboratory tests, and measured the daily loss of nitrogen by excretion of urea in urine.

Results and discussion Patient recovery was faster in G1. The average patient stay in ICU was 5 ± 1 days (G1) vs 10 ± 2 days (G2). The average hospital stay was 22 ± 3 days (G1) vs 29 ± 5 days. Peristalsis was detected on the third day as an average (G1) vs 4.5 days (G2). A decrease in pulmonary complications was achieved in G1 (one pleural effusion) vs G2 (eight pleural effusions). Laboratory tests show that patients in G1 are in lower catabolism compared with G2 patients.

Conclusion Early enteral immunonutrition through jejunostomy is an efficient and safe method of patient nutrition with fewer postoperative complications, and also accounts for a hospital cost decrease of 50%.

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Feasibility of the REDOXS study – reducing deaths due to oxidative stress: a randomized pilot trial of glutamine and antioxidant supplementation in critically ill patients

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Introduction A large randomized trial is needed to evaluate the safety and efficacy of glutamine (GLN) and antioxidant (AOX) supplements. However, high doses of such nutrients via enteral and parenteral routes early in the course of critical illness is often interrupted by high illness acuity and other treatment priorities. The purpose of this pilot trial was to evaluate the feasibility of delivering high-dose GLN and AOX supplements early on in the course of critical illness, and to estimate recruitment for the larger REDOXS study.
Methods In six Canadian centers, using a 2 x 2 factorial design, we randomized mechanically ventilated adults who had two or more organ failures within 24 hours of ICU admission to one of four groups: (1) GLN (0.35 g/kg/day i.v. plus 30 g enterally), (2) AOX (500 μg selenium i.v. and 300 μg selenium, 20 mg zinc, 10 mg β-carotene, 500 mg vitamin E, and 1,500 mg vitamin C enterally), (3) both AOX + GLN, and (4) placebo. Supplementation was continued for a minimum of 5 days up to 28 days and was provided independent of nutrition support. We recorded the time from ICU admission to randomization, the time to start of supplements and nutrition support parameters.
Results From April 2005 to April 2006, 80 patients were randomized (average 2.1/site/month). The median time from ICU admission to randomization was 18.2 hours (range 11.6–21.1 hours). All patients received parenteral supplements, the median (range) time to start was 2.7 hours (2.0–3.8 hours) and 78/80 (98%) received enteral supplements with a median (range) of 2.6 hours (1.9–4.5 hours) from randomization. The mean duration of supplements was 11.1 days (enteral) and 12.2 days (parenteral). The mean volumes of enteral and parenteral supplements received were 84% (range 45–102%) and 93% (range 54–100%) prescribed volumes, respectively. The average prescribed energy and protein intakes were 1,802 kcal/day and 86 g protein/day but the average daily percentage energy and protein received from nutrition support was only 65% (range 4–95%) and 62% (range 2–97%) of that prescribed, respectively.
Conclusion In critically ill patients with organ failure we provided adequate amounts of study supplements via both enteral and parenteral routes in the early phases of acute illness, independent of nutrition support. We estimated recruitment of at least two patients/site/month for our future trial.
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Effect of high-dose selenium substitution on selected laboratory parameters and prognosis in critically ill patients

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Introduction Standard selenium (Se) substitution (30–75 μg/day; 0.4–0.9 μmol/l) in the critically ill is not sufficient for a sustained plasma level (0.58–1.82 μmol/l; 46–143 μg/l). Standard Se substitution keeps the plasma level in the range 0.28–0.42 μmol/l. High-dose Se substitution correlated with a decrease in mortality of patients with SIRS. The influence of high-dose substitution on selected parameters, MAP and mortality in the critically ill were evaluated in a prospective randomized clinical trial.
Methods One hundred and twenty-three patients (78 males, 45 females, median age 62.7 and 60 years, respectively) were randomized into group A (SOFA 19.27) and group B (SOFA 10.23). Group A received standard Se substitution: 30–75 μg NaSelenite i.v./day. Group B received high-dose Se substitution according to a protocol: 1,000 μg at day 1, followed with 500 μg at days 2–14 of NaSelenite i.v. The plasma levels of Se, prealbumin, albumin, CRP, PCT, cholesterol, gluthathionperoxidase GSHPx, D-dimer, creatinine clearance and leucocytes were examined daily. MAP trends and 28-day mortality were evaluated as clinical markers.
Results The Se plasma level was significantly higher in high-dose Se-substituted patients (0.56 μmol/l vs 0.88 μmol/l, $P < 0.001$). GSHPx was significantly higher in high-dose Se-substituted patients (4,864 U/l vs 6,097 U/l, $P < 0.001$). No significant differences were found in the level of albumin, prealbumin, CRP, PCT, leucocytes, fibrinogen, cholesterol, D-dimer and creatinine clearance and MAP. The 28-day mortality was lower in a high-dose Se-substituted patients (33% vs 37%), but not significantly.
Conclusion The critically ill have an increased demand for Se, which is essential for synthesis of Se enzymes and Se proteins. The increased demand for Se is not covered by standard substitution. High-dose Se substitution (500–1,000 μg/day) normalizes its plasma level and increases the GSHPx plasma level. High-dose Se substitution has no adverse reactions. The decrease of 28-day mortality in high-dose Se-substituted patients is not significant. The trial on high-dose Se substitution further continues.

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Magnesium deficiency in the surgical intensive care unit

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Introduction Magnesium (Mg) deficiency is a common and yet underdiagnosed problem. Mg deficiency has been demonstrated in 50% of all ICU patients. These patients have significantly higher morbidity and mortality rate. The aim of this work was to detect the presence of Mg deficiency using a Mg loading test and to evaluate the safety and efficacy of Mg replacement therapy in cancer patients after major gut surgery.

Methods Sixty adult patients admitted to the ICU after major GIT surgery were enrolled in the study, on the basis of a documented Mg serum level < 0.8 mmol/l on arrival at the ICU. Exclusion criteria were cardiac disease, liver dysfunction or serum creatinine > 1.3. Patients were randomly allocated to one of two groups: the Mg group received 20 mmol (5 g) Mg sulfate, infused daily over 6 hours for 3 days; and a control group received an equivalent amount of 5% dextrose. In the Mg group the next scheduled dose of $MgSO_4$ was held if a serum magnesium level > 1.1 mmol/l, hypotension or bradycardia was recorded. Baseline and daily measurements of serum Mg, potassium, sodium, calcium and creatinine were done. Twenty-four-hour urine collection was used to determine the total urinary excretion of Mg. The net Mg balance (total Mg given − total urine Mg) was calculated. In the Mg group, Mg-deficient patients (retainers) who excreted < 70% of the Mg given ((urine Mg in mmol / daily Mg given) x 100) and Mg nondeficient patients (nonretainers) who excreted > 70% of the total Mg given were recorded.
Results Patients in the Mg group showed a statistically significant increase in mean serum Mg at days 1, 2, and 3 compared with the control group and with day 0 (0.73 ± 0.1, 0.81 ± 0.17, 0.8 ± 0.1, and 0.85 ± 0.11 mmol/l at days 0, 1, 2, and 3, respectively). The mean total amount of Mg given, the mean total urine Mg excretion and the net Mg balance were significantly higher in the Mg group compared with the control group (58 ± 0.17 vs 11.3 ± 2.8 mmol, $P > 0.001$; 34.0 ± 2.7 vs 15.5 ± 3.8 mmol, $P > 0.001$; 25.6 ± 1.65 vs 5.2 ± 0.93 mmol, $P > 0.001$). In the Mg group, the numbers of Mg retainer patients were 24 patients on day 1, 21 on day 2 and nine patients on day 3. Mg nonretainer patients were six patients on day 1, nine on day 2 and 21 patients on day 3. Patients in the Mg group showed better haemodynamic stability and fewer ventricular arrhythmias.
Conclusion Mg deficiency is common in ICU patients. Mg sulfate administered according to the above regimen is safe. Early treatment of Mg deficiency significantly increased the serum Mg level and provided a better magnesium, potassium and calcium balance, resulting in a shorter ICU stay.

P157

Parenteral nutrition in the intensive care unit: can we deliver better care to our patients? Preliminary results from a multicenter, prospective, cohort study

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Introduction Nutrition therapy is an integrant aspect of ICU support and can influence outcomes. A delay to starting nutrition support after 24 hours of ICU admission is associated with increased morbidity and mortality [1], and certain lipid emulsions can exacerbate the inflammatory cascade. For an appropriate evaluation of the impact of these and other recent research findings, information regarding the use of parenteral nutrition (PN) in the ICU is needed.
Methods This is the interim analysis of a multicenter, prospective, cohort study aimed to obtain information regarding the use of PN. Data were collected during 3 months from ICU patients over 18 years of age on the use of PN in 20 adult ICUs in Brazil using a web-based clinical research form.
Results One hundred and sixty-six patients were included in this analysis. Among the main results, 63.69% were males and 77.78% were considered malnourished. The mean SOFA score was 6.21, with a mean APACHE II score of 19.39. In total, 97.23% of the PN used in Brazil were manufactured by third-party companies and this was associated with a significant delay in the beginning of the infusion (median time 29.76 hours), and elevated in-ICU (50%) and inhospital (55.17%) mortality rates. A total 24.29% of the patients were immunosuppressed. The most used lipid source was long-chain triglycerides/medium-chain triglycerides (80.69%).
Conclusions The use of PN in Brazil is associated with a significant delay in the start of infusion and high mortality rates. The most used lipid emulsion (long-chain triglycerides/medium-chain triglycerides) has been associated with more apoptosis [2] and compromised lymphocyte proliferation [3]. The overall findings of these study indicate that strategies to reduce the delay in start of PN and the use of better lipid sources must be adopted to provide better assistance for patients in need of PN in Brazil.
Acknowledgement Supported by a research grant from Baxter Hospitalar Ltda.
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P158

Ultrasound-guided vs ultrasound-assisted central venous catheterization

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Introduction Ultrasound (US) significantly facilitates central venous catheterization, reducing the percentage of failure, the percentage of accidental arterial puncture, and the percentage of complications (haematoma, haemothorax, pneumothorax). Nonetheless, it is not clear whether US guidance (USG) (so-called 'dynamic' or 'real-time' US techniques: that is, venipuncture under direct US control) may be better than US assistance (USA) (so-called 'static' or 'indirect' US techniques: that is, US imaging of the vein, with or without skin marking, and then blind venipuncture).
Methods From February 2005 to September 2006, our CVC Team adopted the following protocol for internal jugular vein (IJV) catheterization: (a) both IJVs were evaluated to assess position, dimensions, and other features known to affect the risk of catheterization; (b) then, a decision was made whether to continue with USA or USG; (c) the IJV was accessed via the low lateral Jernigan approach; (d) after two failed USA attempts, USG venipuncture was adopted; (d) when IJVs were not available, USG venipuncture of other central veins was the second choice; and (e) fluoroscopy was used only in paediatric patients, but all patients had a postoperative chest X-ray to rule out pneumothorax and malposition.
Results In 20 months, 821 central venous catheters (CVCs) were inserted in adults (181 short-term CVC + 218 tunnelled + 316 ports) and in paediatric patients (age range 20 days–13 years,

average 5.5 years: 20 short-term + 84 tunnelled + two ports). In adults, the procedure started as USA in 522 and as USG in 299 cases: a shift from USA to USG was necessary in 8%. USG was the first choice in all paediatric cases. The IJV was successfully cannulated in most adult patients, with very few exceptions (innominate vein in 12 cases, axillary vein in two cases, femoral vein in one case, all by USG). In one paediatric patient, the CVC was inserted in the subclavian vein, via a supraclavicular USG approach. Complications were: failure 0%; pneumothorax 0%; haemothorax 0%; accidental arterial puncture 1.1% (1.7% USA vs 0.3% USG); haematoma 0.4% (only for USA); malposition (0.8%, exclusively with the left IJV).

Conclusion In conclusion, (a) we had a minimal incidence of complications, (b) USG was associated with a relevant reduction of the risk of accidental arterial puncture and haematoma, if compared with USA, and (c) choosing the left IJV was associated with a higher risk of malposition.

P159

Advantages of ultrasound-guided peripherally inserted venous access (PICC and midline catheters) in critically ill patients

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Introduction In the critically ill, a reliable peripheral or central venous access is of paramount importance. Nonetheless, access may be difficult or may carry a significant risk of complications (pneumothorax, central line infection, etc.). Peripherally inserted venous catheters – either central (PICC) or peripheral (midline catheters (MC)) – are associated with a low risk of catheter-related bacteremia; also, using the ultrasound guidance and the micro-introducer technique (UG + MIT), they can be inserted in any patient, regardless of the availability of superficial veins.

We have reviewed our experience of 56 peripherally inserted catheters in 53 patients in different ICUs (surgical ICU, trauma unit, coronary unit, neurosurgical ICU, stroke unit, pediatric ICU, etc.); all catheters were positioned at the mid-arm, in the basilic vein or in the brachial veins, using UG + MIT. We assessed the feasibility of this technique in the acutely ill and the rate of complications.

Methods and results We inserted 16 PICC and 40 MC in patients requiring prolonged venous access (estimated >15 days); nine were septic, six had coagulopathy, 21 had tracheostomy. We used both silicone and polyurethane 4 Fr catheters. Procedures were performed by a team of trained physicians and nurses. Catheter insertion was easy in most cases, and immediate complications were few (no failure; one hematoma; no arterial or nerve injury). Late complications were: one local infection; three thrombosis (two requiring removal); four cases of damage of the external catheter (due to poor nursing or to inappropriate use of the catheter during rx procedures), all easily repaired; one dislocation; no catheter occlusion; no catheter-related bacteremia. Most catheters stayed in place for a prolonged time (range 9–65 days, median 19 days); only three were removed because of complications.

Conclusion Our experience with PICC and MC was characterized by an extremely low rate of infective and thrombotic complications. Venous access was achieved in any patient, even with limited availability of peripheral veins. The use of US-inserted PICC and MC should be considered when central access is not advisable or is contraindicated.

P160

A comparison between ultrasound-guided central venous line placement and an anatomical landmark technique

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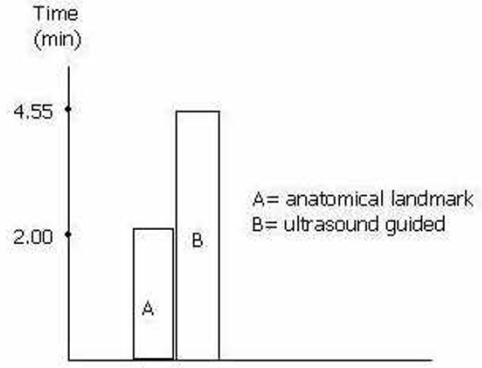
Introduction Ultrasound has been introduced in the insertion of central venous lines to reduce the complications associated with the conventional landmark technique [1]. We compared both techniques; we noted the number of attempts, the duration of insertion and complications.

Methods Thirty patients were randomly selected, from the operating theatre and ICU, who required placement of a central venous catheter. The central venous catheter placement was performed by two experienced anaesthetists with more than 6 years experience in anaesthesia and intensive care. In 15 patients the internal jugular venous catheter placement was performed using the external anatomical landmark technique, and in the other 15 patients the placement was under ultrasound guidance. The duration of insertion was recorded from the moment the needle touched the skin until insertion of the catheter and removal of the guide wire. The numbers of attempts as well as immediate or delayed complications were recorded.

Results The central venous catheter placement was successfully performed from the first attempt in both groups. There were no immediate or delayed complications noted; however, the mean time of insertion was longer in the ultrasound-guided group (4.55 min) compared with the external anatomical landmark group (2 min) (Figure 1).

Discussion Some studies have been designed to evaluate ultrasound-guided central venous catheter placement compared with the conventional method based on external anatomical landmarks. These studies demonstrated the superiority of ultrasound-guided central venous line placement over the external anatomical landmark technique. However, there was no time gain demonstrated in ultrasound-guided placement [2]. On the other hand, a number of studies have expressed several reservations concerning the systematic use of ultrasound guidance for central line placement [3]. In our patients we found that the use of ultrasound neither altered the rate of complication nor the number of attempts in central venous catheter placement. Also the duration of placement of the central line catheter using the external

Figure 1 (abstract P160)



anatomical landmark technique was shorter than in the ultrasound-guided method.

Conclusion The external anatomical landmark technique in central line placement is considered a safe method with experienced hands. The time of insertion of a central line using the external anatomical landmark technique was shorter than the ultrasound-guided placement method. It is essential for all trainees to be taught both methods for central line placement to be able to place a central line catheter quickly and safely in emergency situations and when an ultrasound machine is not available.

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P161

Continuous assessment of inspiratory resistive work during different types of pulmonary oedema in isolated rat lungs

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We recently demonstrated in isolated blood perfused rat lungs subjected to i.t. LPS-induced pulmonary oedema that the continuous measurement of inspiratory resistive work is a good indirect indicator of progressive lung oedema [1]. Here we extend these findings to two other types of pulmonary oedema: hydrostatic oedema induced by elevation of the left atrial pressure, and alveolar oedema (ALV) by infusing normal saline into the trachea at two different infusion rates (2 and 4 ml/hour for 120 min).

See Table 1. Our results indicate that the continuous measurement of inspiratory resistive work is a good indicator of both permeability and hydrostatic lung oedema, but not of pure alveolar oedema (absence of interstitial oedema).

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P162

Prevalence of respiratory support in the community – the Surrey experience

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Introduction This study aimed to establish the prevalence of home ventilatory and respiratory support within the catchment area of Frimley Park Hospital in Surrey. The number of patients receiving respiratory support at home has been increasing nationally since 1990 [1]; however, no local data exist. This trend is likely to continue as domiciliary ventilation gains popularity for the treatment of obstructive sleep apnoea and certain groups of COPD patients [2].

Method A postal survey was sent out to practice managers in the local catchment area. They were asked to provide data for: patients on home ventilatory support for any reason, patients with long-term tracheostomies, patients with COPD who are on home oxygen or who you would classify as end stage, and the total number of patients registered to the practice. This was followed up with a telephone call approximately 2 weeks later. Many were then e-mailed the same questionnaire. A further two telephone calls to each practice were made as necessary in order to obtain data.

Results Out of 67 surgeries contacted, we achieved a response rate of 65%. Thirty-three practices (49%) were able to provide complete data, six (9%) provided partial data, and a further five (7%) were unable or unwilling to provide any data. Twenty-three (34%) practices did not respond. A total of 318,130 patients were listed by the responding practices. Of these: 23 patients live with long-term tracheostomies, a prevalence of 1 in 13,800; 65 patients receive mechanical respiratory support at home, a prevalence of 1 in 4,900; and 207 patients receive oxygen therapy at home, a prevalence of 1 in 1,500.

Discussion This study suggests that the Frimley Park Hospital population of 350,000 currently contains about 100 individuals requiring mechanical respiratory support at home. This is of concern as currently there is no formal support for any of these high-risk patients other than ventilator maintenance. Simple problems precipitate hospital admission and rapidly trigger outreach or intensive care review. The current position is clearly unsatisfactory and must be addressed by PCTs if patient numbers increase.

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Table 1 (abstract P161)

	Dynamic lung compliance (ml/cmH_2O)	Weight gain (g)	Wet/dry lung weight ratio	Inspiratory resistive work (ml x cmH_2O)
Control ($n = 6$)	0.35 ± 0.06	0.54 ± 0.21	6.37 ± 0.35	0.98 ± 0.35
LPS ($n = 12$)	0.28 ± 0.02	4.63 ± 0.63	8.92 ± 0.21	10.45 ± 1.15
Hydrostatic ($n = 7$)	0.38 ± 0.06	1.97 ± 0.24	6.46 ± 0.33	1.65 ± 0.54
ALV 2 ml/hour ($n = 6$)	0.24 ± 0.04	2.66 ± 0.14	10.22 ± 0.60	–1.09 ± 0.54
ALV 4 ml/hour ($n = 4$)	0.07 ± 0.02	3.74 ± 0.79	9.08 ± 0.94	0.96 ± 1.13

Data presented as the mean ± SE after 120 minutes of isolated lung perfusion.

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Intensive care unit patients on mechanical ventilation at a university hospital in southern Brazil: characteristics, mortality, frequency, and mortality risk factors

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Introduction Acute respiratory failure (ARF) is a frequent cause of admission to ICUs and frequently necessitates mechanical ventilation (MV). Knowledge about the frequency and risk factors associated with requirements for MV is crucial to improve outcomes. The objectives of our study were to determine the characteristics, frequency of MV, overall and specific mortality rates and mortality risk factors in patients who required MV in the ICU of a general university hospital in southern Brazil.
Methods A prospective cohort of 751 adult patients admitted to the ICU who needed MV for at least 24 hours, between March 2004 and July 2006. Data were collected on each patient at the inclusion in the study and on a daily basis, during the course of MV for up to 28 days.
Results The frequency of MV was 30%; the overall and specific mortality rates were 15% and 50%, respectively. The mean (±SD) age was 57 ± 21 years; 52% were males; the mean APACHE II score was 22.2 ± 8.2; 69% were medical patients; the mean duration of MV was 11 ± 7.9 days; 93% were on invasive MV. A multivariable analysis was performed to identify the variables associated with death. These included sepsis ($P = 0.02$), MV duration ($P < 0.001$), renal failure ($P = 0.006$) prior to MV, and the following variables that occurred during the MV period: sepsis ($P = 0.004$), acute lung injury/acute respiratory distress syndrome ($P = 0.001$), renal failure ($P < 0.001$), haematological failure ($P = 0.02$) and vasoactive drug use ($P < 0.001$). It should be noted that selected ventilatory monitored variables were included in the multivariate model. However, they were not associated with mortality in our study sample.
Conclusions Our results indicate a frequency of patients on MV of 30% with an elevated specific mortality rate (50%). Sepsis, MV duration, renal failure prior to MV, and sepsis, acute lung injury/acute respiratory distress syndrome, renal failure, haematological failure and vasoactive drug use during the MV period are risk factors for mortality in 28 days after starting MV. Identification of these factors may allow early interventions to attempt to mitigate these poor outcomes.

P164

The effects of adaptive pressure ventilation–synchronised intermittent mandatory ventilation and pressure-controlled synchronised intermittent mandatory ventilation on pulmonary mechanics and arterial gas analyses during laparoscopic cholecystectomy

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Background Hypercapnia and elevated intraabdominal pressure from carbon dioxide (CO_2) pneumoperitoneum can adversely affect respiratory mechanics and arterial blood gases. We tested the hypothesis that adaptive pressure ventilation–synchronised intermittent mandatory ventilation (APV-SIMV) may provide better pulmonary mechanics, CO_2 homeostasis and pulmonary gas exchanges with less frequent ventilatory settings (tidal volume (TV), respiratory rate (RR)) and lower peak inspiratory pressure (P_{peak}) and plateau pressure (P_{plat}) than pressure-controlled synchronised intermittent mandatory ventilation (P-SIMV) in patients undergoing laparocopic cholecystectomy (LP).
Method The study group consisted of 40 patients (APV-SIMV $n = 20$, P-SIMV $n = 20$). LP was performed under total intravenous anesthesia. After induction of anesthesia, a RR of 12 breaths/minute, and an inspiratory:expiratory rate of 1:2 and PEEP of 6 cmH_2O were set for both groups. APV-SIMV was started with a target TV of 8 ml/kg. P-SIMV was started with the inspiratory pressure (P_{ins}) that will provide 8 ml/kg TV. The settings were changed until target parameters to maintain normocapnia and normoxia were achieved ($ETCO_2$ 30–35 mmHg, $PaCO_2$ 35–45 mmHg and SaO_2 >90%). When the target parameters could not be achieved, the first RR was increased by 2 breaths/minute up to 16 breaths/minute, then the volume or pressure was titrated to induce 1 ml/kg increases in TV up to 10 ml/kg. The initial FiO_2 was set to 50%. FiO_2 was increased with increments when the SaO_2 fell below 90%. PaO_2/FiO_2, static compliance, VD/VT, P_{peak} and P_{plat}, $ETCO_2$, inspiratory and expiratory resistances, and arterial blood gas analysis were recorded before, during and after pneumoperitoneum. Statistical analysis were carried out using the chi-square test, paired test and independent samples test when appropriate.
Results Demographic data were similar between groups. Pneumoperitoneum caused significant decreases in static compliance and arterial pH, and increases in P_{peak} and P_{plat}, VD/VT and $ETCO_2$ in both groups. However, APV-SIMV resulted in fewer setting changes, lower peak and plateau pressures, VD/VT, and $ETCO_2$ levels when compared with P-SIMV ($P < 0.025$).
Conclusion APV-SIMV may provide better results then conventional P-SIMV in patients undergoing LP.

P165

The influence of cycling-off criteria and pressure support slope on the respiratory and hemodynamic variables in intensive care unit patients

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Introduction Modern mechanical ventilators allow changes in the flow cycling-off criteria and the pressure slope during pressure support ventilation (PSV). Changes in the cycling-off flow criteria of PSV can modify the expiratory synchrony between the mechanical and neural inspiration termination. The influences of the slope changes on the respiratory parameters in ICU patients are still under investigation.
Objectives To compare the effects of two different flow cycling-off criteria and the effects of two different pressure slopes (150 ms or 300 ms) of PSV on the respiratory parameters of ICU mechanically ventilated patients.
Methods We prospectively evaluated 20 intubated and mechanically ventilated adult ICU patients recovering from acute respiratory failure who could be comfortably ventilated on pressure support mode (PSV) with pressure support of 15 cmH_2O, PEEP of 5 cmH_2O and FIO_2 of 40%. Patients were ventilated on PSV, with 25% and 40% of peak expiratory flow cycling criteria, and were submitted to 150 ms and 300 ms pressure slope delay. We evaluated the respiratory rate, expiratory tidal volume, minute ventilation, VCO_2, $VTCO_2$, $ETCO_2$, mean arterial pressure (MAP), heart rate and SpO_2.

Table 1 (abstract P165)

Slope	Heart rate	SpO_2	Cycling-off (%)	Respiratory rate	Tidal volume (ml)	Minute volume (l/min)	VCO_2	$VTCO_2$	$ETCO_2$	MAP
0.15	83.4	98.8	25	18.2	587.5	10.6	193.6	11.2	27.8	96.4
0.15	83.9	98.8	40	19.2	560.7	10.0	183.7	10.88	28	96.2
0.30	83.6	98.7	25	19.4	588.4	10.5	192.8	11.54	28	98.2
0.30	83.6	98.9	40	19.7	565.2	10.2	187.8	10.61	28.2	97.7

Results Comparisons between different slope and cycling-off values did not result in any statistically significant changes for the evaluated variables (Table 1).
Conclusion Changes in cycling-off criteria from 25% to 40% of the peak flow and on the pressure slope from 150 ms to 300 ms do not affect other respiratory and hemodynamic variables in mechanically ventilated patients.

P166

AUTOPILOT-BT: an approach towards automatic mechanical ventilation

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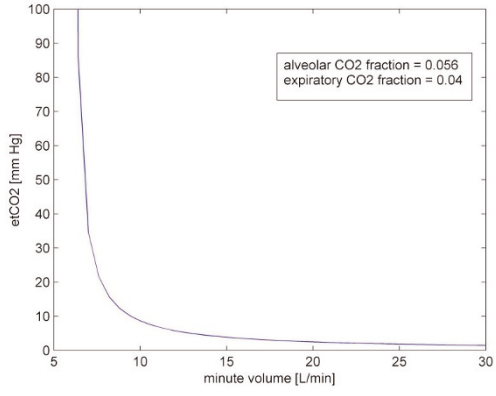
Critical Care 2007, **11(Suppl 2):**P166 (doi: 10.1186/cc5326)

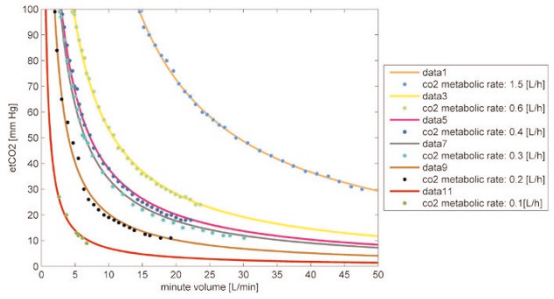
Introduction The clinical use of ventilators is limited due to a huge variety of different ventilation methods. The clinician – often under high cognitive load from the complicated technical equipment on an ICU – just uses a small subset of available parameter settings. The aim of the present study was to develop a closed-loop ventilation controller based on mathematical models and fuzzy logic.
Methods The system was designed to track a desired end-tidal CO_2 pressure ($PaCO_2$), to find a PEEP leading to maximum estimated respiratory system compliance and to maintain the arterial oxygen saturation (SaO_2) at an optimal level. We developed a program in LabView (National Instruments, Austin, TX, USA) on a laptop that is able to read the internal data of a ventilator (Evita 4; Dräger Medical, Germany) in real time. Respiratory signals (for example, SaO_2) are acquired from monitoring. Discrete measurements (for example, PaO_2) are either assumed constant until next measurement or are interpolated using a model-based approach evaluating, for example, the $etCO_2$ data. The course of $etCO_2$ following the setting of optimal frequency was evaluated to calculate the time required for equilibration of $etCO_2$.
Results A module automating the initial settings of the ventilator according to local ICU rules is realized. Modules were added that optimize breathing frequency with respect to $PaCO_2/etCO_2$ and FiO_2 according to SO_2 whenever no PaO_2 is available. A lung simulator (Michigan Instruments Inc., Grand Rapids, MI, USA) connected with the LS4000 (Dräger Medical) was used to evaluate the system. Exemplary results are presented in the figures, which show the minute volume/$etCO_2$ relationship (Figure 1) and a parametric fit of $etCO_2$ data (Figure 2). The adjustment of the frequency is based on the current $etCO_2$ model.
Conclusion Automation is a '*sine qua non*' to achieve optimal patient individualized ventilation support. Our system is enabled to evaluate a therapeutic strategy and to base the settings of the ventilator on current trends/drifts observed in the data.

Figure 1 (abstract P166)



Minute volume/$etCO_2$ relationship.

Figure 2 (abstract P166)



Parametric fit of $etCO_2$ data.

P167

The impact of noninvasive versus invasive mechanical ventilatory support on survival in hematological patients with acute respiratory failure

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Objective To assess the impact on ICU survival of noninvasive (NIPPV) versus invasive mechanical ventilation (IPPV) as the initial ventilatory mode in hematological patients with acute respiratory failure.
Design A retrospective evaluation of a prospectively followed cohort of 277 hematological patients ventilated at the ICU of a tertiary care hospital between January 1997 and June 2006.
Results NIPPV was the initial ventilatory mode in 56 patients. ICU mortality in patients with initial NIPPV versus IPPV was 62.9% and

Figure 1 (abstract P167)

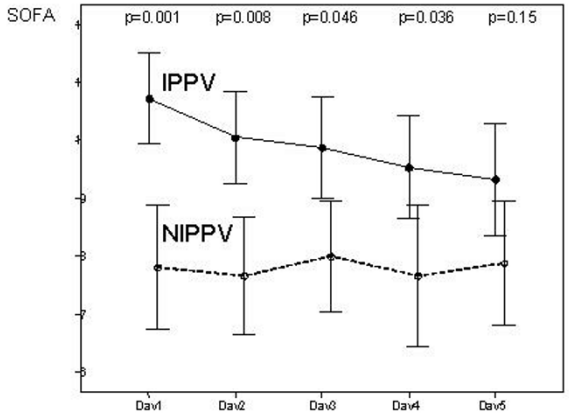
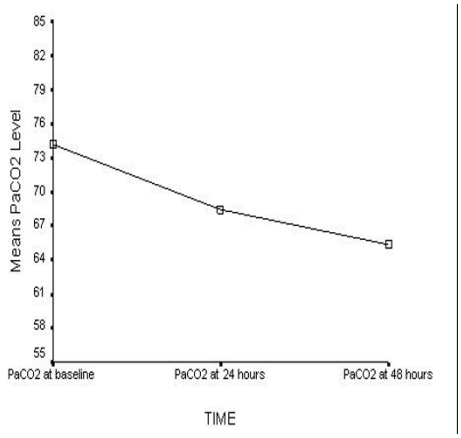


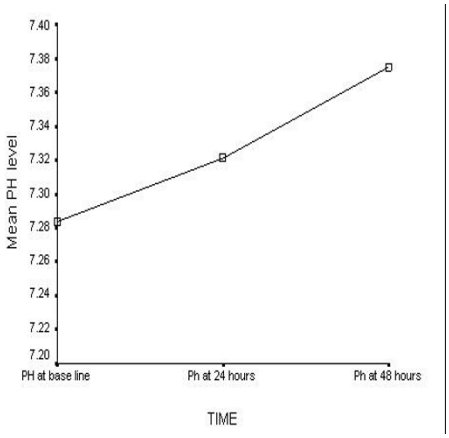
Figure 1 (abstract P168)



62.5%, respectively ($P = 0.99$), but SAPS II at ICU admission was lower in NIPPV patients (45 ± 15 vs 60 ± 18, $P < 0.001$). NIPPV was the sole mode of ventilation in 15 patients and was followed by IPPV in 41 patients (NIPPV–IPPV). ICU mortality in sole NIPPV patients was 35% compared with 76% in NIPPV–IPPV patients. In a multivariable analysis, the ICU mortality of ventilated patients was associated with SAPS II at admission (OR 1.029, CI 1.009–1.048, $P = 0.003$), NIPPV–IPPV (OR 2.73, CI 1.1–6.8, $P = 0.03$), and bacterial infection (OR 0.39; CI 0.21–0.73, $P = 0.003$). The mean change of SOFA between day 1 and day 5 was 0 (±2.6) in NIPPV patients ($n = 33$) compared with −1.6 (±4.3) in IPPV patients ($n = 87$) ($P = 0.001$) surviving beyond 5 days of ICU admission (Figure 1).

Conclusion NIPPV was not associated with better outcome in our population of hematological patients with acute respiratory failure. NIPPV followed by IPPV was an independent predictor of mortality.

Figure 2 (abstract P168)



P168

Physiological variables predictive of survival in patients with acute type II respiratory failure on noninvasive ventilation

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Critical Care 2007, **11(Suppl 2):**P168 (doi: 10.1186/cc5328)

Introduction There are very few data available from the Indian subcontinent regarding the use of noninvasive ventilation (NIV). We carried out this study to determine variables that could be used in the emergency room to predict survival in patients placed on NIV.

Methods This was a prospective, observational cohort study carried out from 2001 to 2005 on all patients presenting with acute type II respiratory failure and meeting criteria for NIV use. NIV was started in the emergency room at settings that were titrated according to arterial blood gases. Univariate and multivariate regression analysis was used to determine the effect on survival. $P < 0.05$ was considered statistically significant. The software used was SPSS 11.

Results The total number of patients enrolled was 119; 52.9% were males, 47.1% were females. The mean age was 63.3 years (±11.9). The most common cause of respiratory failure was COPD in 91.6%. A total of 56.3% patients were stuporus at presentation, and 7.5% fulfilled criteria for severe sepsis. There was no statistically significant difference between the baseline characteristics of the groups that survived or died. The overall survival rate for patients placed on NIV was 76.5%, the intubation rate was 12.6% and the length of hospitalization was 11.4 days (±10.9). Statistically significant improvements in pH and $PaCO_2$ occurred at 24 hours and 48 hours of NIV usage, compared with baseline (7.28 vs 7.37, $P < 0.001$; 74.2 vs 65.4, $P = 0.003$) (Figures 1 and 2). There was no significant change in PaO_2. The variables predicting survival were age (62.1 ± 12.5 years, 67.8 ± 8.7 years, $P = 0.025$), serum creatinine (1.1 ± 0.5 mg/dl, 1.7 ± 0.8 mg/dl, $P = 0.002$), pH at baseline (7.31 ± 0.09, 7.25 ± 0.9, $P = 0.005$), HCO_3 at baseline (36.1 ± 7.5 mEq/l, 32.4 ± 9.3 mEq/l, $P = 0.032$), pH at 48 hours (7.39 ± 0.07, 7.33 ± 0.06, $P = 0.002$), and need for endotracheal intubation (10%, 21%, $P < 0.05$).

Conclusion NIV improves outcomes in our setting. Physiological variables and the need for intubation can predict an improved survival in these patients.

P169

Rapid shallow breathing index – a key predictor for noninvasive ventilation

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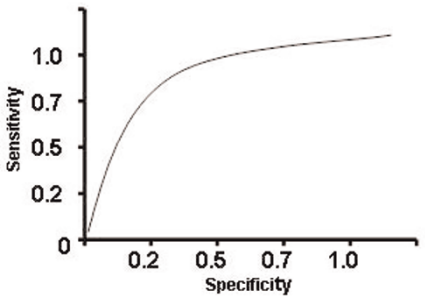
Critical Care 2007, **11(Suppl 2):**P169 (doi: 10.1186/cc5329)

Introduction The rapid shallow breathing index (RSBI) is the ratio determined by the frequency (*f*) divided by the tidal volume (VT). An RSBI <105 has been widely accepted by healthcare professionals as a criteria for weaning to extubation and has been integrated into most mechanical ventilation weaning protocols. We hypothesized that the converse of using the RSBI for weaning might be useful in predicting the need for noninvasive ventilation. Advancements in technology have made it easier to accurately attain bedside RSBI measurements. The purpose of this study was to ascertain a threshold value of RSBI that could predict the need for noninvasive ventilation (NIV) in patients presenting with acute respiratory distress to the critical care area (Cat 1) in the emergency department.
Methods This was a blinded, observational cohort trial that was approved by the Henry Ford Hospital Institutional Review Board. Henry Ford Hospital is an urban, tertiary institution in Detroit, Michigan with an emergency department census of 95,000 patient visits per year. Inclusion criteria: patients > 18 years of age triaged to Cat 1 with acute respiratory distress and for whom the decision to intubate, use NIV or discharge the patient had not been decided. Exclusion criteria: immediate intubation, NIV, or discharge from Cat 1. Baseline demographics and vital signs were collected prior to the initiation of the trial (Figure 1). The CO2SMO Plus! with the $ETCO_2$/flow sensor was used for obtaining bedside measurements. Patients would breathe through the $ETCO_2$/flow sensor for 60 seconds with nose clips.
Results The threshold value for RSBI that discriminated best between no NIV and the need for NIV was determined in 61 patients. Thirty-five patients who did not require ventilatory support had a mean RSBI of 105, and 26 patients with NIV had a mean RSBI of 222 ($P = 0.0001$). A receiver-operating-characteristic curve was constructed based upon the dataset in increments of 10 for the RSBI (Figure 2). An RSBI > 120 yielded a sensitivity of 0.81 and a specificity of 0.74 for determining the need for NIV. A likelihood ratio positive (LR+) of 3.14 further illustrates the formidable predictive value of the 120 RSBI.

Figure 1 (abstract P169)

Variables	No NIV	NIV	pValue
RSBI	105	222	0.001
E_TCO_2	34	36	0.573
Airway Deadspace	85	101	0.073
VCO_2	134	127	0.842
Alveolar Minute Ventilation	4.9	4.5	0.976
BORG Score	4	7	0.00002
PaCO2	41	52	0.110
pH	7.40	7.34	0.041
Lactate	1.8	2.5	0.132
APACHE II	7	11	0.002

Figure 2 (abstract P169)



Conclusion A RSBI of 120 or greater, as reflected by *f*/VT ratio, may be a predictor of when NIV support should be considered. Further prospective randomized studies are needed to validate the value of 120.

P170

Is threshold useful in accelerating weaning from mechanical ventilation?

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Introduction Threshold can be used as a physiotherapic tool in order to increase muscle strength, and this effect can be useful in weaning patients. However, there are still controversies considering its advantages during weaning from mechanical ventilation (MV). The goal of this study is to evaluate its effects in such a situation.
Methods Patients under MV for more than 48 hours and prone to weaning were studied. They were randomized to the control group or to the threshold group and followed daily until extubation, tracheostomy or death. The threshold group was trained twice daily. All cardiorespiratory variables, maximal inspiratory (PImax) and expiratory (PEmax) pressures were registered twice daily during the observation period. The length of weaning and success or failure were registered. Variables were compared by analysis of variance, Mann–Whitney U test and the chi-square test. Results are shown as the median, mean and standard deviation or as percentages. The significance level was $P < 0.05$.
Results Sixty patients were studied (52% men, mean age 64 ± 17 years, 18% with chronic obstructive pulmonary disease in threshold group vs 15% in control group). Comparing initial versus final cardiorespiratory variables in both groups, no important differences were observed with exception of PImax (increased from −33.5 ± 14.4 to −40.2 ± 13.4 cmH_2O in threshold group and changed from −37.1 ± 9.8 to −34.4 ± 9.6 cmH_2O in control group, $P < 0.05$) and PEmax (increased from 24.7 ± 12.7 to 29.4 ± 12.1 cmH_2O in threshold group and changed from 30.9 ± 13.5 to 27.1 ± 9.4 cmH_2O in control group, $P < 0.05$). No reduction was observed in the length of weaning (1.87 days with threshold versus 1.98 days in control group, $P > 0.05$). There was no difference concerning weaning success (73.5% with threshold versus 61.5% in control group, $P > 0.05$).
Conclusions Threshold during weaning from MV can cause an increase in both PImax and PEmax but, at least in these preliminary results, it was not associated with a decrease in length of weaning or an increase in weaning success.

P171

Application of treatment bundles reduces days on mechanical ventilation in critically ill patients

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Critical Care 2007, **11(Suppl 2):**P171 (doi: 10.1186/cc5331)

Background Reduction of time on the ventilator is a key concept to avoid complications. Recommendations include semirecumbent positioning (SRP) [1], low tidal volume ventilation (TV = 6 ml/kg) [2], prophylaxis for stress ulcer (SUP) [3], and deep vein thrombosis (DVTP) [4]. The goal of this study was to investigate whether staff training about these treatments decreases days on ventilation.
Methods All patients of a 50-bed ICU with mechanical ventilation >24 hours were included. From June 2005 to September 2005 (Audit I), patients were examined daily for SRP >30°, low tidal volume ventilation, DVTP, and SUP by an independent task force. Afterwards, nurses and physicians were trained for the monitored treatments. Audit II was then performed from March 2006 to June 2006.
Results One hundred and thirty-three patients (1,389 ventilator-days) were included in Audit I, 141 patients (1,002 ventilator-days) in Audit II. Data are expressed as the median (interquartile range) or percentage of implementation per ventilator-days (Table 1). On average, low tidal volume ventilation was adopted. DVTP and SUP were well implemented without training. There was no effect on frequency of pneumonia, ICU length of stay, or survival.

Table 1 (abstract P171)

	Audit I	Audit II	*P*
APACHE II	24 (10)	25 (11)	0.387
SRP (%)	24.9	49.6	<0.001
TV (ml/kg)	6.3 (2.2)	6.4 (2.3)	0.154
DVTP (%)	89.5	91.9	0.048
SUP (%)	94.5	94.9	0.712
Days on ventilation	6.0 (13)	4.0 (7)	0.017

Conclusion SRP could be successfully improved by staff training. Enhanced implementation was associated with reduction in days on ventilation.
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P172

Comparative study of two methods of weaning from mechanical ventilation in a cancer surgical intensive care unit

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Introduction The aim of the study was to compare the combination of intermittent mandatory ventilation plus pressure-support ventilation (SIMV+PSV) with intermittent trials of spontaneous breathing (ITSB) using a T-tube as two methods of weaning in a surgical ICU.
Methods A total of 104 patients who had been ventilated for more than 48 hours in the postoperative period from October 2005 to October 2006 were enrolled in the study. After fulfilling the weaning checklist they were randomly assigned into two groups: SIMV+PSV group ($n = 53$), and ITSB group ($n = 51$). In patients assigned to the SIMV+PSV group, the ventilator rate was initially set at 6–8 breaths/minute plus PSV of 15 cmH_2O and then both reduced, if possible, by 2 breaths/minute and 2 cmH_2O each time. Patients able to maintain adequate ventilation with SIMV of 2 breaths/minute and PSV of 5 cmH_2O for at least 2 hours without signs of distress were extubated. Patients assigned to the ITSB group were disconnected from the ventilator and allowed to breathe spontaneously through a T-tube circuit. The duration of the trials was gradually increased. Between the trials, assist–control ventilation was provided for at least 1 hour. Patients able to breathe on their own for at least 2 hours without signs of distress were extubated.
Results Until the first attempt was made for weaning, all patients received assist–control ventilation because of haemodynamic instability. The following underlying conditions were present: chronic obstructive pulmonary disease in 67 patients, neuromuscular disorders in nine patients, acute lung injury as a result of surgery in 14 patients, asthma in six patients and miscellaneous causes in eight patients. The duration of mechanical ventilation before weaning was 2.5 ± 0.5 days in the SIMV+PSV group vs 2.4 ± 0.4 days in the ITSB group ($P = 0.02$) and the duration of weaning was 6.2 ± 0.23 hours vs 8.3 ± 0.44 hours in the two groups, respectively ($P < 0.01$). Patients who remained extubated for 48 hours were classified as having successful extubation – the rate of successful extubation in the first 24 hours of starting weaning was higher for the SIMV group (79.2%) than in the ITSB group (64.7%, $P < 0.01$). The total duration of mechanical ventilation was 3.3 ± 0.3 days vs 5.2 ± 1.1 days and the ICU length of stay was 5.6 ± 1 days vs 7.5 ± 1.7 days in the two groups, respectively ($P < 0.01$).
Conclusions The use of SIMV+PSV as a weaning method in the surgical ICU lead to shorter duration of weaning, a higher rate of successful extubation, a shorter duration of mechanical ventilation and less ICU stay than the use of ITSB.

P173

Predicting successful weaning in a cohort of elderly patients

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Critical Care 2007, **11(Suppl 2):**P173 (doi: 10.1186/cc5333)

Introduction Aging causes structural and functional modifications in the respiratory system. The evidence that these changes could impair weaning in elderly patients, until now, was not clear. We designed a protocol to study possible differences between an adult group (AG, up to 60 years) and an elderly group (EG, >60 years) in a daily screening trial.
Methods One hundred and forty-four patients (79 EG and 65 AG) were studied. The primary outcome was weaning success (48 hours of spontaneous ventilation after extubation). The secondary outcome was differences in the conventional weaning predictors. Parameters studied included: respiratory rate (*f*), tidal volume (VT), frequency–tidal volume ratio (*f*/VT), gasometric and ventilatory parameters. The weaning method was a spontaneous breathing trial. Measurements were performed twice: just before the spontaneous breathing trial (T1) and 30 minutes after (T2). The

Table 1 (abstract P173)

Weaning criteria	T1 AG ($n = 65$)	T2 AG ($n = 65$)	T1 EG ($n = 79$)	T2 EG ($n = 79$)
f (breaths/min)	22 ± 59*	22 ± 5.2*	24 ± 5.5*	24 ± 5.4*
VT (ml)	560 ± 200*	550 ± 180*	470 ± 170*	480 ± 150*
f/VT	47 ± 24*	46 ± 19*	59 ± 28*	56 ± 24*

*$P < 0.05$ comparing AG and EG.

chi-square test, analysis of variance and *t* test were used in the analysis.

Results Weaning success was 86% both in EG and AG ($P = 0.989$). There were no differences in gasometric and in ventilatory parameters between groups. Comparisons in TI and T2 in AG and EG are presented in Table 1. Sensitivities of *f*/VT in T1/T2 were: for EG, 94 (86–98)/96 (89–98); for AG, 95 (86–99)/100 (94.8–100).

Conclusion The weaning success in our study is similar to that described in other trials. Older patients showed differences in *f*, VT and *f*/VT when compared with adults. However, there were no differences in weaning success.

P174

Heart rate variability during weaning from mechanical ventilation

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Critical Care 2007, **11(Suppl 2):**P174 (doi: 10.1186/cc5334)

Introduction Weaning from mechanical ventilation (MV) can be associated with cardiovascular changes including elevation of heart rate (HR) and development of arrhythmias. The behavior is not yet known of HR variability during weaning from MV comparing pressure support ventilation (PSV) and the T-tube (TT) in patients with and without heart disease. The aim of this study was to evaluate the impact on heart rate variability (HRV) in these groups of patients during PSV and TT.

Methods Patients with (group 1, $n = 8$) and without (group 2, $n = 22$) heart disease, under MV for at least 48 hours, were observed during 30 minutes of PSV or TT, in a random order. Variables analyzed were: APACHE score, length of stay in the ICU (LOS), and cardiorespiratory variables including the HR, respiratory rate (RR), rapid shallow breathing index (*f*/VT), maximum inspiratory (PImax) and expiratory (PEmax) pressure. Continuous ECG was recorded by the Holter method. The data of HRV were accomplished by analysis of the frequency domain. For statistical analyses, analysis of variance and *t* test were used. The level of significance was $P < 0.05$.

Results Values for the APACHE score, LOS, PImax and PEmax did not show significant differences comparing groups. The RR was significantly higher during TT than during PSV in group 1 (25 ± 6; 20 ± 4; $P < 0.01$), but similar in group 2 (22 ± 5; 22 ± 5; not significant (NS)). *f*/VT was significantly higher during TT in relationship to PSV in group 1 (65 ± 35; 39 ± 17; $P < 0.01$), but similar in group 2 (49 ± 19; 49 ± 22; NS). Changes in the RR interval comparing PSV and TT were significantly different in the entire group (0.48 ± 55; –30 ± 72; $P = 0.02$) as well as changes in the HR interval (–0.3 ± 8; 8 ± 12; $P < 0.001$). Changes in HRV by frequency domain were not significantly different comparing groups 1 and 2 in PSV and TT. The high frequency was in PSV (4 ± 21; 0.4 ± 11; NS), and in TT (–0.64 ± 12; 1 ± 12; NS). The low frequency was in PSV (–11 ± 22; 3 ± 14; NS), and in TT (–6 ± 17; 1.8 ± 19; NS).

Conclusion During weaning from MV, cardiac patients showed higher RR and higher *f*/VT during TT when compared with PSV. Furthermore, there were significant changes in the RR and HR intervals in TT. However, we did not find significant changes comparing HRV in groups, perhaps because the frequency domain analysis had low power to verify those changes.

P175

Assessment of melatonin, cortisol and rest–activity rhythms in critically ill patients weaning from mechanical ventilation

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Introduction Acute illness adversely affects a patient's circadian rhythms. Minimising the delayed restoration of these rhythms may have patient benefits. The aims of this study were to investigate the acute effects of exogenous melatonin on the rest–activity rhythms of patients recovering from critical illness, and furthermore to analyse the rhythms and relationship between plasma melatonin and cortisol levels.

Methods A randomised controlled trial in 24 critically ill patients weaning from mechanical ventilation. Ethics committee approval was granted and all patients provided written consent. Twelve patients in each group received placebo or 10 mg exogenous melatonin at 21:00 hours for four nights. Twelve plasma samples were taken periodically from the first 18 of these patients over a 24-hour period. Actigraphy was used to monitor patient activity. Rhythm analysis of plasma levels and activity data used single cosinor analysis and nonparametric parameters, respectively.

Results Both groups were well matched. There were no significant differences between the groups in any of the rest–activity measures, which were abnormal and comparable with those previously reported [1]. There was a weak inverse correlation between plasma melatonin and cortisol levels ($r = –0.22$, $P = 0.015$). Seven of 18 patients had a circadian rhythm of plasma cortisol levels, while only two patients had a normal acrophase. Four of the nine placebo patients had a circadian rhythm of melatonin, but only one of these had a normal amplitude and acrophase. The plasma melatonin 24-hour area under the curve was significantly reduced compared with healthy elderly people (128.4 (112.6; 217.0) versus 464.5 (372.5; 594.0), $P < 0.001$). A moderate inverse relationship existed between the percentage plasma cortisol rhythm and patient intradaily variability ($r = –0.70$, $P < 0.002$).

Conclusions Acute administration of exogenous melatonin did not result in significant differences in rest–activity rhythms between the groups. Most patients lacked circadian rhythms of plasma melatonin and cortisol levels, which were no longer phase locked. The amplitude of plasma melatonin levels are significantly suppressed.

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P176

Evaluation of patient parameters that predict success using the SmartCare weaning system

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Critical Care 2007, **11(Suppl 2):**P176 (doi: 10.1186/cc5336)

Introduction Our aim was to assess the success of the SmartCare (SC) weaning system, to see what associated factors made a successful wean more likely. SC is a knowledge-based weaning system integrated into the Dräger EvitaXL ventilator, designed to optimise the ventilator settings during weaning so that patients can be weaned as quickly as possible.
Methods The first 100 consecutive general ICU patients where SC weaning had been attempted were identified. Patient age, sex, APACHE score, diagnosis, worst FiO_2 prior to weaning, duration of ventilation prior to weaning, duration of weaning attempt, need for tracheostomy and duration of stay were collected. The patients were then subdivided into unsuccessful and successful weaning attempts based upon whether they required subsequent ventilatory support during the first 48 hours after their weaning ended. The two groups were then analysed to identify the characteristics of the patients where a successful SC wean was achieved.
Results After excluding patients whose weaning was interrupted by transfer or a decision to withdraw treatment, we had 89 weaning attempts to analyse. These represented 43 successful (S) and 46 unsuccessful (US) weans. Comparison of mean ± SD ages (S 61 ± 14.3 years, US 57.3 ± 16.1 years, $P = 0.28$) and APACHE scores (S 16.2 ± 4.9, US 17.7 ± 6.5, $P = 0.23$) for the two groups showed no major differences. Logistic regression demonstrated that the worst FiO_2 prior to weaning and the duration of ventilation prior to weaning were both significantly associated with an unsuccessful SC weaning attempt ($P = 0.002$ and $P = 0.005$, respectively). ROC curve analysis suggested patients with an FiO_2 below 0.47 and a duration of ventilation prior to weaning of below 43 hours were more likely to be successfully weaned.
Conclusions SC proved most successful in those patients who had a lower worst FiO_2 prior to weaning and a lower duration of ventilation prior to commencing weaning.

P177

Assessing the impact of introducing the 'ventilator bundle' on outcomes for mechanically ventilated patients

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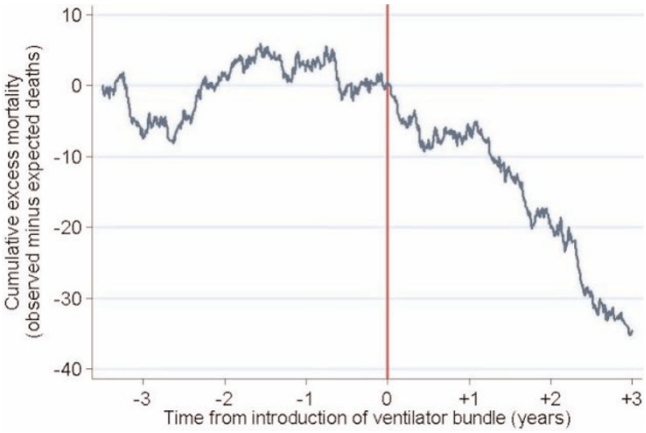
Background The concept of bundles was developed by the Institute for Healthcare Improvement. Individual bundle elements are built on evidence-based practice, and the bundle concept is that when these elements are executed together they produce better outcomes than in isolation. There is, however, limited evidence linking the use of bundles to demonstrable changes in patient outcomes. As a preliminary analysis to inform a multicentre evaluation, we explored the effect of the introduction of the 'ventilator bundle' on the outcomes for mechanically ventilated patients in a single critical care unit.
Methods Data were extracted for mechanically ventilated admissions from a single unit participating in the Case Mix Programme that was an early adopter of the ventilator bundle. A risk prediction model was developed using data from admissions during the 3.5 years prior to the introduction of the bundle and applied to admissions during the 3 years since introduction to estimate the cumulative excess mortality (observed minus expected deaths).
Results There were 762 ventilated admissions prior to the introduction of the bundle and 618 since. The cumulative excess mortality plot suggested a reduction in mortality after introduction of the bundle (Figure 1) but this was not statistically significant (relative risk reduction 10.9%, 95% confidence interval −10.2% to 31.8%).
Interpretation The results suggest that it will be beneficial to carry out a multicentre evaluation of the ventilator bundle in Case Mix Programme units, and will inform the design of this study.

Figure 1 (abstract P177)



P178

Hemodynamic changes due to expiratory positive airway pressure by facial mask in the postoperative period of cardiac surgery

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Introduction Expiratory positive airway pressure (EPAP) is used as physiotherapic tool in the management of patients after major surgeries such as cardiac surgery but its hemodynamic effect is not well studied. The goal of this study was to evaluate hemodynamic changes caused by EPAP use after cardiac surgery in patients monitored by Swan-Ganz catheter.
Methods Patients in the first or second day after cardiac surgery, with respiratory and hemodynamic stability and with a Swan-Ganz catheter, were included. They were evaluated at rest and after using EPAP of 10 cm, by facial mask, in a randomized order. Variables studied were oxygen saturation (SPO_2), heart rate (HR), respiratory rate (RR), mean arterial systemic and pulmonary pressures (MAP and MPAP), central venous pressure (CVP), pulmonary capillary wedge pressure (PCWP), cardiac index, stroke index, stroke work index from left and right ventricles, and systemic and pulmonary vascular resistance. Patients were studied as a whole group and divided into subgroups (with ejection fraction <50% or >50%) and values were compared with a *t* test and analysis of variance. Results are shown as the mean ± standard deviation. The significance level was $P < 0.05$.

Results Twenty-eight patients were studied (22 men, mean age 68 ± 11 years). The most common surgery was myocardial revascularization ($n = 17$). EPAP was well tolerated in the patients studied. Comparing rest and EPAP periods, increases were observed in: PCWP (11.9 ± 3.8 to 17.1 ± 4.9 mmHg, $P < 0.001$); CVP (8.7 ± 4.1 to 10.9 ± 4.3 mmHg, $P = 0.014$); MPAP (21.5 ± 4.2 to 26.5 ± 5.8 mmHg, $P < 0.001$); MAP (76 ± 10 to 80 ± 10 mmHg, $P < 0.035$). All other variables did not show significant changes. These results were observed in the total group and when divided concerning ejection fraction >50% or <50%.
Conclusions EPAP was well tolerated in this group of stable patients after cardiac surgery and the hemodynamic changes due to its use were an increase in the measurement of right and left filling pressures as well as a small increase in arterial pressure.

P179

Predicting successful nasal continuous positive airway pressure treatment in newborn infants: a multivariate analysis

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Background The use of nasal continuous positive airway pressure (nCPAP) in newborn infants is common, especially for weaning after mechanical ventilation. We have reported on the successful transition to the use of the infant flow method as a standard of practice in Poland.
Objective The authors present results of multivariate logistic regression (MLR) analysis of 481 newborns treated with the infant flow method in an effort to improve related clinical guidance.
Methods We collected data on the baseline demographic, physiological characteristics and outcomes of 1,299 newborns treated with nCPAP in 57 neonatal ICUs in Poland over a 2-year period. We conducted a stepwise MLR of 481 newborns with the two most common indications for use. We evaluated three outcomes: need for intubation in newborns treated electively with nCPAP (RDS), weaning failure requiring reintubation in the mechanically ventilated newborns (weaning), and bad outcome.
Results In the RDS group of patients we found that nCPAP failure was highly significantly related to estimated gestational age and clinical risk index for babies (CRIB). While in our population less mature RDS newborns were only slightly less likely to avoid intubation, the MLR model showed that, controlling for initial CRIB, they were less than one-half as likely to avoid intubation. Failure of nCPAP in weaning was highly significantly related to only pH, prior to beginning nCPAP. Bad outcomes were highly related to estimated gestational age and CRIB in the RDS group, but not the weaning population.
Conclusions We believe that understanding the risk of both nCPAP failure and also bad outcomes for a specific patient will enhance clinical decision-making. That is, for patients with the highest risk of poor outcome or nCPAP failure, more aggressive use of intubation and surfactant might be warranted. Likewise, such aggressive therapy might also be avoided for those with a seemingly low chance of poor outcome.

P180

Airway pressure release ventilation in acute lung injury/acute respiratory distress syndrome patients

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Introduction Advocates of airway pressure release ventilation (APRV) suggest that this mode is lung-protective for patients with ALI/ARDS, while providing additional benefits of spontaneous breathing, including improved haemodynamics, decreased need for sedation, and better patient comfort. However, there are few available data on the clinical experience with APRV.
Methods We conducted a retrospective audit of consecutive patients receiving APRV from January 2004 to August 2006 in three academic ICUs in Toronto. APRV was initiated at the discretion of the attending physician; a protocol guiding the implementation of APRV was introduced in July 2006. We recorded data describing: baseline characteristics; how APRV was used; its potential ramifications including oxygenation and sedation/analgesia doses; and outcomes.
Results Thirty patients, all with ALI/ARDS, received 39 trials of APRV during the study period – median age 52 years, 60% male, 50% pulmonary ALI risk factor, median APACHE II score 28. They had ALI for a median of 4.5 days with a median 135 hours of CMV before APRV. They received a median of 38 hours APRV. By 12 hours, oxygenation improved significantly (P/F ratio from 103 to 159, $P < 0.01$), with a concomitant decrease in FiO2 requirements (from 0.70 to 0.50, $P < 0.0006$). At 72 hours, the median P/F ratio had improved to 196 on a median FiO_2 of 0.40 (both $P < 0.01$). Administration and dosages of sedatives (midazolam equivalents, propofol) and analgesics (morphine equivalents) did not change significantly over the period from 24 hours before to 24 hours after APRV initiation. There were two episodes of barotrauma during APRV; neither required therapeutic drainage. The 30-day mortality was 13/30 (43%), most commonly due to multiorgan failure and withdrawal of life-support.
Conclusions In our patients APRV use appeared safe, led to improved oxygenation, but did not change needs for sedation/analgesia. Future studies are needed to determine the optimal timing and methods for ARPV use; these should be followed by randomized trials to confirm safety and document the effects of APRV on patient-centered outcomes.

P181

Importance of nonlinearities to quantify mechanical pulmonary stress under dynamic conditions: stress index and SLICE method

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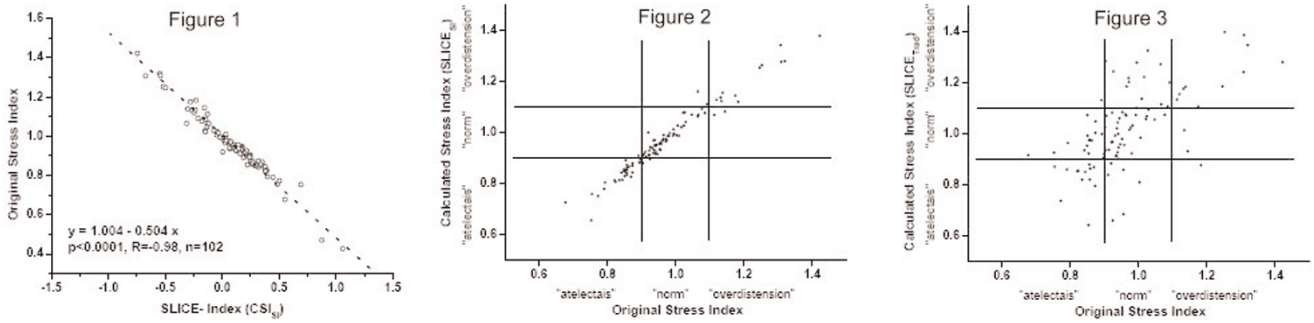
Introduction Recent data suggest that dynamic measurements of respiratory mechanics should be preferred to static measurement for lung protection [1]. The aim of this study was to analyze similarities and differences between dynamic methods: the stress index (SI) [2] and SLICE [3].

Figures 1-3 (abstract P181)



Methods One hundred and two respiratory datasets from 70 patients (28 ARDS, 24 postanesthesia care, 18 other) were analyzed. The SI and SLICE were performed using exactly the same database (SLICE_SI) in addition to the conventional SLICE that includes inspiratory and expiratory data (SLICE_CONV). A compliance-based index (CSI) directly comparable with the SI was generated from the compliance data.

Results The SI and CSI highly correlated when calculation of the CSI was based on the same database (Figure 1). According to the resulting regression formula (Figure 1), the SI can be reliably predicted from SLICE_SI (Figure 2). However, if SLICE_CONV was used for calculation of the SI (Figure 3), noticeable differences were found. Analysis of individual datasets showed three major reasons for the observed differences: differences in excluded data at low volumes respective to high volumes, nonlinearity of resistance, and differences in mechanics between inspiration and expiration.

Conclusion The SI and SLICE similarly measure the nonlinearity of compliance. The SI can be predicted from SLICE. However, nonlinearities of the respiratory system are not restricted to compliance alone; it might therefore be necessary to include nonlinearities of resistance and asymmetries between inspiration and expiration in the analysis of dynamic respiratory mechanics.

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P182

Contribution of HMSE-1 to surfactant conversion under acute inflammatory conditions

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Introduction A reduced content of biophysically active large surfactant aggregates is a common finding in acute inflammatory lung disease. Cyclic surface area changes and a carboxylesterase activity (surfactant convertase) are thought to mediate this subtype conversion. However, data concerning regulation of surfactant convertase are scarce. We therefore investigated the expression and activity of lung surfactant convertase and HMSE-1, a potential macrophage-derived human convertase, under normal and acute inflammatory conditions.

Methods Convertase activity in lavage fluid (BALF) was assessed using the *in vitro* cycling assay. The relative large surfactant aggregate content was determined by phospholipid quantification in the pellet following centrifugation at 48,000 x *g*. Esterase activity was assessed by means of a chromogenic substrate assay. Expression of both convertase and HMSE upon LPS challenge was assessed by real-time (TaqMan) PCR in murine alveolar macrophages, murine primary type II cells, and the human monocytic cell line U937, respectively.

Results Lavage fluid from ARDS patients displayed an increased esterase activity when compared with BALF from healthy controls. In addition, a pronounced large to small aggregate conversion was observed for BALF from LPS-challenged mice or BALF from ARDS patients. Incubation with LPS resulted in a significant increase in convertase gene expression in primary mouse type II cells as well as in HMSE-1 gene expression in U937 cells and monocytes from peripheral blood. No convertase expression was found in cultured murine alveolar macrophages.

Conclusions An increased convertase activity was found under acute inflammatory conditions of the alveolar compartment, and type II cells seem to be a relevant source of this increased convertase activity. However, leakage of esterase activity from the vascular space and other inflammatory cells cannot be ruled out.

P183

Transgenic mice expressing a surfactant protein B–urokinase fusion protein in the distal respiratory epithelium are protected against acute lung injury and postinflammatory fibrosis

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Introduction Persistent deposition of fibrin in the distal lung is thought to play a significant role in the pathogenesis of acute lung injury (ALI) and postinflammatory lung fibrosis. The therapeutic concept of the correction of the alveolar hemostatic balance, although effective in most models, needs further improvement in view of specific targeting of surfactant-containing alveolar fibrin clots.

Methods In the present study we generated transgenic mice that express a surfactant protein B–urokinase fusion protein (SPUC) in the distal respiratory epithelium under the control of the 3.7 kb human SP-C promotor. Survival was determined in a lethal ALI model (inhalative LPS administration) in SPUC mice compared with wild-type mice of the same genetic background. Furthermore, the outcome, lung function, collagen content and histology were assessed in the model of bleomycin-induced pulmonary fibrosis.
Results Transgenic mice showed an improved survival after inhalative LPS or bleomycin administration as compared with wild-type mice. The fibrotic response to inhalative bleomycin challenge was markedly attenuated in transgenic mice, as evident by reduced histological appearance of fibrosis, improved pulmonary compliance and reduced lung hydroxyproline content. As potential underlying mechanisms for the attenuated fibrotic response we observed an improvement in alveolar surface activity, a decrease in pulmonary fibrin deposition, increased hepatocyte growth factor levels and decreased gelatinase activity in the BAL fluids of transgenic mice as compared with control animals.
Conclusions Lung-specific expression of a surfactant protein B–urokinase fusion protein protects against ALI after inhalative LPS challenge and prevents fibrosis associated with bleomycin-induced lung injury.

P184

Mini-bronchoalveolar lavage with and without surfactant in the treatment of recurrent atelectasis in pediatric intensive care patients

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Introduction Since traditional treatment of atelectasis is often insufficient to reopen the collapsed airways, mini-bronchoalveolar lavage (mini-BAL) is performed. We retrospectively compared the treatment effects of mini-BAL only and mini-BAL combined with surfactant in the treatment of pediatric ICU patients with recurrent atelectasis.
Methods A retrospective analysis included a heterogeneous group of 18 mechanically ventilated pediatric ICU patients with recurrent atelectasis. Nine patients (mean age, 4.4 ± 3.4 years) who received surfactant after standard mini-BAL were compared with nine patients (mean age, 4.7 ± 3.0 years) who underwent only standard mini-BAL. Gas exchange and pulmonary mechanic parameters in the two groups were compared. The peak inspiratory pressure (PIP), positive end-expiratory pressure (PEEP), paO_2/FiO_2, and partial arterial carbon dioxide pressure ($paCO_2$) were analyzed with 3 x 2 multivariate analysis of variance, with the time of measurement (before treatment, 6 and 12 hours after treatment) as a within-subject factor and the type of treatment (mini-BAL only vs mini-BAL with surfactant) as a between-subject factor.
Results The groups did not differ in age (independent sample *t* test = 0.698). The parameters significantly changed with time after treatment (Wilks' $\lambda = 0.027$, $F = 25.277$, $P < 0.001$), and the treatment procedures had significantly different effects (time x treatment, Wilks' $\lambda = 0.103$, $F = 6.070$, $P = 0.013$). A significant univariate time–treatment interaction was not present only for SpO_2 ($F(2,32) = 2.167$, $P = 0.629$). Subsequent analyses showed different effect of surfactant administration on PEEP compared with mini-BAL alone. In the mini-BAL only group, PEEP changed from 6.44 ± 1.13 cmH_2O before treatment to 5.22 ± 0.83 cmH_2O 6 hours after the treatment ($P = 0.019$), and remained the same 12 hours after the treatment. The group that received surfactant had significantly lower PEEP values compared with the mini-BAL only group 12 hours after the treatment (3.44 ± 0.72 before vs 5.22 ± 0.44 mmH_2O after treatment, $P = 0.025$).
Conclusion Mini-BAL is efficient in the treatment of recurrent atelectasis in pediatric ICU patients. Beneficial effects of surfactant administration after mini-BAL should be confirmed prospectively in a larger number of patients.

P185

Automated mechanical ventilation based on the ARDS Network protocol in porcine acute lung injury

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Introduction The results of the ARDS Network trial [1] demonstrated a significant reduction of mortality by using a mechanical ventilation protocol with tidal volumes (VT) of 6 ml/kg predicated body weight. Additionally, a computer-driven weaning protocol was successfully performed and a reduction of mechanical ventilation duration could be demonstrated [2]. The implementation of the ARDS Network protocol in routine ICU practice remains modest [3]. A possible reason is the increased organisational and temporal burden. An automated execution of the protocol would help to propagate its day-to-day use. To test the ability to automate such a complex protocol, we designed a pilot study in porcine acute lung injury using an experimental medical expert system capable of continuously controlling respiratory parameters and global as well as regional ventilation with electrical impedance tomography (EIT).
Methods After induction of saline lavage-induced lung injury in pigs ($n = 3$), automated mechanical ventilation was initiated. The medical expert system used a closed-loop fuzzy controller with a rule base of if/then rules based on the ARDS Network protocol reference card. The protocol's algorithmic rules and therapeutic goals (oxygenation, pH, I:E, VT) were continuously controlled and ventilatory settings electronically adjusted accordingly. The medical attendant personnel was constantly informed with status messages about the decisions made. During the trial, all measurements were made using an online blood gas monitor (TrendCare Satellite; Diametrics Medical Inc., UK), a monitor for hemodynamic parameters (Sirecust 1281; Siemens, Germany), a capnograph (CO_2SMO+; Respironics, Inc., USA), and an EIT prototype system (EIT Evaluation Kit; Draeger Medical, Germany). Subjects were ventilated for between 40 and 90 minutes.
Results The computer-driven ventilator settings could stabilise the ventilation of the lung-injured subject in the predefined thresholds. Compared with the beginning of the study, a reduction in ventilation pressure and $PaCO_2$ could be observed. Despite the initial low PaO_2/FiO_2 ratio (<200 mmHg) of the subjects, FiO_2 could be decreased by the system in the given time without penetrating the thresholds for oxygenation.
Conclusion Robust execution of an automated ARDS Network protocol with an electronically controlled ventilator is possible and leads to pulmonary stabilisation. Further trials have to be undertaken before this successful approach can be realised in ARDS patients.

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P186

Efficacy of prone ventilation in adult patients with acute respiratory failure: a meta-analysis

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Background The use of prone ventilation in acute respiratory failure has been investigated by several randomised controlled trials in the recent past. To date there has been no systematic review or meta-analysis of these trials.
Objectives The primary objective was to assess the efficacy of prone ventilation in reducing mortality of adult patients with acute respiratory failure. The secondary objective was to evaluate changes in oxygenation, incidence of pneumonia, duration of mechanical ventilation, ICU and hospital stay, and adverse effects including pressure sores, endotracheal tube or intravascular catheter complications and cost-effectiveness of using prone ventilation.
Methods A systematic literature search was performed between 1966 and July 2006 to identify randomised controlled trials evaluating prone ventilation.
Measurements and results Of 229 studies evaluating prone ventilation, five were suitable for inclusion. Prone ventilation was not associated with a reduction in mortality (OR = 0.99; 95% CI = 0.74–1.30), but improvement in oxygenation was significant (mean difference 21.2; $P < 0.001$). There was no significant difference in the incidence of pneumonia, ICU stay and endotracheal tube complications. There was a trend towards an increased incidence of pressure sores in prone-ventilated patients. The data on duration of mechanical ventilation, intravascular catheter complications or hospital stay were not suitable for meta-analysis. No study reported cost-effectiveness.
Conclusions The use of prone ventilation is associated with improved oxygenation. It is not associated with a reduction in mortality, pneumonia or ICU stay and may be associated with an increased incidence of pressure sores.

P187

Continuous long-term prone position ventilation effects in pulmonary acute respiratory distress syndrome patients

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Introduction The optimal duration of prone position ventilation (PPV) in acute respiratory distress syndrome (ARDS) is uncertain. It has been pointed out that pulmonary ARDS patients respond less than extrapulmonary ARDS patients.
Objective To study effects of continuous long-term PPV on gas exchange, PEEP, lung injury score and multiorgan failure in pulmonary ARDS patients.
Materials and methods The design was a prospective (cohort). We studied 42 PPV periods in 33 pulmonary ARDS patients. Measures were taken in the supine position before PPV and at 1 hour after PPV, and then every 6 hours until the end of PPV. Statistical values are expressed as the median and interquartile range. Wilcoxon and Kruskal–Wallis tests were used. $P < 0.05$ was considered significant.
Results The mean age was 44 (25–57) years, the initial lung injury score (LIS) was 3.1 (2.75–3.6), and PPV was maintained for 91 (51–117) hours. The PaO_2/FIO_2 ratio was 125 (99–181) mmHg before PPV and 256 (170–298) mmHg after 1 hour of PPV ($P = 0.001$). This difference with the supine PaO_2/FIO_2 ratio was sustained until the end of PPV. Initial values of PEEP were set at 15 (12–18) cmH_2O by constructing a PEEP-compliance curve; there were no differences in PEEP values along the study. Initial values of $PaCO_2$ were 47 (41–69) mmHg and there were no significant differences along the study period. After 24 hours of PPV, the LIS was significantly decreased in comparison with the supine value before PPV: 3 (2.25–2.7) vs 2.5 (2.25–2.75), $P = 0.001$. There were no significant complications.
Conclusions PPV had a positive effect on gas exchange even after 6 hours. This effect lasts through the PPV period. Because of its effect on the LIS, a duration of 24 hours for continuous PPV could be useful in this patient setting.

P188

Maximal recruitment strategy guided by thoracic CT scan in severe acute respiratory distress syndrome patients: a case series report

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Introduction There is great controversy concerning protective ventilation in ARDS. Recruitment maneuvers and PEEP titration sufficient to avoid collapse and tidal recruitment are the major goals of the maximal recruitment strategy (MRS).
Objectives To describe clinical and demographic data. To evaluate the incidence of complications related to transportation and to the MRS.
Methods Forty-three patients with ARDS were transported to CT and submitted to the MRS, which consisted of 2-minute steps of ventilation with a fixed PCV = 15 cmH_2O and progressive PEEP levels (10–45–25–10 cmH_2O), RR = 10, I:E = 1:1, and FiO_2 = 1.0. Opening (recruitment) and closing (PEEP titration) pressures were determined according to the least amount of collapse observed at the CT, and were used to ventilate the patients afterwards.
Results Clinical data are presented in Table 1. There were no complications due to transportation and one patient developed pneumomediatinum after the protocol.

Table 1 (abstract P188)

Mortality (%)	28
Age (years)	49 ± 17
APACHE II score	20 ± 6
SOFA D1 score	9.4 ± 3
SOFA D7 score	5.2 ± 4
Maximal recruitment pressure (cmH_2O)	60 ± 5
Maximal PEEP day 1 (cmH_2O)	25 ± 3
Maximal plateau pressure day 1 (cmH_2O)	40 ± 5
PaO_2/FiO_2 ratio before recruitment protocol	130 ± 43
PaO_2/FiO_2 ratio after recruitment protocol	317 ± 99

Conclusions MRS was well tolerated in this series of patients, rendered the gas distribution through the lung more homogeneous, improved gas exchange and was related to low mortality. A RCT to test the MRS is necessary.

P189

Low sensitivity of measurements of respiratory mechanics in detecting lung edema from high tidal volume mechanical ventilation

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Introduction High tidal volume mechanical ventilation (HTVMV) leads to pulmonary edema from increased endothelial permeability. The lungs show evidence of inflammation with endothelial adhesion molecule expression, infiltrates of white blood cells and cytokine production. In order to understand the molecular mechanisms responsible for the pathogenesis of ventilator injury, mouse models are beneficial but technically difficult due to the small size of the animal. To study the time course of lung edema formation we compared lung elastance measured by forced oscillations with invasive methods of lung edema detection (for example, wet–dry weight ratio and histology).

Methods C57Black6 mice were anesthetized with i.p. sodium pentothal and paralyzed with succinylcholine. A tracheostomy was performed and the animals were connected to a Flexivent ventilator (Sqirec). The HTVMV group received a tidal volume of 25 ml/kg and 33 breaths/minute for 4 hours. The control group received 7 ml/kg at 120 breaths/minute. Temperature was kept at 36–37°C with the aid of a heated pad. The heart rate was monitored with surface EKG electrodes. Lung elastance and tissue energy dissipation were measured every 30 minutes using the forced oscillation technique. At the end of the experiment a sternotomy was performed. A ligature was placed around the right hilum and the right lung was cut, briefly rinsed in PBS, blotted dry and weighed. The dry weight was obtained following desiccation at 60°C for 48 hours. The left lung was inflated with 500 µl formalin injected slowly into the tracheal canula and embedded in paraffin. Paraffin blocks were sectioned with a microtome at 5 µm thickness and stained with hematoxylin–eosin.

Results The wet-to-dry weight ratios rose from 4.82 ± 0.16 in control animals to 6.34 ± 0.83 in the HTVMV group ($P < 0.05$, $n = 4$). Light microscopic examination of histologic sections showed mononuclear white cell infiltrates around small arteries and within the alveolar walls of mice in the HTVMV group but not in control mice. Elastance rose nonsignificantly during the HTVMV protocol.

Conclusions In this *in vivo* mouse model, high tidal volume mechanical ventilation caused pulmonary edema and lung tissue infiltration with white blood cells. However, measurements of lung mechanics showed minimal changes during the course of the experiment, indicating that they are less useful in detecting early edema.

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Pressure dependency of respiratory resistance in patients with acute lung injury and acute respiratory distress syndrome

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Introduction The analysis of the nonlinearity of respiratory compliance to guide ventilator settings in ALI and ARDS is well established. The pressure dependency (or volume dependency respectively) of respiratory resistance of these patients is mostly ignored. This study was performed to investigate the pressure dependency of resistance in ALI and ARDS over a wide range of pressures.

Figure 1 (abstract P190)

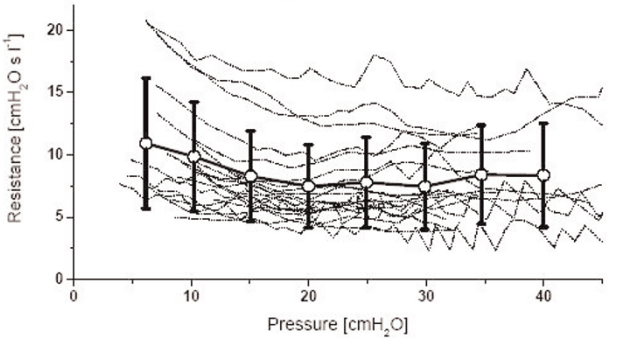
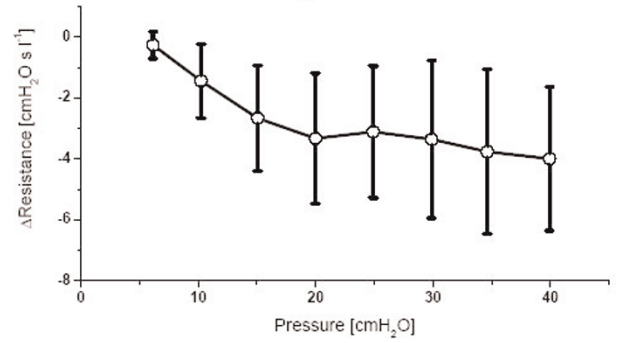


Figure 2 (abstract P190)



Methods Twenty-one patients with ALI or ARDS were analyzed. Ventilation was interrupted by a respiratory manoeuvre: the volume was increased from ZEEP in steps of 100 ml with constant inspiratory flow until the plateau pressure reached 45 cmH_2O. Each step was followed by a hold of 3 seconds. Inspiratory resistance during each step was determined by a least-squares fitting procedure.

Results Resistance decreased from 10.7 ± 5.1 $cmH_2O \cdot s/l$ at 5 cmH_2O to 8.1 ± 4.0 $cmH_2O \cdot s/l$ at 40 cmH_2O ($P < 0.05$). Figure 1 shows individual absolute values and means ± SD of all patients. Most of the decrease was found up to 20 cmH_2O; at higher pressures, changes were not uniform. The average relative changes in inspiratory resistance (±SD) of all patients are shown in Figure 2.

Conclusion Inspiratory resistance in ALI and ARDS is not constant. Especially at higher pressures, individual resistance may change unpredictably. The assumption of a constant resistance should therefore be avoided.

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Alveolar microscopy: on the automatic determination of alveolar size during ventilation

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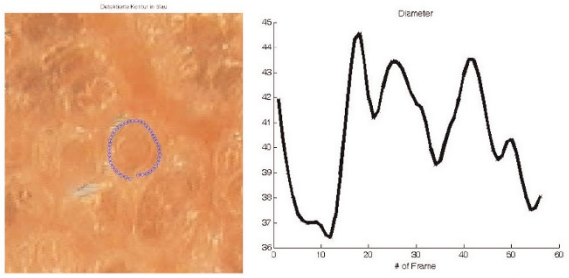
Introduction Alveolar microscopy seems to provide important insight into alveolar dynamics during mechanical ventilation [1,2]. The utility of this method is limited due to high efforts needed to evaluate sequences of images with respect to alveolar geometry. The evaluation – done by hand – is time consuming, places a high cognitive load on the examiner and is error prone. Reproducibility of results is low. This project aims to establish a computer-assisted tool that provides semi-automatic evaluation of video sequences acquired with alveolar endoscopy.
Methods We developed a computer program based on Matlab (Mathworks, Natick, MA, USA), which analyses video sequences acquired with an alveolar endoscope (Schölly, Denzlingen, Germany) [2]. The user has to provide a pointer to the alveoli that shall be traced and whose changes in size and shape are to be determined. Filters, smoothing splines and expectation-driven fine tuning is performed to achieve robust and predictable results of the intratidal change in alveolar geometry.
Results Animal studies related to alveolar mechanics during artificial ventilation were conducted. Figure 1a shows a plot of a frame taken from a video obtained during an experiment performed on a healthy anesthetized rat. Overlaid circles indicate identified boundaries of a selected alveolus. Figure 1b presents a trace of alveolar diameter during a tidal breath. Evaluation of successive frames allows one to compensate for motion artifacts and to analyze the intratidal changes in alveolar geometry.

Figure 1 (abstract 191)



(a) Marked areas of a traced alveolus. **(b)** Changes in diameter during ventilation.

Conclusion Given a synchronization with respiratory data, this tool will allow one to quantify pressure-related changes of alveolar size. Thus it will allow one to monitor the alveolar distension in a variety of animal models (for example, lavage-induced ARDS) and to correlate these findings, for example, with outcome.

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P192

Assessment of breath by breath recruitment by electrical impedance tomography in saline lavage lung injury

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Introduction Alveolar recruitment and maintenance of lung volume are important goals in the treatment of acute lung injury (ALI) and essential for improving oxygenation. The most usual employed strategy to achieve this goal is the use of positive end-expiratory pressure (PEEP). Recruitment and collapse are highly dynamic phenomena that are difficult to monitor. Dynamic effects of regional ventilation can be monitored by electrical impedance tomography (EIT) at the bedside [1]. We investigated the ability of EIT for providing a useful tool to detect dynamic changes of regional breath by breath recruitment at the bedside during an incremental and decremental PEEP trial in experimental lung injury. In addition, we analyzed pressure–volume (P–V) curves computed by EIT data.
Methods ALI was induced in six pigs by repetitive lung lavage. After stabilization of the lung injury model (> 1 hour) a stepwise PEEP trial was performed consisting of 2-minute steps of tidal ventilation (10–30 cmH_2O; 30–5 cmH_2O). During the PEEP trial subjects were ventilated pressure-controlled. Global ventilatory and gas exchange parameters were continuously recorded. Offline we analysed EIT data by computing the amount of breath by breath recruitment (ΔV EIT) at each pressure level before and after lung lavage. Nondependent and dependent regions of interest were defined in the tomograms. ΔV EIT was defined as the mean increase or decrease in end-expiratory global impedance per breath.
Results Ventilatory parameters clearly showed a recruitment of nonaerated lung areas at the descending part of the pressure ramp. The shape of the P–V curve from EIT data, in particular the increasing slope (lower level > upper level), reflected the recruitment of poorly ventilated lung regions. The flattening of the curve at higher pressures, especially at the upper level, reflected less amount of recruitment but more overdistension. Regional pulmonary recruitment/derecruitment was very high in the lower level. These phenomena were more impressive after induced lung injury.
Conclusions Stepwise PEEP recruitment maneuvers can open collapsed lungs and certain PEEP levels are necessary to keep the lungs open. Monitoring of ΔV EIT is capable of detecting the dynamic process of recruitment and derecruitment at bedside. Plotting regional P–V curves from EIT data provides continuous information that may be of use in determining the PEEP level to maintain recruitment in acute lung injury.

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P193

Nonlinearity of intratidal airway resistance

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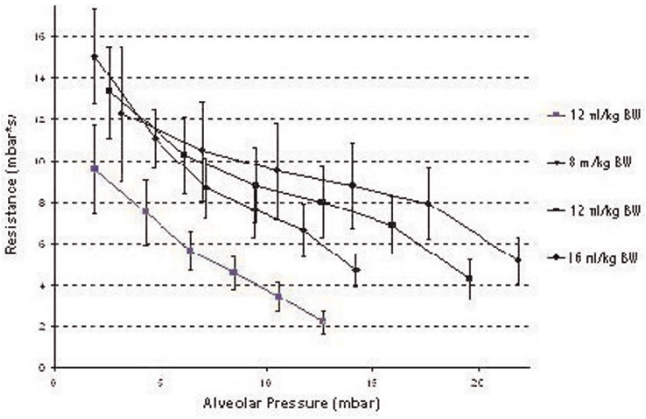
Introduction Acute respiratory distress syndrome is a disease associated with high mortality. Understanding the interdependence

Figure 1 (abstract P193)



of ventilator settings and respiratory mechanics is crucial for further developments of protective lung ventilation. Up to now, the nonlinearity of compliance has mainly been the focus of interest. We hypothesized that airway resistance also changes intratidally. Therefore, this study was performed to analyze the dependence of resistance on tidal gas volume.

Methods After induction of anesthesia and tracheotomy, the lungs of 14 surfactant-depleted piglets were ventilated at zero end-expiratory pressure with three different tidal volumes (8, 12, 16 ml/kg) in a randomized order. In addition, baseline measurements (12 ml/kg) were performed before saline lavage. Before any change of the ventilator settings a recruitment maneuver was performed. The nonlinear intratidal airway resistance was analyzed using the SLICE method [1].

Results Figure 1 shows the intratidal resistance before lavage (grey) and after surfactant depletion (black) plotted against the alveolar pressure. Each curve in the diagram represents the intratidal course of resistance for one ventilator setting. Resistance is increased after surfactant depletion and is intratidally declining before and after lavage.

Conclusion The analysis of resistance shows a dependence on intratidal volume. The nonlinear course of intratidal resistance can be interpreted as a volume-related caliber effect leading to an increase of cross-sectional area of the large and small airways.

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P194

Noninvasive alveolar recruitment maneuver induces cytokine release in healthy volunteers

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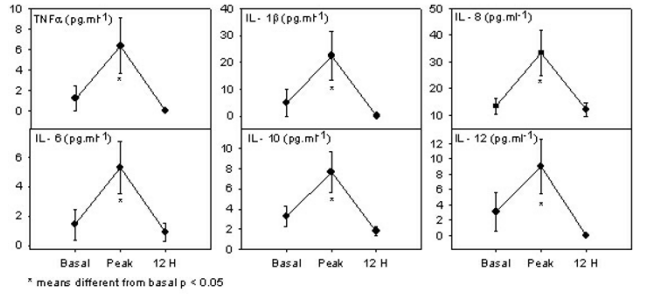
Introduction Alveolar recruitment maneuver (ARM) using high airway pressures has been shown to re-expand atelectasis and to improve gas exchanges after general anesthesia; however, ARM may lead to lung stretching-induced inflammatory response. The objective of this study was to evaluate plasma cytokine behavior after an ARM in healthy volunteers.

Figure 1 (abstract P194)



Methods After obtaining ethical committee approval and informed consent, a basal blood sample was collected in 10 healthy volunteers. Continuous positive airway pressure (CPAP) was noninvasively applied (BiPAP Vision®; Respironics, USA) using a total face mask. CPAP was increased by 3 cmH_2O from 5 to 20 cmH_2O every five breaths. At CPAP of 20 cmH_2O, an inspiratory pressure of 20 cmH_2O above CPAP was implemented during 10 breaths. After that, CPAP was stepwise decreased in an inverse fashion. Pulse oximetry, arterial pressure and heart rate were measured before and after ARM. Additional blood samples were drawn at 30 minutes, 2 and 12 hours. TNFα, IL-1β, IL-6, IL-8, IL-10 and IL-12 were measured by the flow cytometry technique (Cytometric Bead Array BD™ Kit). The highest cytokine value at 30 minutes or 2 hours after ARM was considered the peak value measurement. Data were analyzed using a paired *t* test and one-way RM ANOVA. $P < 0.05$ was significant.

Results Four men and six women with a mean age of 26 ± 1 years and mean BMI of 23.8 ± 3.6 kg/m^2 were studied. No changes were observed in heart rate or MAP after ARM, while pulse oximetry increased from 97.2 ± 0.8% to 98.4 ± 0.7% ($P = 0.009$). As shown in Figure 1, ARM induced a significant increase in the peak plasma level concentration of all cytokines that returned to basal levels within 12 hours. No adverse effects were observed during and after ARM.

Conclusions Despite beneficial effects in reversing atelectasis, ARM-induced lung stretching was associated with an inflammatory response in healthy volunteers.

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Recruitment/derecruitment models fitted to respiratory data of acute respiratory distress syndrome/acute lung injury patients

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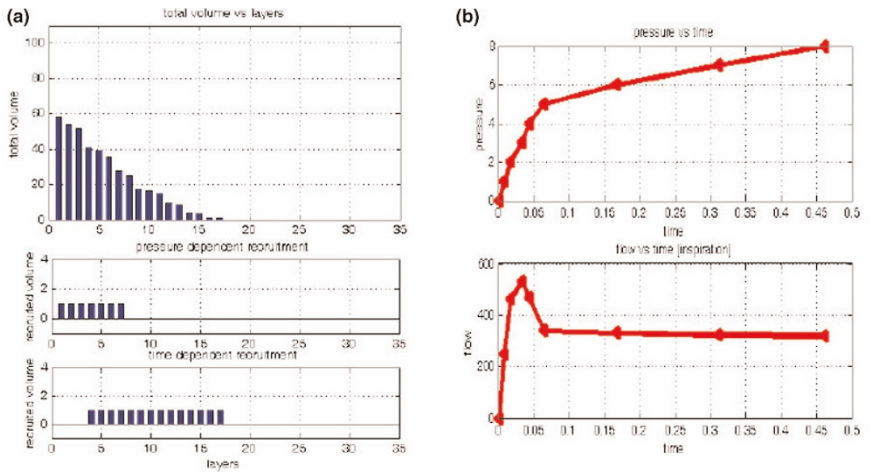
Introduction Recruitment/derecruitment (R/D) seems to play an important role in the development of VILI [1]. Many clinicians base their determination of PEEP settings during mechanical ventilation of ARDS/ALI patients on an estimate of alveolar recruitability [2]. This project aims to establish an online tool that provides estimates of R/D in patients at the bedside.

Methods We developed a computer simulation of R/D based on Matlab (Mathworks, Natick, MA, USA), which incorporates different

Figure 1 (abstract P195)



approaches [1,3,4]. Our model is fitted (currently offline) to patient data acquired during controlled mechanical ventilation. For data acquisition the internal respiratory data of a ventilator (Evita 4; Dräger Medical, Lübeck, Germany) is read in real time. The simulation assumes a quantitative partition into pressure-dependent and time-dependent recruitment. Pure pressure-related approaches (for example [1]) are not able to describe transients (for example, a volume shift after a change in PEEP).

Results A multistep optimization process is performed to reduce the difference between measured data and model prediction. At any moment during a tidal breath or during some respiratory maneuver the current state of the model can be visualized. The inflated volume splits up into extension of open alveoli and into temporal or pressure-dependent recruitment. Distribution of these compartments over time during a tidal inflation is depicted in Figure 1a. The pressure vs time and flow vs time curves are shown in Figure 1b.

Conclusion The fitting of recruitment models provides interesting insight into not directly observable R/D. It may be used for monitoring trends and drifts in recruitment. Currently results rely on certain assumptions; for example, distribution and quantity of superimposed pressure. With modern imaging techniques (for example, CT, EIT) a validation of the fitted models will come into reach and will be performed as a next step.

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P196

A novel system for evaluation of pulmonary functional residual capacity in the intensive care unit: preliminary data

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Introduction The aim of this study is to evaluate the efficacy of pulmonary recruitment by the use of functional residual capacity (FRC) measurement with the Engström Carestation FRC INview™ system (GE Healthcare), in patients with high pulmonary recruitment range (group A) and in patients with low recruitment range (group B).

Methods Five patients without pulmonary disease (group A) admitted to the ICU for a postoperative course and five patients admitted to the ICU for acute respiratory failure (group B) were studied with the Engström Carestation FRC system based on the evaluation of nitrogen wash-in and washout by the COVX metabolic module. The FRC, ratio (PaO_2/FiO_2) and static compliance (C_{stat}) are registered in three clinical steps: 1: ICU arrival; 2: after pulmonary recruitment with high inspiratory pressure; and 3: 3 hours after recruitment. Data are shown as the mean ± standard deviation; intragroup variables are analyzed with the Wilcoxon test (W), and intergroups variables are analyzed with the Mann–Whitney test (MW). $P < 0.05$ is taken as statistically significant.

Results FRC increase in group A is statistically significant (W) (step 1: 1,525 ± 360 ml; step 2: 1,937 ± 583 ml, $P < 0.05$ vs step 1; step 3: 2,592 ± 659 ml, $P < 0.05$ vs step 2 and $P < 0.01$ vs step 1) while the FRC increase in group B is not significant (step 1: 1,697 ± 210 ml; step 2: 1,757 ± 367 ml; step 3: 1,982 ± 365 ml); the FRC of group A is statistically higher than the FRC of group B in step 2 ($P < 0.05$ MW) and in step 3 ($P < 0.01$ MW). The ratio increase in group A is statistically significant (W) (step 1: 256 ± 133; step 2: 407 ± 187, $P < 0.01$ vs step 1; step 3: 379 ± 169, $P < 0.05$ vs step 1) while the ratio increase in group B is not significant (step 1: 194 ± 50; step 2: 253 ± 83; step 3: 276 ± 73); the ratio of group A is statistically higher than the ratio of group B in step 2 ($P < 0.01$ MW) and in step 3 ($P < 0.05$ MW). The C_{stat} increase in both groups is not significant, but in group A C_{stat} is statistically higher than C_{stat} of group B in every step ($P < 0.05$ MW) (step 1: 38 ± 2 ml/cmH_2O for group A vs 28 ± 7 ml/cmH_2O for group B; step 2: 44 ± 6 ml/cmH_2O vs 36 ± 8 ml/cmH_2O; step 3: 47 ± 5 ml/cmH_2O vs 36 ± 8 ml/cmH_2O).

Conclusion With the limit of low sample size, these preliminary data suggest that the FRC evaluation system is a good parameter to optimize pulmonary recruitment and seems to be in a position to overcome the C_{stat} limit for the evaluation of pulmonary recruitable parenchyma.

P197

High-frequency oscillatory ventilation for trauma patients with acute respiratory distress syndrome who fail conventional mechanical ventilation

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Introduction The purpose of this study is to report our clinical experience with high-frequency oscillatory ventilation (HFOV) for rescuing trauma patients with acute respiratory distress syndrome (ARDS) and severe hypoxemia despite optimal conventional ventilation. Experimental and clinical data suggest mechanical ventilation can contribute to mortality in ARDS, and modern ventilatory strategies require protective measures such as low tidal volume, low airway pressure and fraction of inspired oxygen (FIO_2), which is not always possible with conventional ventilation. HFOV could be an alternative to achieve protective ventilation and adequate oxygenation.
Methods We retrospectively analyzed nine trauma patients who presented with ARDS criteria and failed conventional mechanical ventilation requiring HFOV. The mean airway pressure was initially set 3–5 cmH_2O higher than that for conventional ventilation and was subsequently adjusted to maintain oxygen saturation >90% and FiO_2 <0.6. The $PaCO_2$ target range was 35–60 mmHg with a pH >7.25. We collected demographic data, injury severity scale (ISS), APACHE II score, time to HFOV, time spent on HFOV, ventilation settings and arterial blood gas before and after HFOV and mortality.
Results Data on nine trauma patients were available for analysis; the severity of respiratory dysfunction can be estimated by the mean PaO_2/FiO_2 of our patients, 131. Two patients received a trial of inhaled nitric oxide as part of the management of ARDS failing conventional ventilation. The last mean measurements before initiation of HFOV were: pH 7.24, PaO_2 116, PCO_2 67.4, FiO_2 0.899. No significant hemodynamic instability was associated with initiation and administration of HFOV. The mean frequency was 4.3 (mode 4), mean power was 8.5, mean FiO_2 was 0.83. The successful weaning rate from HFOV to extubation or trach mask was 70%, and mean total time of mechanical ventilation (conventional + HFOV) was 347.76 hours and the time spent on HFOV was 107.5 hours.
Conclusion HFOV is a possible alternative for safely correcting oxygenation failure associated with ARDS in trauma patients. Further research is necessary to identify the best strategy and patients for HFOV.

P198

Hemodynamic effects of high-frequency oscillatory ventilation in acute respiratory distress syndrome

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Introduction High-frequency oscillatory ventilation (HFOV) is a promising ventilatory modality for ARDS patients having refractory hypoxemia despite standard ARDS ventilation. Hemodynamic alterations while switching the patient from volume-controlled ventilation (VCV) to HFOV are not yet well studied.
Objective To evaluate immediate (within 3 hours) hemodynamic effects of HFOV in ARDS patients with septic shock needing vasopressor support.

Figure 1 (abstract P198)

Trends of hemodynamic parameters during study period

	on VCV	1 hr HFOV	2 hr HFOV	3 hr HFOV
Heart rate /min	115.2±14.8	122.2±16.4	110.4±71.2	105±18.1
MAP mmHg	77.5±13.7	72.4±11.4	74.2±14.2	79.8±13.3
C.O. L/min	5.45±0.6	5.81±0.5	5.21±0.3	5.9±1.2
C.I. L/min/m^2	3.26±0.26	3.47±-0.22	3.12±0.32	3.53±0.6
SVRI Dynes.sec.cm^{-5}	1431±369	1310±308	1457±512	1793±617
SVV %	7.87±3.90	7.9±4.1	7.82±2.4	7.75±1.8

Methods Patients having a PO_2/FiO_2 ratio ≤150, PEEP >12 cm and FiO_2 requirement ≥0.7 on VCV (6 ml/kg) were switched to HFOV. The initial continuous distending pressure (CDP) of HFOV was 5 cm above the mean airway pressure during VCV. Other HFOV settings were FiO_2 1, bias flow 30 l/min, amplitude 70 cm and frequency 7 Hz. The CDP was adjusted to maintain oxygen saturation >88%. Fluid bolus before switching to HFOV was avoided. All the patients were sedated and paralysed during the study period. A drop in the mean arterial pressure (MAP) ≤65 mm or cardiac index (CI) ≤2.5 l/min/m^2 were treated with escalation of inotrope if required. Hemodynamic monitoring was done with the Flotrac-Vigileo monitoring system.
Results Eight ARDS patients needing vasopressor support were switched to HFOV from VCV. Baseline data of these patients were: age 58.87 ± 11.69 years, APACHE II score 21.02 ± 8.14, mean CDP of HFOV 26.67 ± 3.22 cm, frequency 7 Hz, amplitude 70 cm. Figure 1 presents the trends of hemodynamic parameters during the study period. Only one patient needed escalation of the dopamine dose during the trial period.
Conclusion Switching of an ARDS patient from VCV to HFOV does not impart significant hemodynamic instabilities and can be safely done.

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Outcome predictors of high-frequency oscillatory ventilation in acute respiratory distress syndrome

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Introduction Outcome predictors of high-frequency oscillatory ventilation (HFOV) in severe ARDS are not well studied.
Objective To evaluate outcome predictors of HFOV in adult patients with ARDS.
Methods ARDS patients receiving mechanical ventilation as per the ARDSnet protocol with PO_2/FiO_2 <150, PEEP ≥12 cm and FiO_2 ≥0.7 were considered for HFOV. The continuous distending pressure (CDP), frequency, amplitude, inspiratory time and bias flow of HFOV were optimised, guided by frequent blood gas analysis. Weaning from HFOV to pressure support ventilation was attempted once the PO_2/FiO_2 ratio remained ≥200 with CDP ≤18 cm FiO_2 ≤0.5. Responders (R) were defined as patients who were successfully weaned to a state without any ventilatory support for >12 hours. Nonresponders (NR) could not be weaned off any ventilatory assistance.
Results Fifteen out of the total 28 patients were R and 13 were NR. Both the groups were similar prior to HFOV in terms of APACHE II score, number of organ failures, PEEP and plateau pressures, and duration of ventilation before HFOV. The baseline PO_2/FiO_2 ratio and improvement in it at 6 hours and 24 hours in the R group were statistically significantly higher as compared with

Figure 1 (abstract P199)

PARAMETERS	RESPONDERS	NON-RESPONDERS	P VALUE
PO_2/FiO_2 ratio on VCV	102.85±33.04	85.56±26.28	P<0.01
O.I. on VCV	22.09±7.99	26.61±11.70	P< 0.05
PO_2/FiO_2 ratio at 6 hrs HFOV	218.48±112.44	123.64±80.61	P<0.01
O.I. at 6 hrs HFOV	15.25±7.25	32.18±17.61	P<0.01
PO_2/FiO_2 ratio at 24 hrs HFOV	299.22±94.34	183.66±120.69	P<0.01
O.I. at 24 hrs HFOV	9.85±3.75	22.41±13.61	P<0.01

VCV, volume controlled ventilation.

that in the NR group. The difference in improvement in the oxygenation index (OI) of the two groups at 6 and 24 hours was also statistically significant. The rate of improvement in the PO_2/FiO_2 ratio and OI in NR was slower than that in R, and this difference was statistically significant (trend test). See Figure 1.

Conclusion A lower PO_2/FiO_2 ratio and higher OI prior to HFOV and slow improvement in the PO_2/FiO_2 ratio and OI at 6 and 24 hours on HFOV are significant negative outcome predictors of HFOV in ARDS.

P200

Monitoring slow recruitment manoeuvres with high-frequency oscillatory ventilation in adult acute respiratory distress syndrome patients using electrical impedance tomography

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Introduction Recruitment manoeuvres (RM) during high-frequency oscillatory ventilation (HFOV) are increasingly used in ARDS. However, the changes in lung volume during a RM (lung recruitability) are difficult to quantify at the bedside, and the use of CT is impractical in patients on HFOV. We studied the effects of a standardised protocol of slow RM (SRM) on regional lung volumes assessed noninvasively by electrical impedance tomography (EIT).

Methods SRM were performed by progressive increases of continuing distending pressure (CDP) starting from the mean airway pressure on CMV + 5 cmH_2O, by increments of 3 cmH_2O every 10 minutes until a CDP of 50 cmH_2O was reached or haemodynamic instability ensued. Subsequently, CDP was reduced by 2 cmH_2O every 5 minutes until optimal CDP was established on gas exchange. EIT measurements were performed using 16 electrodes, acquired via the Goe-MF II EIT system (Viasys Healthcare, USA). Offline analysis of EIT measurements was performed using the AUSPEX software (University of Amsterdam). Changes in impedance (ΔZ) during tidal breathing were calibrated against set tidal volumes during conventional mechanical ventilation. Changes in lung volume after each increase in CDP on HFOV were expressed as the fold change compared with the previous CDP level.

Results Four patients with ARDS, who underwent rescue HFOV, were enrolled. Following the SRM, there was a mean 2.38-fold increase in PaO_2/FiO_2 and a 19.7% reduction in $PaCO_2$. EIT showed a mean 4.66-fold increase in global lung volume, with preferential ventilation of the ventral regions (59.4% of global volume change). Despite these differences, both dorsal and ventral regions showed a similar degree of volume change compared with their own baseline (V/D of 4.7/4.5-fold). This may be consistent with a more homogeneous recruitment with HFOV. The inflation limb of the changes in lung volumes during SRM fitted the Venegas–Harris equation ($r^2 = 0.99$).

Conclusion EIT can noninvasively assess lung recruitability and quantify the changes in global and regional lung volume during SRM with HFOV in ARDS patients.

P201

pH: an overlooked criterion for success in high-frequency oscillatory ventilation in acute respiratory distress syndrome?

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Critical Care 2007, **11(Suppl 2):**P201 (doi: 10.1186/cc5361)

Introduction High-frequency oscillatory ventilation (HFOV) is used for patients with refractory hypoxia and or severe oxygenation failure in our ICU. There is a unit policy regarding the timing of initiation of HFOV, and all patients were initiated with a single static recruitment manoeuvre and then managed according to local guidelines. The aim of this study was to understand which ventilatory parameters best predicted successful outcome following HFOV.

Methods After institutional approval, we retrospectively reviewed the case notes all the adult patients who were ventilated with HFOV during the 18-month period between January 2005 and July 2006. The data were analysed using SPSS® version 13 software.

Results There were 33 episodes of HFOV in 31 patients; 19 females and 12 males; mean age of 56 years. First-day median APACHE II scores and predicted mortality were 23 and 41%, respectively. All the patients had acute respiratory distress syndrome (ARDS) at the time of initiation of HFOV. The main causes of ARDS were pneumonia leading to sepsis (50%), sepsis from other sources (18%), postoperative emergency laparotomy and abdominal aortic aneurysm repair (18%). Patients were ventilated with conventional ventilation for a median period of 35 hours (0–519 hours) before being ventilated with HFOV for a median period of 58 hours (7–1,080 hours). Fourteen patients (45%) were successfully weaned to conventional ventilation while two (7%) died because of cardiac arrest and in the remaining 15 patients (48%) treatment was withdrawn. Eight patients (25.8%) survived to discharge to the ward. An admission pH of less than 7.20 was found to be significantly associated ($P = 0.09$) with failure of treatment.

Conclusion Although we believed that the unit's approach to HFOV was one of 'treatment' rather than 'rescue', our results suggest we are still using HFOV in a 'rescue' mode. While our results support the findings of other studies that earlier initiation of HFOV shows a trend towards improved outcome in adult patients with ARDS, further studies are still required to identify appropriate parameters for selecting patients in a timely manner who may benefit from HFOV. However, progressive acidosis in ARDS appears to be a relatively more important predictive criterion than parameters of failing oxygenation and ventilation.

P202

Acoustic monitoring of one-lung ventilation with vibration response imaging

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Critical Care 2007, **11(Suppl 2):**P202 (doi: 10.1186/cc5362)

Introduction Inadvertent endobronchial intubation and one-lung ventilation (OLV) with a standard endotracheal tube may lead to serious complications, such as a nonventilated lung, pneumothorax and hypoxemia. Auscultation of breath sounds was found to be

Figure 1 (abstract P202)

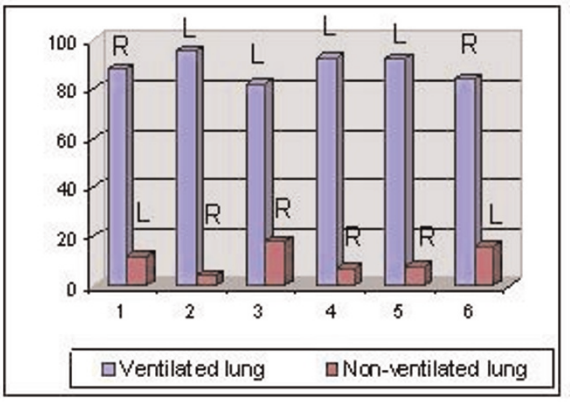
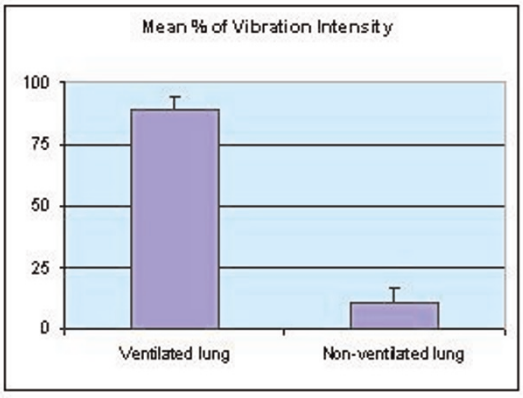


Figure 2 (abstract P202)



inaccurate for the detection of OLV with a high margin, up to 60% error [1]. Vibration response imaging (VRI) is a novel technology that measures vibration energy from the lungs and displays regional intensity in both visual and graphic format. The time from the start of the procedure to display takes less than 1.5 minutes. We investigated the effectiveness of VRI to detect OLV using a double-lumen endotracheal tube in lung surgery patients.

Methods Double-lumen tubes were placed at the time of surgery. Tracheal and endobronchial lumens were alternately clamped to produce unilateral lung ventilation of the right and left lungs. VRI was performed after each occlusion. Two images were excluded *a priori* (prior to analysis) due to technical failure (external artifact).

Results The right and left lung distribution of vibration intensity is shown in Figure 1. The mean percentage change of vibration intensity clearly demonstrates the increased vibration in ventilated lungs (89.1 ± 5.47% vs 10.9 ± 5.4%, $P < 0.05$) (Figure 2).

Conclusions Auscultation is insensitive to endobronchial intubation and chest radiography may not be immediately available. VRI offers the potential to rapidly and noninvasively determine endobronchial intubation. Currently VRI is performed in the sitting position, but the capability of supine imaging will soon be available.

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P203

Correlation of lung vibration and airflow

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Critical Care 2007, **11(Suppl 2):**P203 (doi: 10.1186/cc5363)

Introduction Airflow into a mechanically ventilated patient is easily measured in the inspiratory limb of the ventilator. Regional airflow inside the lungs, up to this point, is a black box. Vibration response imaging (VRI) is a novel technology that measures vibration energy from the lungs to create a real-time structural and functional image of regional vibration during respiration. Sophisticated surface skin sensors are placed on the subject's back to record, analyze and display vibrations noninvasively. Our goal was to assess the correlation of vibration measured at the chest wall with airflow into the lungs.

Methods To assess the effect of constant inspiratory flow on lung vibration, VRI was performed on a mechanically ventilated patient on assist volume control, and airflow in the tubing was recorded concurrently. To assess the effect of increasing flow rates on lung vibration, healthy subjects were recorded several times with VRI while taking tidal volumes of 200–1,300 ml at the same respiratory rate. The inspiratory tidal volume was recorded.

Figure 1 (abstract P203)

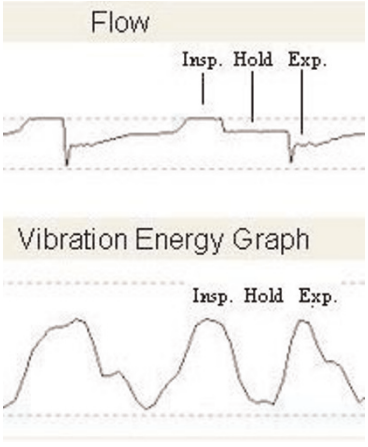
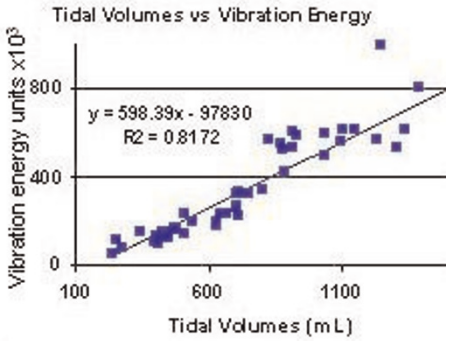


Figure 2 (abstract P203)



Results In the mechanically ventilated patient, when there is minimal flow, the vibration was at its lowest. When flow begins at the ventilator, the vibration measured over the lungs increases and when the flow stops, the vibration decreases. An inspiratory hold was performed to separate inspiratory from expiratory vibrations (Figure 1). As the subject takes increasing tidal volumes, the vibration during the breath cycle increases linearly. A sample subject is shown in Figure 2 ($R^2 = 0.81$).

Conclusion Vibration measured using VRI correlates with lung airflow. Given the difficulty in assessing airflow in the lungs, measuring lung vibration could potentially serve as a surrogate for regional lung airflow.

P204

The Gliding-SLICE method: an enhanced tool for estimation of intratidal respiratory mechanics

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Introduction Focusing on lung-protective ventilation, the analysis of nonlinear dynamic respiratory mechanics appears crucial. Based on the SLICE method we developed the Gliding-SLICE method as a tool to determine respiratory system mechanics. This tool was tested in a nonlinear water-filled two-chamber lung model.

Methods The classic SLICE method [1] determines parameters of the respiratory system for abutted volume ranges. The Gliding-SLICE method enhances this method by moving a window of analysis along the volume axis. This way, a quasi-continual course of intratidal mechanics can be determined. To test the new method we build up a physical model that consists of two connected chambers filled with water. During inspiration water is displaced from one chamber to the other resulting in a counter pressure. Using wedges of certain shapes we simulated volume-dependent nonlinear compliances.

Results Using the Gliding-SLICE method we determined a nonlinear course of compliance in a patient (Figure 1) and in model data (Figure 2).

Conclusion The Gliding-SLICE method allows one to calculate mechanical parameters of the respiratory system quasi-continually. This allows a more intuitive interpretation of data. The method is not limited to principle constrictions but can be enhanced by ventilatory maneuvers; for example, for separated view on inspiratory and expiratory respiratory mechanics.

Figure 1 (abstract P204)

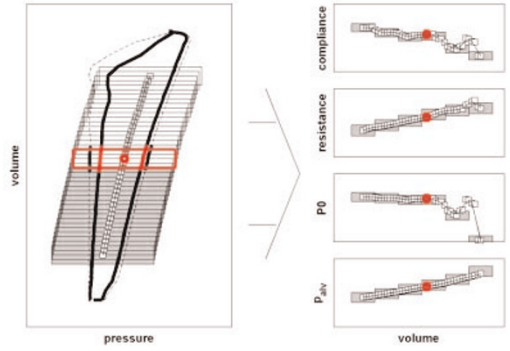
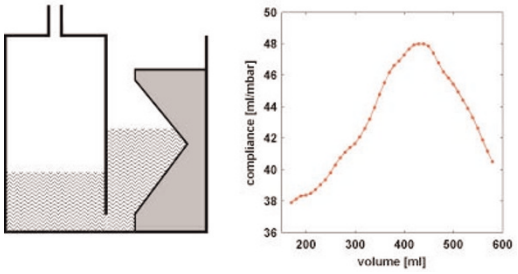


Figure 2 (abstract P204)



Reference

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P205

Functional residual capacity measurement during mechanical ventilation in order to find the optimal positive end-expiratory pressure

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Critical Care 2007, **11(Suppl 2):**P205 (doi: 10.1186/cc5365)

Introduction In patients with ALI/ARDS, a protective ventilation strategy has been introduced in order to diminish ventilator-induced lung injury. It has become clear that these patients require sufficient levels of PEEP to prevent alveolar derecruitment, but also not too much PEEP that alveolar overdistension occur. To achieve the optimal level of PEEP in patients with ALI/ARDS, different concepts have been introduced. GE Healthcare, along with Dr Ola Stenqvist, has developed a technology to measure functional residual capacity (FRC) in ventilated patients without interruption of the ventilation. The aim of this study was to test the feasibility of this device and to test whether decreasing the PEEP affects FRC in mechanically ventilated patients with and without lung disease.

Methods For this survey we examined 10 patients under mechanical ventilation. The FRC examinations were performed with the Engström Carestation equipped with the FRC Inview™ monitoring feature. FRC is determined using the change of lung nitrogen volume after a step change in the inspired oxygen fraction. With this system, there is no need to use supplementary gases or specialized gas monitoring devices. Furthermore, a series of FRC measurements can automatically be obtained at different PEEP levels that can be chosen prior to the measurement. During this procedure, all ventilator settings will remain constant other than the FiO_2 and the PEEP settings. In patients with ALI, the PEEP was decreased from 25 to 5 cmH_2O in five steps and the FRC was measured. In the patients without lung disease, PEEP was decreased from 15 to 0 cmH_2O in four steps and the FRC was measured.

Results The best FRC measurements were obtained in well-sedated patients during controlled mechanical ventilation. During pressure support ventilation, a constant breathing pattern is necessary for accurate FRC measurements. In patients that received pressure support ventilation, FRC values were lower at the highest studied PEEP level. In two patients that received controlled ventilation, lower levels of FRC were found at the highest PEEP level but this was due to a pneumothorax that was diagnosed a day later. In patients with ALI, the FRC decreased after each PEEP reduction step. However, the FRC decreased more when PEEP was lowered from 15 to 10 cmH_2O in these patients. In patients without lung disease, the FRC did not

decrease after PEEP was reduced from 15 to 5 cmH_2O but decreased after PEEP was reduced from 5 to 0 cmH_2O.
Conclusion Accurate measurements of FRC are obtained during a constant breathing pattern that is easier to obtain during controlled ventilation in comparison with pressure-support ventilation. In patients with ALI/ARDS, the FRC decreased during each PEEP reduction, but whether the largest change in FRC indicates the optimal PEEP needs further research.

P206

Analysis of the nonaerated lung volume in combinations of single computed tomography slices – is extrapolation to the entire lung feasible?

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Introduction The nonaerated lung volume (V_{non}) can be quantified from computed tomography (CT) images. Analysis of the CT slices covering the entire lung is time-consuming and thus limits potential clinical and experimental applications. This could be improved by analyzing only a few representative CT slices. The number and anatomical location of CT images required for analyses that are representative for the entire lung, however, is discussed controversially.
Methods The percentage of V_{non} ($\%V_{non}$) relative to the total lung volume was quantified in CT-image series ($n = 21$) of sheep with gross anesthesia-induced atelectasis. This was performed for different combinations of number and anatomical location of CT slices and the results were compared with the $\%V_{non}$ of the entire lung (lung). The combinations were: one juxtadiaphragmatic slice (juxta), three apical, hiliar and juxtadiaphragmatic slices (3old), and three consecutive juxtadiaphragmatic slices (3new). The correlation between $\%V_{non}$ and the arterial oxygen partial pressure (PaO_2) was examined for all combinations. The PaO_2 was measured at the time of the CT and transformed logarithmically ($lnPaO_2$) to linearize the relation between PaO_2 and $\%V_{non}$. Linear regression and Bland–Altman plots were used for statistical analysis.
Results The R-squared (R^2) values for the correlation between $lnPaO_2$ and $\%V_{non}$ of lung and the slice combinations juxta, 3new and 3old were 0.61, 0.60, 0.57 and 0.55, respectively. The $\%V_{non}$ of lung correlated best with the $\%V_{non}$ of slice combinations juxta and 3new ($R^2 = 0.96$ and 0.95, respectively). Comparison of these slice combinations with lung also resulted in the least bias in the Bland–Altman analyses (6.3 and 5.9%, respectively). R^2 for the correlation between lung and 3old was 0.93, and the bias for lung vs 3old in the Bland–Altman analysis was 6.8%.
Conclusion Depending on the precision required, the use of single juxtadiaphragmatic CT slices can help to speed up the analysis process and thereby propel the clinical implementation of CT-derived information. Our data suggest that juxtadiaphragmatic slices may be better suited than the 'traditional' combination of apical, hiliar and juxtadiaphragmatic slices.

P207

Pulmonary expansion and disobstruction maneuver with a closed system in patients with acute lung injury and acute distress syndrome, and its effect on gas exchange

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Introduction Respiratory physiotherapy is ever more utilized for the treatment of critical patients. However, it is known that there are few studies on the effect on gas exchange in patients with acute lung injury (ALI) and acute respiratory distress syndrome (ARDS) and physiotherapy techniques. The purpose of this study was to assess the effect of a pulmonary expansion and disobstruction maneuver with a closed system on the gas exchange of patients with ALI and ARDS.
Methods The patients with the diagnosis of ALI and ARDS who met the inclusion criteria were randomized to one of the two groups: those of the intervention group were subjected to a pulmonary expansion and bronchial disobstruction maneuvers, for approximately 10 minutes by the association of the following physiotherapy techniques: sighs, side-lying position, expiratory rib-cage compression and endotracheal suctioning with a closed system and after observed for 10 minutes; the patients of the control group did not receive any treatment, they were only observed for 20 minutes. Ventilatory parameters and arterial blood gases were measured before (Time 1) and 10 minutes after the procedures (Time 2). The analysis of variance test for repeated measurements was used for comparing variables at different times. Results are shown as the mean and standard deviation. The significant level was $P < 0.05$.
Results At Time 1, the control group ($n = 21$) had ratio of arterial partial pressure of oxygen to fraction of inspired oxygen (PaO_2/FiO_2) and partial arterial carbon dioxide pressure ($PaCO_2$) of 167.7 ± 56.2 and 40.3 ± 10.1, respectively, and the intervention group ($n = 19$) had PaO_2/FiO_2 of 180.5 ± 67.0 and $PaCO_2$ of 38.6 ± 10.5. At Time 2, the control group had, respectively, PaO_2/FiO_2 and $PaCO_2$ of 165.9 ± 63.8 and 38.9 ± 10.3, and the intervention group of 177.2 ± 4.5 and 39.0 ± 10.8. No variable was significantly different between the groups at Time 1 and Time 2 ($P > 0.05$).
Conclusion The proposed maneuver was not beneficial for gas exchange in the sample studied.

P208

Dry powder nebulization of a recombinant surfactant protein C-based surfactant for treatment of acute respiratory distress syndrome

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Critical Care 2007, **11(Suppl 2):**P208 (doi: 10.1186/cc5368)

Introduction Nebulization of pulmonary surfactant for treatment of ARDS represents a desirable therapeutic approach but was hitherto impossible under clinical conditions due to the technical limitations of currently available devices. In the present study we investigated a new dry powder nebulizer for administration of a recombinant surfactant protein C (rSP-C)-based surfactant.
Methods The nebulizer device consists of a cylindrical glass housing that, at the bottom, ends up in a spherical lower housing part that serves as the dry powder reservoir. A gas inlet portion with a nozzle at its end is coaxially aligned with the housing, almost reaches the bottom of the dry powder reservoir, and induces aerosol generation when gas pressures between 1 and 2 bar are applied. The upper portion of the housing contains a cap with an aerosol exit port. Several nozzles ensure a discharge of unsuitably large aerosol particles. Aerosol characteristics were determined by laser diffractometry. The efficacy of an inhalative rSP-C surfactant application was assessed in three animal models of acute lung injury, including rabbits with acute lung injury due to either repetitive lavage with prolonged and injurious ventilation, or due to inhalative application of bleomycin at day 4, and bleomycin-challenged, spontaneously breathing mice.
Results The generated aerosol had a mass median aerodynamic diameter of 1.6 μm, with 85% of all particles being smaller than

5 μm, and the average mass of surfactant being nebulized under these conditions was approximately 1 g/min. Biochemical and biophysical studies showed that the composition and surface tension reducing properties of the rSP-C surfactant remained unaltered after nebulization. In both rabbit models, administration of 130 mg/kg body weight rSP-C surfactant resulted in a far-reaching restoration of gas exchange and compliance. In bleomycin-challenged, spontaneously breathing mice, surfactant aerosolization resulted in a restoration of compliance.
Conclusions Nebulizer characteristics and results from the *in vivo* studies suggest that the herein-described dry powder nebulizer might proffer for surfactant therapy of ARDS.

P209

Changes in respiratory mechanics after fiberoptic bronchoscopy with bronchoalveolar lavage in mechanically ventilated patients

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Introduction Nonuniform findings have been reported about the effects of bronchoalveolar lavage (BAL) on respiratory mechanics.
Objectives (1) To study the effects of BAL on respiratory mechanics in mechanically ventilated patients with suspected pneumonia, and (2) to find out whether these effects are related to the extension of radiographic infiltrate and preceding respiratory mechanics measurements.
Methods BAL was performed with 150 ml sterile isotonic saline in three aliquots of 50 ml. Respiratory mechanics (static compliance and airway resistance) was measured using the rapid airway occlusion technique immediately before and after the BAL and 90 minutes later. The heart rate, arterial blood pressure and body temperature were recorded continuously in all patients. Patients were classified according to the presence of unilateral or bilateral infiltrates.
Results Fifty-eight critically ill patients undergoing mechanical ventilation were included. Following the BAL, compliance of the respiratory system (Crs) decreased from 50.9 ± 36.1 to 35.6 ± 14.8 ml/cmH_2O ($P < 0.01$) and airway resistance increased from 16.2 ± 7.6 to 18.1 ± 11.3 cm H_2O/l/seg ($P < 0.05$); 90 minutes later, both parameters had returned to pre-BAL values (P = not significant). Patients who showed >20% decrease in Crs had higher pre-BAL Crs than patients with less severe decrease (55.8 ± 20.1 vs 36.9 ± 14.1; $P < 0.001$). On the contrary, neither pre-BAL airway resistance nor the extension of the radiographic infiltrates were related to the changes in respiratory mechanics.
Conclusions (1) BAL in mechanically ventilated patients can lead to a significant but transitory deterioration on pulmonary mechanics characterized by a decrease in Crs and an increase in airway resistance. (2) Patients with better initial Crs showed the more severe affectation.

P210

Diagnosis accuracy of thoracic ultrasonography in severely injured patients

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Critical Care 2007, **11(Suppl 2):**P210 (doi: 10.1186/cc5370)

Introduction Thirty-three percent of severely injured patients suffer from thoracic trauma [1]. Diagnosis of pleural and pulmonary lesions at the bedside in the emergency department is difficult. Clinical examination (CE) and chest X-ray (X-ray) have limited sensibility and specificity. Contrast-enhanced computed tomography (CT scan) is the gold standard. CT scan has limitations: it takes time to be performed, implies transport of severely injured patients, and has ionising effects. Thoracic ultrasonography (US) can be quickly performed at the bedside in the emergency room. It has good diagnosis accuracy in ARDS patients [2]. The purpose of this study is to evaluate the diagnosis accuracy of US in severely injured patients in the emergency room.
Methods We prospectively evaluated 90 patients (median age: 41 (7–89) years) who were admitted to the emergency room of the Grenoble University Hospital over a period of 9 months. Pneumothorax, hemothorax and alveolar consolidation were diagnosed by CE, X-ray and US. The physician who performed the US was not involved in the patient's management. The diagnosis accuracy of each technique is compared with the CT scan interpreted by the radiologist.
Results Sixty percent of patients had a chest trauma IGS II 22 (8–104), ISS 20 (0–59), thorax AIS 2 (0–5), SOFA 1 (0–11), oxygen saturation at the entrance 100% (74–100), mechanical ventilation for 56% of patients. We studied 179 hemithorax. For hemothorax (n = 16), the sensitivity/specificity/positive predictive value/negative predictive values (%) were CE: 13/95/18/92; X-ray: 13/95/20/92; US: 63/95/56/96. For pneumothorax (n = 30), CE: 20/96/50/86; X-ray: 17/100/100/86; US: 53/93/62/91. For alveolar consolidation (n = 100), CE: 17/95/81/47; X-ray: 29/98/94/52; US: 69/82/83/67.
Conclusion Ultrasonography has a better sensitivity than CE and X-ray with a comparable specificity. In the emergency room it is a reliable modality for the diagnosis of pneumothorax, hemothorax and alveolar consolidation in the severely injured patient.
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P211

Prehospital emergency endotracheal intubation using the Bonfils intubation fiberscope

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Critical Care 2007, **11(Suppl 2):**P211 (doi: 10.1186/cc5371)

Objective Difficult intubating conditions are prevalent in 7–10% of patients who require out-of-hospital emergency endotracheal intubation. Airway anatomy can further be deteriorated through trauma, bleeding, and the use of cervical spine (CS) immobilization collars. We evaluated the feasibility of the Bonfils intubation fiberscope for prehospital emergency endotracheal intubation.
Materials and methods The Bonfils intubation fiberscope (Karl Storz GmbH, Tuttlingen, Germany) is a reusable, rigid, straight fiberoptic device with a 40° curved tip, 40 cm long and 5 mm in diameter. A flexible eyepiece is mounted on the handle of the scope. The fiberscope has a connector that fits onto the 15-mm tracheal tube adapter and thereby allows oxygen insufflation. A cold light source or a small battery handle (powered by two 1.5 V alkaline batteries) can be attached to the stylet handle. The tip of the Bonfils intubation fiberscope is positioned just proximal to the tip of the attached endotracheal tube, thereby preventing the lens from being soiled with blood or secretions. Having adopted the Bonfils technique in our institution, we felt that because of its battery-powered light source the Bonfils intubation fiberscope could also be used in prehospital settings, independent of a

110/220 V cold light source. After appropriate inhospital training with the Bonfils intubation in anesthetized patients, our hospital's mobile emergency unit staffed with an emergency physician was equipped with a battery-powered Bonfils intubation fiberscope.
Results During 123 missions, 15 adult patients underwent prehospital endotracheal intubation (cardiac arrest $n = 9$, multiple injuries $n = 4$, drug poisoning $n = 1$, pulmonary edema $n = 1$) with the Bonfils intubation fiberscope, the use of which was either planned ($n = 13$) or unplanned ($n = 2$). All intubations were successful in the first attempt, even in two cardiac arrest victims who had an unexpected difficult airway (Cormack&Lehane grade IV under direct laryngoscopy). In those patients with multiple injuries the cervical immobilization collar did not need to be unfastened or removed for endotracheal intubation. Sufficient retropharyngeal space – which is mandatory for sufficient use of the Bonfils – was created by a digital jaw thrust maneuver in the first three patients. Using a standard Mackintosh laryngoscope blade significantly enhanced ease of insertion of the Bonfils fiberscope and visualization of the glottic aperture, thereby decreasing the procedure time from 35–40 seconds to 20–25 seconds.
Conclusion Despite this first promising series of in-the-field use, physicians and paramedics should familiarize themselves with the Bonfils device under optimal clinical conditions before using it under emergency or prehospital conditions. In our experience, the learning curve with the Bonfils device is steep, and 10 intubations supervised by an instructor usually prove effective for achieving sufficient skills to use the Bonfils on one's own and under less optimal conditions. In summary, we believe that the Bonfils fiberscope will prove its value as an additional airway management device in both, emergency and prehospital settings.
Acknowledgement The Bonfils intubation fiberscope was generously provided by Karl Storz GmbH, Tuttlingen, Germany.

P212

Airway equipment on the intensive care unit for management of the unanticipated difficult intubation

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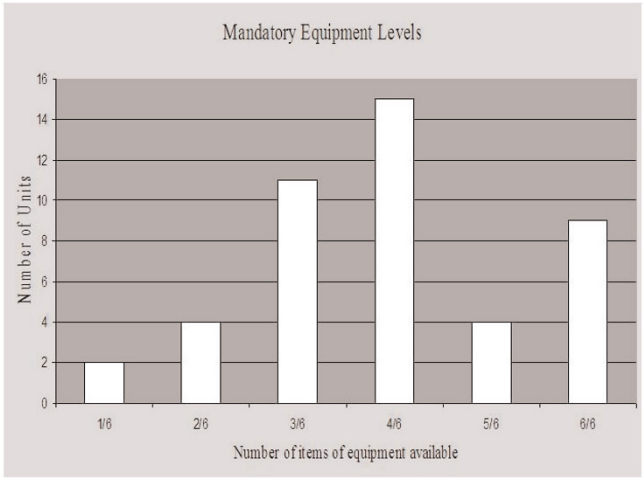
Introduction This study was designed to assess the ability of ICUs to deal with the unanticipated difficult intubation. The ICU is a location in which the incidence of difficult intubation has been found to be significantly higher than in theatre (8–22.5% vs 1.5%).
Method We contacted all adult general ICUs in the South of England and invited the physician responsible for airway management to take part in a structured interview. The interview was designed to follow the Difficult Airway Society (DAS) guidelines. We designed six equipment-related questions that identified a unit as achieving the minimum levels of equipment necessary. These included availability of laryngoscopes, capnography, LMA/ILMA, and rescue techniques.
Results Forty-five of 51 units responded (88%). Mandatory equipment levels are shown in Figure 1.
Discussion Difficult intubation is more likely on the ICU, yet only 20% of units keep sufficient equipment immediately available. The most serious omissions were the 29% of units without a rescue technique immediately available and the one-third of units not routinely employing capnography.

Figure 1 (abstract P212)



Airway equipment available on ICUs. A score of 6/6 is considered the minimum.

P213

Potential of the AirWay Scope for tracheal intubation in a confined space

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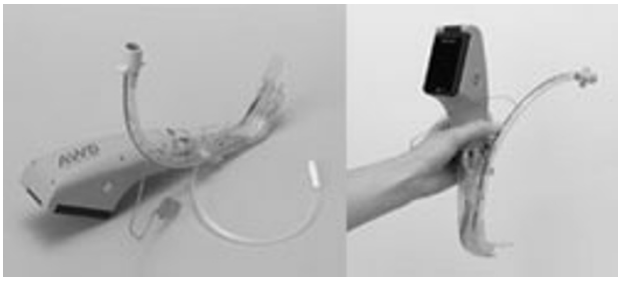
Critical Care 2007, **11(Suppl 2):**P213 (doi: 10.1186/cc5373)

Introduction Occasionally, rescuers are confronted with a hard situation to establish tracheal intubation compared with doctors in the anesthetic room. Especially in the confined space, the tracheal intubation must enter technical difficulties with any supporting device. This may be caused by the fact that there was no device developed specially from a standpoint in the clinical emergency use.
Objective The AirWay Scope (AWS) is one of the newest intubation devices, manufactured using modern technology to alleviate the tracheal intubation in emergency scenes. The AWS is equipped with a full-colored CCD, a LCD monitor and a specially configured introducer guiding a tracheal tube into the glottis (Figure 1). The aim of this study is to confirm the potential of the AWS as an intubation-supporting device in emergency scenes.
Method Six doctors in the emergency department were enrolled in this study. All doctors have experienced using the AWS in cases on the operation table but have no experience in special situations such as patients on the ground (POG) or no space over the head of the patient (NSH). Doctors tried intubation with the AWS and Macintosh Laryngoscope (Mac) in the simulated POG and NSH situations using a Laerdal Airway manikin. Technical training was not carried out in advance. The NSH/Mac situation was not investigated because it was theoretically impossible. The time to intubate (TTI) was recorded.
Result All doctors successfully established intubation in each situation, POG/Mac, POG/AWS and NSH/AWS. Although the intubation of a manikin having no space over the head was thought to be difficult without prior training, all doctors successfully achieved the intubation from the foot using the AWS. The TTI (s) was 12.0 ± 1.5 in POG/Mac, 7.4 ± 1.1 in POG/AWS and 12.9 ± 1.4 in NSH/AWS. The TTI with AWS in POG situation was significantly shorter than that with Mac ($P = 0.0135$).

Figure 1 (abstract P213)



Conclusion With its portability, easy handiness, excellent visual information and the tube-guiding function of the introducer, the AWS may have potential to alleviate the various difficulties in intubation in emergency scenes, even in a confined space.

P214

A comparison of two types of new bronchial blockers, Uniblocker™ and Coopdech endotracheal blocker tube, for one-lung ventilation during thoracoscopy

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Critical Care 2007, **11(Suppl 2):**P214 (doi: 10.1186/cc5374)

Introduction The purpose of this study was to compare the use of a wire-guided bronchial blocker, Uniblocker™ (Fuji Systems Corporation, Tokyo, Japan), with a spread type of bronchial blocker, Coopdech endotracheal blocker tube (Daiken Medical Corporation, Osaka, Japan), for lung isolation during elective thoracic surgical cases.
Materials and methods Twenty ASA I–II patients signed written informed consent before being enrolled into the study. We designed a prospective, randomized trial to compare the effectiveness of lung isolation among the two types of bronchial blockers: Uniblocker™ group (UBB; $n = 10$), and Coopdech endotracheal blocker tube group (CBB; $n = 10$). Patients were randomized to intubate with a single-lumen tube with concomitant use of a UBB or a CBB. Both groups were subdivided in two: bronchial blocker placed in the right mainstem bronchus (UBBR/CBBR), and in the left mainstem bronchus (UBBL/CBBL). Comparisons between groups included: (1) the number of unsuccessful placement attempts with the blinded insertion technique, (2) the number of malpositions of the devices, (3) the time required to place the device in the correct position, (4) surgical satisfaction with the lung deflation, (5) complications and (6) the quality of lung deflation.
Results The number of unsuccessful placement attempts was none in the UBBR group (0/10) and one in the CBBR group (1/10), two in the UBBL group (2/10) and five in the CBBL group (5/10). A fiberoptic aided technique should be more appropriate for the left-sided blocker in both groups. There was no statistical difference in bronchial blocker malpositions, the lung to collapse and the number of complications among the two groups. Furthermore, for elective thoracic surgical cases, once the lung was isolated, the management seemed to be similar for both groups.
Discussion This study demonstrates that the wire-guided bronchial blocker (Uniblocker™) provides a high torque control and can be easily manipulated into the desired site of the lungs. In conclusion, our study shows that the Uniblocker™ is more useful than the Coopdech bronchial blocker tube.

P215

Comparison of the LoTrach and the Portex Soft Seal cuff: tracheal wall pressure and fluid leakage in a benchtop study and a clinical study

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Critical Care 2007, **11(Suppl 2):**P215 (doi: 10.1186/cc5375)

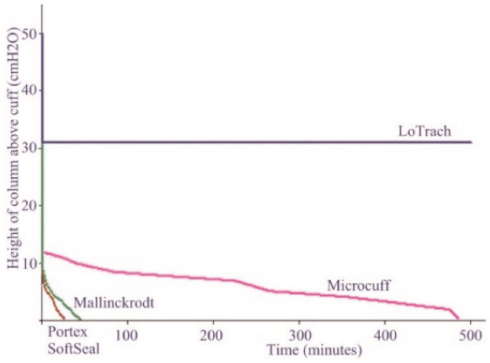
Introduction The objective of the study is to demonstrate two methods of measuring tracheal wall pressure (*in vitro* and in patients), with the LoTrach (LVLP) cuff and with conventional high-volume low-pressure (HVLP) cuffs. The LoTrach (VTSL, Singapore) is a new tracheal tube designed for use for mechanical ventilation in the critically ill. The LoTrach has been shown to prevent the ubiquitous problem of micro-aspiration of secretions associated with conventional HVLP cuffs [1]. Aspiration prevention is achieved by the properties of the LoTrach's low-volume low-pressure (LVLP) cuff, and these have been previously described [1,2]. It is important that, alongside achieving aspiration prevention, there is also tracheal wall pressure control. The LoTrach LVLP cuff is calibrated such that the sum of the elastic forces within the cuff remain constant throughout the inflation profile. Thus, at the working intracuff pressure of 80 cmH_2O, only a consistent and acceptable 30 cmH_2O is transmitted to the tracheal wall [2].
Methods *Benchtop model*. Four tracheal tubes (8 mm internal diameter) were studied; the LoTrach, Portex SoftSeal, Microcuff and Mallincrokdt HiLo Evac. The model trachea had an internal diameter of 2.4 cm and the cuff was inflated with a Tracoe constant pressure device. The cuff was overpressured while fluid was instilled above the cuff to a height of 50 cm. The stopwatch was started as the pressure was reduced to the test pressure of 30 cmH_2O. The rate of fall of the resulting column of fluid was then measured.
Clinical study. Intubated patients underwent a staged recruitment manoeuvre while the intracuff pressure was maintained with a Tracoe cuff inflator. The PEEP was set to 15 cmH_2O and then increased in 5 cmH_2O increments every 5 seconds until 40 cmH_2O was achieved. A second observer auscultated the anterior neck and the pressure at which air leak was heard was recorded. Two tubes were studied; LoTrach (at 80 cmH_2O intracuff pressure = 30 cmH_2O calculated wall pressure) and Portex Soft Seal (30 cmH_2O).
Results Conventional HVLP cuffs do not prevent leakage of fluid past the cuff, hence the negative slope on the graphs. The LoTrach cuff does not leak and therefore the line is horizontal (see Figure 1). The clinical study shows that both the LoTrach and Portex cuffs demonstrate a gross air leak at equal and acceptable tracheal wall pressures at 33.4 and 29.7 cmH_2O, respectively (see Table 1).

Table 1 (abstract P215)

Type of tube	Number of measurements	Tracheal wall pressure (cmH_2O)
LoTrach (LVLP)	45	29.7 (SD = 3.7)
Soft Seal (HVLP)	41	33.4 (SD = 3.1)

Conclusions In the benchtop model, the LoTrach LVLP cuff demonstrates an acceptable wall pressure of 30 cmH_2O (at an intracuff pressure of 80 cmH_2O), while achieving the prevention of leakage of fluid past the cuff. The clinical study demonstrates that the tracheal wall pressure was both acceptable and equal for both the Portex HVLP and the LoTrach LVLP cuffs. The LoTrach prevents micro-aspiration in the benchtop model with acceptable tracheal wall pressures in both the benchtop and clinical studies.

Figure 1 (abstract P215)



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P216

Safety of semi-open percutaneous tracheotomy when performed in critically ill burn patients

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Critical Care 2007, **11(Suppl 2):**P216 (doi: 10.1186/cc5376)

Introduction Lung injury and generalized edema from a burn and resuscitation complicates airway management and patient care. The need for long-term ventilation and multiple surgeries warrant early tracheostomy. Percutaneous techniques are well described; however, the burned and swollen neck increases all of its recognized complications. We report a modified semi-open technique for performing percutaneous tracheotomies (PT) in acutely burned patients, which we consider safer.
Methods We reviewed the medical records of 20 patients admitted to a regional burn center requiring tracheostomy for prolonged mechanical ventilation. The procedure took place in the OR if burn excision was planned; otherwise it was performed at the bedside. The Blue Rhino tracheostomy kit was used for all PT. Major differences from other approaches included dissecting down to the pretracheal fascia, allowing the trachea to be seen and palpated; bleeding was controlled using an electrocautery, and blood vessels were retracted from the field or ligated. The trachea was palpated as the endotracheal tube was withdrawn into the proximal trachea and a flexible bronchoscope was used only to confirm the proper placement of the guidewire. Proper placement of the tracheal tube was confirmed by capnography. In patients with a deep trachea due to severe neck swelling, a proximal-long tracheostomy tube was substituted for the standard one. In the event that the airway or ventilation became compromised, this technique could be converted rapidly to an open procedure.
Results Of 350 patients admitted to the burn center from July 2005 to December 2006, 20 (6%) required a tracheostomy. Eighteen were performed percutaneously, 13 at the bedside. The total burn surface area averaged 46% (range 2–95%). PT were performed within an average of 10 days from admission (range 0–32 days). Overall mortality in the tracheostomy group was 35%. There were no short-term complications associated with this method.
Conclusion PT can be performed safely in severely burned patients using a semi-open percutaneous technique. Exposing the trachea and palpating the trachea avoids the risk of losing the airway and permits immediate access to the trachea in the event of an untoward loss of the airway. We believe that this method is safer than the more commonly used technique requiring bronchoscopic visualization.

P217

Outreach-led tracheostomy service in a cardiothoracic centre: early and safe facilitated discharge from critical care

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Critical Care 2007, **11(Suppl 2):**P217 (doi: 10.1186/cc5377)

Introduction A retrospective analysis of a year cohort of tracheostomies discharged from intensive care in a specialist cardiothoracic centre was undertaken to analyse whether facilitated outreach-led discharge was safe.
Methods A retrospective analysis of the ICU database was undertaken to identify all patients who had a tracheostomy (percutaneous or surgical) inserted in the ICU, and a chart review of patients discharged from the ICU with a tracheostomy *in situ* was performed. The following variables were collected: patient demographics; diagnosis; number of days of tracheostomy *in situ*; number of days on noninvasive ventilation (CPAP); and tracheostomy-related complications. A review of the risk management database was performed to identify any tracheostomy-related reported adverse events.
Results One hundred and eight tracheostomies were performed in intensive care in the 2-year period. Sixty-two patients were discharged with tracheostomy *in situ* and were reviewed by the outreach team for a cumulative total of 710 days until decannulation. There were 383 days whereby patients with a tracheostomy *in situ* had been noninvasively ventilated. There were three reported critical events relating to tracheostomy and no deaths.
Conclusion More than 60% of patients who had a tracheostomy inserted are discharged from critical care with a tracheostomy *in situ*. With the support of the outreach team these patients were successfully managed in Level 2 and Level 1 areas. This reduced the requirement for critical care (Level 3) bed-days. There was a low rate of complications. We concluded that outreach services can facilitate early and safe discharge of tracheostomy patients from critical care.

P218

Prevention of airway control loss during percutaneous tracheostomy

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Background Loss of airway control during percutaneous tracheostomy (PCT) is one of the serious complications. It may happen due to an unstable position of the endotracheal tube (ETT) with its tip in the larynx and cuff above the vocal cords. This

position of the ETT is the main request for PCT performance. We retrospectively reviewed our experience with additional use of the fiberoptic bronchoscope (FOB) and tube exchanger (TE) for stabilization of ETT during PCT.

Patients and methods From the 160 adult critically ill patients that underwent PCT by the Griggs technique between January 2000 and August 2001, we selected 33 patients receiving anesthesia from the same anesthetist. From this group 12 patients were ventilated through ETT by the standard technique: in 11 patients a pediatric FOB was used to control and stabilize the position of ETT during PCT, and in the remaining 10 patients a 15-Fr TE was used with the same aim instead of a pediatric FOB. The optimal diameters of FOB and TE suitable for ETT (7.5 mm, 8 mm) were found in our previous experiments, using a mechanical lung simulator.

Results Loss of airway control during PCT occurred in three patients, where ventilation through the ETT was performed by the standard technique. This complication was corrected by expeditious actions of the anesthetist and surgeon. In the other patients, additional use of a pediatric FOB or TE has created secure and proper position of the ETT and PCT passed smoothly without complications. Moreover, we could not register a negative influence of a pediatric FOB and 15-Fr TE presence in the ETT on ventilation parameters during PCT performance.

Conclusions Stabilization of the ETT position and prevention of airway control loss during PCT performance can be reached by use of a pediatric FOB or by 15-Fr TE with the same reliable results. Employment of a pediatric FOB is more expensive than a TE.

P219

Routine chest radiography following percutaneous dilatational tracheostomy

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Critical Care 2007, **11(Suppl 2):**P219 (doi: 10.1186/cc5379)

Background and objective The role of routine chest radiography (CXR) following percutaneous dilatational tracheostomy (PDT) has recently been questioned [1].

Materials and methods We performed a prospective observational study, on a mixed medical–surgical critical care unit, in 291 patients undergoing PDT under bronchoscopic guidance to assess the utility of routine postoperative CXR. Data were collected on all patients undergoing PDT from 1 November 2003 to 5 December 2006. Two postprocedure CXRs were reviewed and compared with those taken prior to PDT. Significant findings were barotraumas (pneumothorax, pneumomediastinum) and consolidation not noted on the preprocedure film. Postprocedural films reviewed were those taken immediately after PDT and, to exclude the possibility of overlooking evidence of minor barotrauma, one further film taken between 24 and 96 hours.

Results A total of 291 patients underwent PDT. Two hundred and six (71%) were uncomplicated. Complications were recorded in 85 (29%) patients. Of these, 71 (24%) were minor procedural complications (multiple attempts at needle insertion (>2), minor bleeding, tracheal ring fracture) and there were 14 (5%) major complications (malplacement, major bleeding). Two hundred and thirty-six (81%) patients had two postprocedural CXRs reviewed. Of the remainder, 44 (15%) patients had at least one CXR reviewed after PDT and in 11 (4%) patients neither the report nor the CXR could be reviewed. New abnormalities were noted on 25 (9.0%) postprocedure CXRs. No new pneumothoraces were seen (Table 1). In 11 (4%) patients, neither the report nor the CXR could be reviewed.

Table 1 (abstract P219)

	Number (%)	New problem seen on CXR (*n* (%))
Two CXRs reviewed		
Uncomplicated PDT	167 (57)	15 (5)
Complicated PDT	69 (24)	10 (3)
One CXR reviewed		
Uncomplicated PDT	36 (12)	0
Complicated PDT	8 (3)	0
Total	280	25

Conclusions Routine CXR following uncomplicated PDT performed under bronchoscopic guidance appears unwarranted. Review of later films failed to reveal new abnormalities. The role of CXR following PDT appears to be restricted to those patients undergoing complicated procedures. This will lead to reductions in both medical costs [2] and exposure to ionising radiation.

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P220

Biphasic DC shock as a first-line therapy in recent-onset stable atrial fibrillation in the emergency department

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Critical Care 2007, **11(Suppl 2):**P220 (doi: 10.1186/cc5380)

Objective To evaluate the efficacy of early electric cardioversion (EC) with a biphasic defibrillator and the impact on atrial function in recent-onset atrial fibrillation (AF).

Methods The study population consisted of 21 consecutive patients (mean age 58 years; range 35–76 years) with AF lasting from less than 48 hours. Hemodynamically stable AF was treated via DC shock if sinus rhythm (SR) was not restored in 6 hours after i.v. antiarrhythmic drug therapy. All patients were pretreated with heparin 5,000 U i.v. The defibrillator used was the Heartstart MRX using a biphasic waveform and low energy (70–120 J). A transthoracic echo was performed pre-EC and 1 hour post-EC. All patients were sedated with midazolam (*in vivo* titolation). Atrial function (ejection fraction, surface area, A wave) and ventricular function (ejection fraction) were evaluated. The patients returned to the emergency department after 7 days for follow-up. Data were analyzed using descriptive statistics (Table 1).

Results DC shock was successful for all patients (100%) and in 19/21(90.4%) at first shock. There was a significant increase in atrial function with the reappearance of the A wave. There were no

Table 1 (abstract P220)

		Pre-EC	Post-EC
Number of patients	21		
Age average	59		
Sinusal rhythm restoration	21/21		
Left atrial ejection fraction two chambers		30	35 ($P = 0.02$)
Left atrial ejection fraction four chambers		29	35 ($P = 0.02$)
Left ventricular ejection fraction		52	54 ($P =$ NS)
A wave (m/s)			0.54

thromboembolic complications. After 7 days, results showed that 19/21 (90.4%) patients were in SR.

Conclusion Early electric cardioversion in the emergency department setting is a simple technique that allows the restoration of SR without complications. The biphasic waveform uses lower energy with a positive impact on atrial function. Higher energy can cause transient tissue damage due to electroporation that can affect the outcome of defibrillation therapy being both pro-arrhythmic and anti-arrhythmic. The recovery of atrial function is also due to the short duration of arrhythmia. The early cardioversion avoids atrial remodelling and allows a longer duration of SR.

P221

Incidence and diagnosis of patients developing atrial fibrillation in intensive care

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Critical Care 2007, **11(Suppl 2):**P221 (doi: 10.1186/cc5381)

Introduction Atrial fibrillation (AF) is a common arrhythmia encountered in critically ill patients. In this study we evaluated the incidence and risk factors associated with the occurrence of AF in a general ICU.

Methods One hundred and ten patients admitted to the ICU during a 3-month period were screened for AF. Case notes and daily management charts of these patients were analysed retrospectively.

Results Twenty-nine (26.3%) out of 110 patients developed AF. The mean age of patients was 71.8 (±9.2) years and the APACHE II score was 21.3 (±6.3). Electrolytes were within the normal range in 85% of the patients. The main cardiac factors identified in our patients with AF were hypertension (71.4%) and coronary artery disease (48.3%). Less commonly encountered cardiac diagnoses were congenital heart disease and history of previous atrial fibrillation. Inotropic support and sepsis were the leading noncardiac factors found in 24 (82.8%) and 22 (75.9%) patients, respectively. Diabetes mellitus and obesity contributed in 17.2% of patients.

Troponin T was determined in 13 patients and found to be elevated in 10 patients (34.5% of AF patients). Transthoracic echocardiography was performed on 10 patients with persistent AF (34.5%). Seven patients had valve pathology whereas left ventricular dysfunction was present in five patients. Only one echocardiography was reported normal. Patients were treated according to local guidelines with amiodarone (19 (65.5%)), digoxin (5 (17.2%)) and β-blockers (4 (13.8%)), and DC cardioversion was used in only one patient. Eighteen (62.1%) patients were successfully cardioverted.

Conclusion Apart from known risk factors for AF such as increased age, hypertension or ischaemic heart disease, sepsis and inotropes increase susceptibility for AF. Less frequently associated causes such as congenital heart disease, obesity and diabetes can contribute towards AF. Echocardiography could reveal less obvious causes of AF like valvular pathologies and left ventricular dysfunction, and could be a useful diagnostic tool in critically ill patients with AF.

P222

The calcium sensitizer levosimendan reduces the brain natriuretic peptide levels as compared with dobutamine in intensive care unit septic patients with decompensated heart failure

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Introduction The brain natriuretic peptide (BNP) is a useful index to follow-up patients with heart failure as well as a special diagnostic and prognostic tool. This study aims at investigating the impact of levosimendan in comparison with dobutamine on the BNP levels in ICU patients with decompensated heart failure related to septic shock. The role of levosimendan in septic patients is still under consideration.

Methods Twenty-nine patients (20 males and nine females) of a 70.5 ± 9.2 average age rate with persisting left ventricular dysfunction related to severe sepsis, after receiving a 48-hour conventional treatment including inotropic agents, were randomised to either 24-hour i.v. levosimendan (0.2 γ/kg/min) (n = 15) (Group A) or dobutamine (5 γ/kg/min) (n = 14) (Group B) therapy. Serial BNP measurements were performed before, at 48 hours and 5 days later.

Results Levosimendan therapy significantly reduced the BNP levels both in 48 hours and in 5 days as compared with dobutamine. Group A: 1,138 ± 93.7, 740.2 ± 106, 445 ± 118.3 and Group B: 1,561 ± 370.2, 1,436 ± 368, 1,850 ± 520.5, before, 48 hours and 5 days later, respectively. P = 0.025 for 48 hours and P = 0.037 for 5 days.

Conclusion Levosimendan therapy reduces BNP levels, reflecting a beneficial haemodynamic effect on the ICU patient with septic myocardial depression.

P223

The ADHERE classification and regression tree model overestimates mortality rates in clinical trials: results from REVIVE I & II

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Background Blood urea nitrogen (BUN), systolic blood pressure (SBP), and serum creatinine (Cr) were significant predictors of inhospital mortality by classification and regression tree (CART) analysis of ADHERE. REVIVE I & II (REVIVE) compared levosimendan with placebo, in addition to standard-of-care (SOC), in patients with acute decompensated heart failure. We hypothesized that mortality in REVIVE would be similar to ADHERE in all CART-defined risk subgroups.

Methods REVIVE (n = 700) mortality data were mapped using the same variables/cut-points as the ADHERE CART analysis.

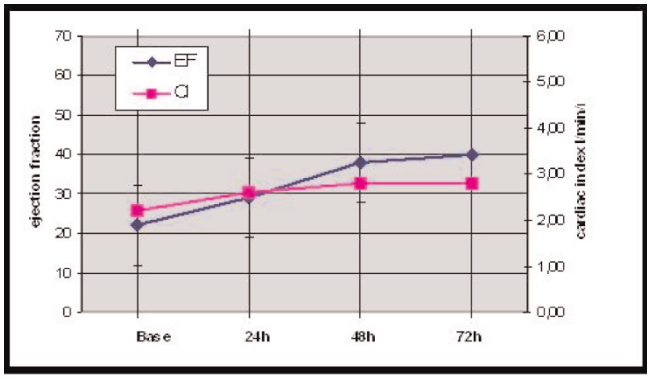
Results Compared with ADHERE, proportionately more patients in REVIVE had SBP <115 mmHg (56.4% vs 18.6%; P < 0.001) with more patients (3.0% vs 1.9%; P < 0.05) in the highest mortality risk subgroup (SBP <115 mmHg, BUN ≥43 mg/dl, and Cr ≥2.75 mg/dl). For the total population and for every CART-defined subgroup, REVIVE inhospital mortality rates were lower than those from ADHERE. See Figure 1.

Figure 1 (abstract P223)

BUN, mg/dL	All	<43			≥43				
SBP, mmHg	All	All	<115	≥115	All	<115		≥115	
Creatinine, mg/dL	All	All	All	All	All	All	<2.75	≥2.75	All
		Patient Population, %							
ADHERE	100.0	78.2	12.5	65.1	21.8	6.1	4.2	1.9	15.5
REVIVE	100.0	76.4	41.6	34.8	23.6	14.8	11.8	3.0	8.8
		In-Hospital Mortality, %							
ADHERE	4.0	2.8	5.6	2.2	8.7	15.3	12.8	20.9	6.0
REVIVE	3.2	1.8	2.5	0.9	7.7	10.2	7.7	20.0	3.4

Mortality rates from REVIVE for subgroups defined by the ADHERE classification and regression tree model.

Figure 1 (abstract P224)



Conclusion Clinical trials (REVIVE) may enroll proportionately more patients at increased risk of mortality in comparison with the general population (ADHERE). Despite the predicted increased mortality risk, mortality rates were lower in REVIVE than in ADHERE for the total population and for every CART-defined risk subgroup. Differences in SOC or additional risk factors, such as age or other comorbid conditions, may contribute to the poorer prognosis in nontrial populations.

P224

Levosimendan in patients with acute cardiogenic shock, not responders to conventional therapy

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Critical Care 2007, **11(Suppl 2):**P224 (doi: 10.1186/cc5384)

Introduction Cardiogenic shock remains the leading cause of death in patients hospitalized for myocardial infarction, acute valvular disease and after cardiac surgery. Levosimendan (LS) is a new inodilator that has been shown to improve hemodynamic function in patients with decompensated systolic heart failure without increased myocardial oxygen consumption. The aim of this study was to evaluate the use of LS as rescue medication in patients with low ejection fraction (EF) that are not responders to conventional therapy.
Methods Twelve patients with acute cardiogenic shock admitted to the ICU were enrolled. The diagnosis of cardiogenic shock was made on cardiac index (CI) measured by thermodilution catheter <2.5 l/min/m^2, and baseline echocardiography with EF measured by the biplan Simpson method <30%. LS (Orion Pharma, Helsinki, Finland) at the dose of 0.1 γ/kg/min for 24 hours continuous infusion was added to standard inotropic agents (dobutamine, enoximone, epinephrine) or IABP when CI and EF seemed not to improve or when the patient's condition worsened. Hemodynamic measurements and echocardiography data were recorded at ICU admission and when pharmacological therapy was changed at 24, 48 and 72 hours.
Results The data collection showed: an increase in CI (baseline to standard therapy) of 2.6 ± 0.51 ($P < 0.001$), and standard therapy to LS of 2.93 ± 0.67 ($P < 0.003$) that seem to be additive. Significant increase in EF was noted in comparison with standard therapy (29.88 ± 6.15, $P < 0.035$) and after LS therapy (38.44 ± 6.56, $P < 0.001$) (Figure 1). To find differences between baseline and pharmacological therapy changes at 24, 48 and 72 hours a *t* test was performed.
Conclusion We found an additive effect of dobutamine, enoximone and LS that theoretically can be explained by the different mechanism of action. Catecholamines increase Ca^{2+} availability and LS increases myocardial cell calcium sensibility.

P225

Retrospective study of proarrhythmic effects of levosimendan during the therapy of heart failure

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Critical Care 2007, **11(Suppl 2):**P225 (doi: 10.1186/cc5385)

Introduction Levosimendan is a new, effective inodilator agent, which is a new alternate drug beside conventional inotropic drugs in treatment of acute and chronic heart failure. Positive inotropic effects of levosimendan is based on myocardial Ca-sensitising. Few clinical data are available about the occurrence of proarrhythmic effects of levosimendan, particularly administered in parallel with catecholamines.
Method From 1 January 2006 until 30 July, 41 levosimendan-treated patients' data were processed in our retrospective study. Indication of levosimendan therapy was acute heart failure due to myocardial infarction in 23 cases and acute progression of chronic heart failure (NYHA III–IV) in 18 cases. After a 10-minute bolus levosimendan infusion was administered at rate of 0.1 μg/kg/min for 6 hours and 24 hours in each group, respectively. We investigated the occurrence of sustained ventricular or supraventricular arrhythmias for the first 48 hours from the beginning of infusion.
Results The ratio of hypertension, diabetes, earlier myocardial infarction and ACBG were 58%, 27%, 32% and 15%, respectively, in the monitored population (13 females, 28 males; mean age: 68 years). Three ventricular arrhythmias and one supraventricular arrhythmia were observed during the 48-hour period, all of them occurred in acute heart failure patients with acute myocardial infarction. Parallel usage of catecholamines (noradrenalin and/or dopamine) and levosimendan therapy was observed in three cases, in one of them ventricular tachycardia was observed 3 hours after starting levosimendan infusion. No arrhythmia was observed in chronic heart failure patients. The incidence of proarrhythmic effects during levosimendan therapy was 9.75% of the whole analysed population and was 17.4% at acute heart failure during acute myocardial infarction.
Conclusion With these results the authors would like to draw attention to the proarrhythmic effects of levosimendan during acute heart failure therapy, especially in the case of parallel usage with catecholamines.

P226

Levosimendan in myocardial depression due to severe sepsis

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Introduction Myocardial depression in sepsis, among other factors, is due to calcium (Ca^{2+}) desensitization in the myofilament. So using a Ca^{2+} sensitizer drug may play a beneficial role in this situation. Levosimendan has a dual mechanism; it causes Ca^{2+} sensitization through binding to Troponin C and opening of ATP-dependent K^+ channels in vascular smooth muscle.
Methods A prospective observational case-series study extending over a period of 18 months from November 2004 to April 2006. We analyze the data of 18 patients receiving levosimendan for myocardial depression due to severe sepsis and compare them with our historical data in the previous year of the same group of patients regarding mortality. All those patients were included in the study who had a pulmonary artery catheter (PAC) and who after initial resuscitation (early goal-directed therapy (EGDT)) did not respond to treatment and their cardiac index (CI) was <2.2. Each patient than received an infusion of levosimendan at 0.1 μg/kg/min without a loading dose. Hemodynamic parameters such as the CI, mixed venous saturation (SvO_2) and mean arterial pressure (MAP) were recorded at 0, 12, 24 and 48 hours. Noradrenaline was used to maintain a MAP above 65 mmHg. Patients were followed for 30 days to document the 7th-day and 30th-day mortality. SPSS 11 was used for statistical analysis. The Student *t* test was used as a test of significance.
Results The average age was 67.6 ± 10.39 years and the APACHE II score was 26.33 ± 2.37. Patients were divided into three subgroups: survivors, 7th-day and 30th-day mortality groups. There was no significant difference in these subgroups regarding age and APACHE II score. Levosimendan group 7th-day and 30th-day mortality was 33% and 66% as compared with historical data of 37% and 71%, respectively. The change in CI in the survivor group was significant ($P = 0.021$), from 2.11 ± 0.17 to 3.8 ± 0.28, while in the 7th-day and 30th-day mortality groups it was insignificant. SvO_2 increased in the survivor and 30th-day mortality groups significantly ($P = 0.011$ and $P = 0.035$, respectively). It did not show any significant improvement in the other group. MAP also showed significant improvement in the survivor group ($P = 0.026$) and insignificant in others.
Conclusion It is evident from our study that levosimendan improves hemodynamic response in septic patients. Although it improves the mortality, we cannot say with full confidence that these improved hemodynamic parameters are responsible. Randomised control trials are needed to answer this question, which are underway.

P227

The elderly acute coronary syndrome patient: a neglected population?

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Introduction Cardiovascular disease is the commonest cause of death in the elderly (>75 years). The elderly acute coronary syndrome (ACS) patient forms a particular high-risk cohort. Clinical trials traditionally concentrate on younger patients for both ACS treatment strategies and secondary prevention, despite the elderly being the fastest growing section of the population. The literature suggests the elderly do not receive appropriate therapy in this setting. What is the current UK experience?
Objective and method To assess the secondary preventative treatment received by the elderly ACS patient. Retrospective analysis of our Myocardial Infarction National Audit Project (MINAP) database 2003–2006. Patients were divided into three age groups: <50 years, 50–75 years and >75 years old. Data were collected from hospital admission to discharge.
Results A total of 1,501 consecutive patients were included in the analysis, 530 patients (35.3%) were >75 years, mean age 83.6 years (±5.1). The discharge diagnosis was ST elevation myocardial infarction in 619, UA/NSTEMI in 870 and unspecified in 12 patients. The overall inpatient all-cause mortality rate was 8.06% (121/1,501). See Table 1.

Table 1 (abstract P227)

	<50 years	50–75 years	>75 years
Total	149	822	530
STEMI	84	364	172
Inhospital mortality	0	33 (4%)	88 (17%)
Aspirin (%)	98.7	94.5	90.4*
ACE-I (%)	84.6	83.4	66.4*
β-Blocker (%)	93.8	82.4	72.9*
Statin (%)	96.5	95.6	89*

*$P < 0.001$, chi-squared.

Conclusions The elderly ACS patient forms a high-risk group. The therapeutic approach in this group should be justifiably as aggressive as that in younger patients, balancing risks with benefits. The elderly patient should be prescribed secondary preventative measures, and our data show considerably greater numbers can benefit from standard treatment than suggested by the published literature.

P228

Long-term prognosis of octagenarian patients with ST-elevation acute myocardial infarction treated by primary angioplasty

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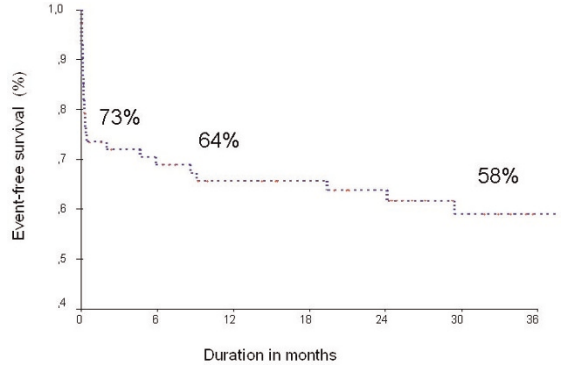
Introduction The incidence of acute myocardial infarction (AMI) in old patients is increasing due to rapid aging of the population. This is of particular concern because AMI in patients who are ≥80 years old is associated with high mortality. However, the role of reperfusion therapies is not clear in these patients.
Objective To evaluate the mid-term and long-term prognosis of octogenarian patients with ST-elevation myocardial infarction (STEMI) treated with primary coronary angioplasty (PCA).
Methods We studied retrospectively, from January 2000 to March 2005, 73 patients ≥80 years with STEMI treated with PCA. At the end of follow-up, we assessed the incidence of death, myocardial infarction and necessity of new procedures of revascularization of the treated vessel.
Results The average age was 84 ± 3.6 years, 39 (58%) were women. The location of the AMI was anterior in 56%, and 25% were diabetic. The average follow-up time was 19 ± 17 months. During the follow-up, 43 patients developed events, most of them

Figure 1 (abstract P228)



($n = 28$) consisting of death (23 by cardiac death). However, most of these events occurred in the first month after the admission, the mortality between 1 month and 3 years being low (Figure 1).
Conclusion Our data show that the octogenarian patients with STEMI treated by primary PCA developed a very high mortality. However, this mortality especially concentrates in the first month after the procedure, being low between 1 month and 3 years.

P229

Outcome in myocardial infarction is related to the morphologic pattern of ST elevation

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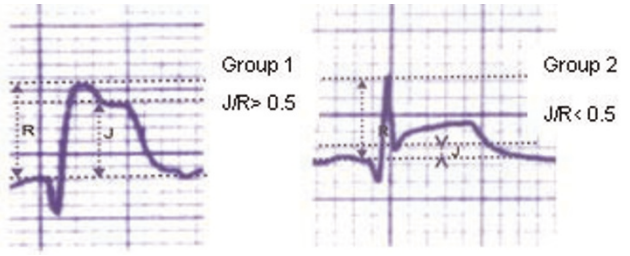
Purpose Although invasive management of ST-segment elevation myocardial infarction (STEMI) has improved the clinical outcome, early mortality remains an important issue. Our purpose is to assess the utility of the initial electrocardiographic (ECG) pattern in detecting patients who are at increased risk despite the current recommendations of revascularization.
Methods We analyzed 446 consecutive patients (age 61.9 ± 13.8 years, 76.5% male) admitted in the first 12 hours of STEMI to our coronary unit. Exclusion criteria were left bundle branch block at admission or previous myocardial infarction. Most patients (87%) were treated with primary angioplasty. Patients treated with thrombolytics and with early reperfusion criteria were programmed to coronary angiography the following day. Two groups were defined according to the presence of ST-segment elevation (STE) together with distortion of the terminal portion of the QRS in two or more adjacent leads (group 1) or the absence of this pattern (group 2) (Figure 1).
Results There were 102 (22.8%) patients in group 1 and 344 (77.2%) in group 2. No differences in age or risk factors were seen between both groups. The number of diseased vessels was similar. Group 1 had higher CK, MB-CK and cardiac troponin I. The maximal Killip class was >2 during hospitalisation in 38% of group 1 vs 24% ($P = 0.009$). Group 1 had more mortality (8.8% vs 2.6%, $P = 0.005$) and more cardiogenic shock. Other ECG characteristics related to mortality were the sum of STE in all leads, the number of leads with STE and ST segment depression. After a logistic regression analysis including all ECG characteristics, the pattern of group 1 remained significantly related to mortality ($P = 0.013$) together with the number of leads with STE.
Conclusion The initial STE pattern is useful in detecting patients at higher risk of death or cardiogenic shock, despite the adequate revascularization therapy in STEMI.

Figure 1 (abstract P229)



P230

Percutaneous coronary intervention in acute coronary syndrome complicated by states Killip 3 and 4 in 2005

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Introduction Early percutaneous coronary intervention (PCI) is the most effective treatment for acute coronary syndrome (ACS, ST-elevation myocardial infarction (STEMI), non-STEMI, unstable angina pectoris) complicated by states Killip 3 and 4.
Method A total of 1,187 patients suffering from high-risk acute coronary syndrome (hrACS) were treated in our center in 2005. States Killip 3 and 4 have developed perioperatively in 186 of these patients. International studies have proven high mortality in these patient groups – especially in state Killip 4. Our aim was to analyze the inhospital mortality of the state Killip 3 and 4 patient group treated in our center in 2005.
Results Seven hundred and two patients with STEMI and 485 patients with hrACS were admitted to our center in 2005. The mortality of these patients was 4.84% (STEMI) and 3.71% (hrACS), and the main cause of this mortality (37.7%) was the Killip 3/4 state, which was observed in 11.9% of the STEMI patients and in 17.9% of hrACS patients ($n = 84$ and 87). The mean age of the Killip 3/4 patients was 70 ± 10 years. Angiologically successful PCI was performed in 97.9% of the cases. The ratio of revascularized coronaries was left anterior descending coronary artery (LAD): 66 (35.9%), right coronary artery (RCA): 33 (17.9%), circumflex coronary artery (CX): 28 (15.2%), PCI in left main coronary artery: 28 (12.5%), LAD + CX: 15 (8.15%), RCA + LAD: 7 (3.8%), CX + RCA: 6 (3.26%), venous bypass graft: 2 (1.1%). No PCI was performed in two cases. Adjuvant therapies of intraaortic balloon counterpulsation in 67 (36%), mechanical ventilation in 62 (33.3%), continuous veno-venous hemofiltration in 12 (6.45%), and levosimendan therapy in 86 (46.2%) patients were used. Ten (5.4%) of the patients had advanced adult life support (cardiopulmonary resuscitation) (AALS) before arrival at our center, and AALS was performed in the perioperative period in 16 (8.6%) patients. The early inhospital mortality of hrACS aggravated by state Killip 3/4 was 10.7% (20 patients) – according to subgroup: Killip 3: 0.06%; Killip 4: 30.5%.

Conclusion The prognosis of state Killip 3/4 and successive multiorgan failure as the high-mortality complication of hrACS can be improved by early successful PCI, and the concomitant pharmacologic and nonpharmacologic supportive therapy.

P231

Abstract withdrawn

P232

Symptom onset to balloon time in patients with ST-segment elevation myocardial infarction treated by primary coronary angioplasty: influence on ST-segment resolution and on mortality

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Introduction With controversy in the field, we wanted to assess the influence of symptom onset to balloon time in ST-segment elevation myocardial infarction (STEMI) treated by primary coronary angioplasty (PCA), on ST-segment resolution and on the 1-year mortality.
Methods Retrospectively (January 1998–August 2004), we studied 558 consecutive patients with STEMI treated by PCA. The symptom to balloon time (SBT) was defined as the elapsed time between symptom onset and the first balloon inflation, and the procedural success (PS) as the TIMI III flow post-PCA with estenosis <50%.
Results Table 1 summarises clinical features according to SBT. After adjustment of potentially confounding variables, SBT was the variable associated with less ST-segment resolution (HR 1.772, 95% CI 1.46–4.15, $P = 0.02$).

Table 1 (abstract P232)

Symptom to balloon time	<2 hours	2–4 hours	4–6 hours	>6 hours	*P* value
ST-segment resolution (%)	95	92	86	78	0.0001
Procedural success (%)	97	95	91	84	0.03
Mortality (%)	6	9	12	29	<0.001

Conclusion This study shows that, in patients with STEMI treated by PCA, SBT is related to ST-segment resolution, to PS and to mortality

P233

Coronary collateral circulation status is correlated with the initial electrocardiographic pattern in ST-elevation myocardial infarction

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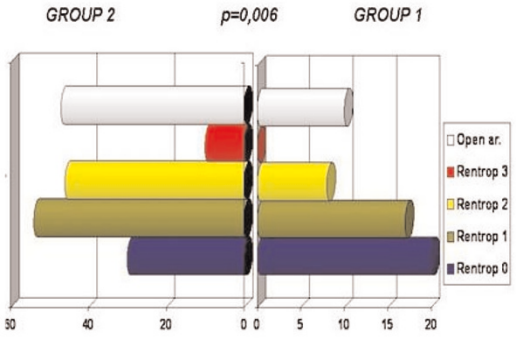
Introduction The status of coronary collateral circulation (CC) in the first hours of ST-elevation myocardial infarction (STEMI) may influence outcome. Early recognition of the CC status may have therapeutic and prognostic implications. Our purpose was to correlate the electrocardiogram (ECG) pattern and CC in STEMI.

Figure 1 (abstract P233)



Methods We analyzed ECG and angiographic CC in 242 consecutive patients (62 ± 14 years, 79% male) with STEMI treated with primary angioplasty. Patients were divided into two groups based on the magnitude of ST elevation with/without distortion of the terminal portion of the QRS (group 1/group 2). The degree of collateral filling (Rentrop) was assessed as grade 0 = none, grade 1 = filling of side branches of the occluded artery, grade 2 = partial epicardial filling, and grade 3 = complete epicardial filling of the occluded artery.
Results ST elevation with distortion of the terminal portion of QRS were present at initial ECG in 55 patients (23%). This group had a lower incidence of Rentrop grade 2/3 than group 2 ($P = 0.006$, Figure 1). Moreover, group 1 had higher enzyme release, worse maximal Killip class and more frequently the combined variable death/shock. Group 1 more often had proximal occlusion of the infarction-related artery and nonreflow. Multivariate analysis found ECG to be an independent predictor of outcome.
Conclusion ST elevation with distortion of the terminal portion of QRS predicts impaired CC. Early recognition of this pattern should warrant prompt treatment.

P234

Hemoglobin concentration on admission influences the rate of inhospital 30-day mortality and complications in patients with acute myocardial infarction: a retrospective analysis of 660 Chinese patients

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Objective To determine the association between hemoglobin concentrations on admission and inhospital 30-day cardiac mortality and complications among patients with acute myocardial infarction during their hospital course.
Methods We conducted a retrospective study of data on 660 Chinese patients who were hospitalized with acute myocardial infarction. Patients were categorized according to the hemoglobin concentration on admission, and data were evaluated to determine whether there was an association between the hemoglobin concentrations on admission and inhospital 30-day mortality and complications. Complications were defined as cardiogenic shock, congestive heart failure, arrhythmia, ventricular tachycardia or fibrillation and pneumonia.

Results Patients with hemoglobin values between 140 and 159 g/l were used as the reference; cardiovascular mortality increased as hemoglobin levels fell below 140 g/l or rose ≥160 g/l. The in-hospital 30-day mortality was 25.0% in patients with hemoglobin concentrations <100 g/l, 20.4% in patients with hemoglobin concentrations of 100–119 g/l, 10.6% in patients with hemoglobin concentrations of 120–139 g/l, 4.3% in patients with hemoglobin concentrations of 140–159 g/l, and 8.5% in patients with hemoglobin concentrations of 160 g/l or greater. The increase in risk of complications associated with a low hemoglobin concentration was more pronounced in patients with anemia than in patients without. Compared with patients with hemoglobin concentrations of 140–159 g/l, those with hemoglobin concentrations <140 g/l had more inhospital complications and those with hemoglobin concentrations ≥160 g/l also had more arrhythmia and pneumonia ($P < 0.001$, respectively). As expected, a significant inverse correlation between hemoglobin concentrations and ages ($r = -0.51$; $P < 0.001$) was observed, and a significant positive correlation between hemoglobin concentrations and albumin concentrations and in the patients with acute myocardial infarction.
Conclusion It is demonstrated in this study that a reverse J-shaped relationship between baseline hemoglobin values and major adverse cardiovascular events is observed in patients with acute myocardial infarction. There is a greater incidence of patients with a hemoglobin concentration on admission in the elderly population than that in the younger one.

P235

Anaemia at the moment of admittance is associated with higher heart failure and mortality among patients with acute coronary syndrome

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Background The search for novel and modifiable risk factors in acute coronary syndrome (ACS) can open new strategies. We decided to evaluate the prevalence of anaemia and determine its influence on the prognosis of hospitalized ACS patients.
Patients and methods Four hundred and twenty-eight consecutive patients hospitalized for ACS between 2005 and 2006 in a coronary care unit (CCU) of a cardiology department of a tertiary hospital were studied. During their hospitalization we registered cardiovascular risk factors; we determined the presence of microalbuminuria (>3 mg/dl) in a 24-hour urine sample. We also took blood samples during the first 24 hours of their admittance to the CCU for a complete haemogram, levels of total cholesterol, HDL cholesterol, LDL cholesterol, triglycerides, creatinine, creatinine clearance (Cockroft–Gault equation), glucose, HbAc1, high-sensibility C-reactive protein and a follow-up of levels of Troponin, CK and CK-MB.
Results The prevalence of anaemia (Hb < 11 g/dl in women and Hb < 12 g/dl in men) in patients with an ACS was 15.4%. This group was characterised by the following: woman ($P < 0.0001$), higher age ($P = 0.0001$), less weight ($P = 0.01$), higher frequency of high blood pressure ($P = 0.0001$), diabetes mellitus ($P = 0.0001$), history of ischaemic heart disease ($P = 0.002$) and peripheral artery disease ($P = 0.0001$). This group presented a major proportion of the NSTEMI ($P = 0.015$), higher level of renal dysfunction (77% to 32%, $P = 0.0001$), and microalbuminuria (61% to 32%, $P = 0.0001$). Patients with anaemia presented a worse intrahospital prognosis: major incidence of cardiac insufficiency (42% to 20%, $P = 0.0001$), refractory angina pectoris (14% to 6%, $P = 0.01$), more electric complications (12% to 9%, $P = 0.01$) and a higher mortality (14% to 7%, $P = 0.009$). The presence of anaemia was an independent predictor of cardiac insufficiency and death at the moment of admittance to the CCU (OR = 2.20, 95% CI = 1.10–4.35; $P = 0.002$)
Conclusion The presence of anaemia is a powerful predictor of a worse prognosis in patients with ACS. Anaemia is associated with other factors of a worse prognosis such as renal dysfunction, peripheral artery disease and diabetes mellitus.

P236

Long-term prognostic impact of anemia in patients with ST-elevation acute myocardial infarction treated by primary coronary angioplasty

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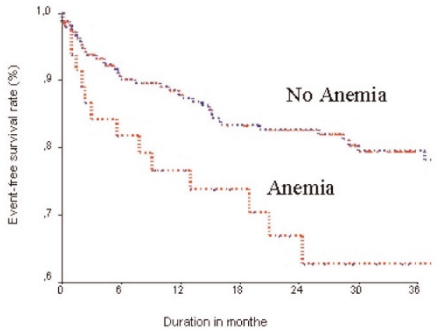
Introduction Anemia has been shown to be a powerful and independent predictor of 30-day outcomes among patients presenting with acute coronary syndrome. However, there are limited and conflicting data about its long-term independent predictive value in this setting.
Objectives To investigate the long-term prognostic impact of anemia in patients with ST-elevation acute myocardial infarction (STEMI) treated by primary coronary angioplasty (PCA).
Methods Retrospectively, from January 2001 to December 2003, we studied 298 consecutive patients with STEMI treated with PCA. Patients were classified into two groups according to having anemia or nonanemia at admission (for men Hb < 13 vs ≥13 g/dl, and for women Hb < 12 vs ≥12 g/dl). We defined the composite endpoint as death or rehospitalization for heart failure or acute coronary event. The average follow-up time was 24 months and was determined in 97%.
Results Anemia was present in 41 patients (14%). At the end of follow-up, 109 patients (37%) developed ≥1 component of the composite endpoint (52 deaths and 66 rehospitalization). The event-free survival was 62% in the group with anemia versus 82% in the other group ($P < 0.001$). After controlling for a variety of baseline clinical, laboratory, and angiographic variables, anemia was a strong and independent predictor of death or rehospitalization for heart failure or acute coronary event (HR 1.96, 95% CI 1.21–3.17, $P = 0.006$). Figure 1 shows that patients with anemia present a worse prognosis.

Figure 1 (abstract P236)



Conclusion Our data demonstrate that baseline anemia is a strong and independent predictor of future adverse events at 2 years in patients with STEMI treated with PCA.

P237

Cardiogenic shock in the Aachen Digital Myocardial Infarction Registry

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Introduction Guideline-oriented therapy of acute coronary syndrome (ACS) with ST-elevation myocardial infarction (STEMI) calls for quick and early treatment. The creation of an infarct network has been associated with streamlined treatment and a reduction of hospital mortality. Whether patients with cardiogenic shock (CS) receive similar, optimized treatment as regular STEMI patients is unclear.
Methods We created the Aachen Digital Myocardial Infarction Registry (ADMIRE) database according to the European Cardiology Audit and Registration Data standards for clinical cardiology practice. Patients were labelled according to the presenting form of ACS. The infarct network included local ambulance services (LA), local hospitals (LH) and the interventional center with an emergency department (ED) and a 24/7 cath lab crew. To improve performance we introduced prehospital triage, fax-transmission of ECG, and direct alert of the cath lab crew by telephone. We determined treatment variables, median index-to-door (IDT) and door-to-sheath (DST) times and hospital mortality.
Results Between April and December 2006 we treated 593 patients including 119 STEMI (20.1%) and 45 CS patients (7.6%); 66.7% were male, mean age was 67.4 years. CS presented with ST elevation in 48.9%, as non-STEMI in 33.3%, rescue percutaneous coronary intervention (PCI) in 11.1% or with subacute ACS in 6.7%; 30.4% of CS were admitted through LA, 67.4% through LH and only one patient through the ED. Upon admission, 50% of CS had required CPR, 69.6% were on mechanical ventilation. In total 89.1% of CS underwent angiography, with revascularization in 69.8% and intra-aortal balloon pump treatment in 68.1%. The median DST for CS vs STEMI was 82 vs 59.5 minutes ($P = 0.07$), and the IDT was shorter for CS (172 vs 385 min, $P < 0.05$). Stratified by admission source, the DST was equal between LA and LH (66 vs 84 min, $P = 0.75$). CS patients with ST elevation were not treated significantly faster than those without or CS with rescue PCI (64 vs 84 vs 94 min, $P > 0.05$ for each). Prehospital CPR did not lead to significantly altered DST. The DST was <60 minutes in 31.3% of CS compared with 50% STEMI patients. Mortality in CS patients was significantly higher than that of STEMI patients (56.5% vs 7.6%, $P < 0.05$) but equal among CS subgroups (50% for ST-elevation CS, 80% for non-STEMI CS, 40% for rPCI CS, no deaths for CS with subacute ACS). It did not differ by admission source and was not influenced by a DST < 60 minutes, intra-aortal balloon pump or revascularization status.
Conclusion Despite their higher complexity, patients with CS were treated as fast as patients with STEMI, yet there was room for improvement to increase the number of patients treated within the first hour of admission for both STEMI and CS. Structural changes and further implementation of standard operating procedures might achieve this. We could not show a mortality difference for any of our treatment variables, which might be due to the low number of patients.

P238

Intra-aortic balloon counterpulsation: impact on patient hemodynamics in acute myocardial infarction complicated by cardiogenic shock

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Introduction Evaluation of hemodynamics in patients with acute myocardial infarction (AMI) is crucial. Hemodynamic changes during intra-aortic balloon counterpulsation (IABC) are monitored using invasive methods for assessment of hemodynamics in patients with cardiogenic shock (CS).
Objective To evaluate hemodynamic indices in patients with AMI, complicated by CS and managed with IABC during initial days of treatment.
Methods Hemodynamic indices including cardiac output (CO), cardiac index (CI), mean pulmonary artery pressure (MPAP) and pulmonary capillary wedge pressure (PCWP) were measured by pulmonary artery catheterization using an intermittent thermo-dilution technique for patients with AMI complicated by CS, admitted within 12 hours from the onset of pain and managed by IABC. All measurements were performed within 48 hours after initiation of IABC.
Results Twenty-nine patients were investigated according to the study protocol: 15 (51.7%) men and 14 (48.3%) women. Average age was 71.4 ± 6.9 years. Anterior AMI was diagnosed for 19 (65.5%) patients, and inferior in 10 (34.5%) patients. Primary percutaneous transluminal coronary angioplasty (PTCA) was successfully performed for 22 (75.9%) patients, primary PTCA was unsuccessful for four (13.8%) patients, and seven (24.1%) patients underwent scheduled cardiac surgery within the first 2 weeks. The inhospital mortality rate was 41.4% (12 patients).
The initial (after initiation of IABC) CO was 3.7 ± 1.2 l/min, CI was 1.9 ± 0.7 l/min/m^2, MPAP was 30 ± 7.1 mmHg (maximum 43 mmHg), PCWP was 19.1 ± 5.1 mmHg (maximum 26 mmHg). After the first 24 hours of IABC, the CO was 3.8 ± 1.6 l/min, CI was 2 ± 0.9 l/min/m^2, MPAP was 23.7 ± 7.1 mmHg (maximum 36 mmHg), PCWP was 16.8 ± 4 mmHg (maximum 24 mmHg). After 48 hours of IABC, CO was 4.1 ± 1.7 l/min, CI was 2.1 ± 0.8 l/min/m^2, MPAP was 23.8 ± 6.5 mmHg (maximum 44 mmHg), PCWP was 16.8 ± 4.6 mmHg (maximum 24 mmHg).
Conclusion Intra-aortic balloon counterpulsation has a positive impact on hemodynamic changes of patients with acute myocardial infarction complicated by cardiogenic shock during the initial days of treatment.

P239

Elevation of Troponin T in critically ill septic patients is common: but does it matter?

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Critical Care 2007, **11(Suppl 2):**P239 (doi: 10.1186/cc5399)

Background Troponin T (TnT) is an established marker of adverse outcome in acute coronary syndrome patients and aids risk stratification. Myocardial dysfunction and elevated of TnT are common in critically ill patients and cardiology advice is often sought.
Objective To evaluate the role of TnT as a predictor of all-cause mortality in patients with severe sepsis/septic shock as defined by international criteria.

Methods A prospective observational study was performed on patients admitted to a general adult ICU within 24 hours of the development of severe sepsis/septic shock. Serial TnT samples were taken over the first 96 hours. Patients were grouped into three groups: A, TnT < 0.01 ng/ml; B, TnT 0.01–0.099 ng/ml; and C, TnT > 0.099 ng/ml.
Results Blood from 49 patients was analysed. The peak Troponin level was elevated (>0.01 ng/ml) in 39/49 patients (80%). There was no significant difference between the three groups in terms of hypertension, history of angina, myocardial infarction or systolic blood pressure at time of ICU admission. Patients with undetectable TnT levels (<0.01 g/ml) had significantly lower 6-month mortality rates than those with detectable levels (group A 2/10 (20%) vs Group B/C 23/39 (59%), $P = 0.037$; group B 8/15 (53%), group C 15/24 (63%)). See Table 1.

Table 1 (abstract P239)

Group	Number	APACHE II score	Mean age (years)	Inotropic support	Mortality
A	10	18.5 (8.2)	52 (17)	8	2/10
B	15	20 (5.7)	63 (15)	15	8/15
C	24	22.2 (6.8)	65 (14)	22	15/24

Conclusions Elevated biochemical markers of cardiac myocyte damage are common in patients with severe sepsis/septic shock. TnT elevation is a predictor of 6-month all-cause mortality. Clinicians should be aware of the significance of an elevated TnT assay in this patient population.

P240

Prognostic markers in the acute phase of myocardial infarction

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Introduction The aim of the study was to assess the prognostic value of heart rate variability, arrhythmias and left ventricular systolic and diastolic function for the course and the outcome of myocardial infarction (MI).
Methods We prospectively studied 57 consecutive patients admitted to the ICU of the Department of Cardiology of Kaunas Medical University Hospital between 2002 and 2004 with acute MI. The study protocol included 24-hour ECG monitoring on the first day and the third day of admission and echocardiography performed at days 2–4. Inhospital prognostic endpoints were death and nonfatal events: postinfarction angina, progressive heart failure, pulmonary edema and cardiogenic shock. Heart rate variability (HRV) was assessed at days 1 and 3 by a 24-hour recording using the 'HeartLab' system. A logistic regression model was used to select the combination of statistically significant variables and predict the complications.
Results In our model statistically significant independent variables for prediction of inhospital MI complications were HRV frequency domain parameter low-frequency power (LF) on day 3, and left ventricular end-systolic volume (LV ESV), atrial fibrillation/flutter and inotropic agent administration on day 1. According to the results, atrial fibrillation/flutter (odds ratio 25.6) and increased LV ESV (odds ratio 1.067 (6.7%) for increase in 1 ml) increase the probability of inhospital complications, while increased LF on day 3 (odds ratio 1.29 for 1,000 units) and no administration of inotropic drug on day 1 (odds ratio 34.5) decrease the probability of inhospital complications. The average efficacy of prognostication reached 96.5%; the presence of complications was correctly predicted in 88.9% of cases, and the absence of complications in 100% of cases.
Conclusion The HRV parameter LF on day 3, and LV ESV, atrial fibrillation/flutter and inotropic agent administration on day 1 are statistically significant independent predictors of inhospital complications of MI with an average predictive efficacy of 96.5%.

P241

The relationship between blood pressure and plasma magnesium level in hypertensive patients

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Introduction The aim of this study was to investigate the relationship between blood pressure and plasma magnesium levels in patients referred to the emergency department with hypertensive attack. Epidemiological evidence on the effects of magnesium on blood pressure is inconsistent. Metabolic and experimental studies suggest that magnesium may have a role in the regulation of blood pressure. Magnesium regulates various ion channels in many tissues, including those of the cardiovascular system. Magnesium is the second most abundant intracellular cation, and the important element that has numerous biological functions in the cardiovascular system. Furthermore, magnesium acts as a calcium antagonist, regulating the calcium metabolism.
Methods Patients were included who were taken to the emergency department due to hypertensive attack. Their age, gender, systolic and diastolic blood pressure were recorded. In order to see the plasma magnesium levels, venous blood samples were taken. The results were compared with a chi-square test. The values $P < 0.05$ were accepted as significant.
Results Seventy-three patients (35 of whom were female, 38 males) were included in the study. The average age was 47 ± 6.3 (ranging from 33 to 68 years). The average blood pressure of the patients was found as systolic 200 ± 10 (range 185–240) mmHg, diastolic 105 ± 7 (range 95–110) mmHg. The average plasma magnesium levels were 1.4 ± 0.3 (range 0.9–2.2) mg/l. The plasma magnesium levels were low in 29 patients (ranging from 0.9 to 1.7 mg/l). There was a negative relationship systolic blood pressure and plasma magnesium level ($P < 0.05$). In addition, there was a negative relationship diastolic blood pressure and plasma magnesium level ($P < 0.05$).
Conclusion Low plasma magnesium levels would be an important factor for elevated blood pressure and hypertensive attack.

P242

Precise and ultrarapid control of blood pressure with clevidipine, an arterial selective calcium channel blocker

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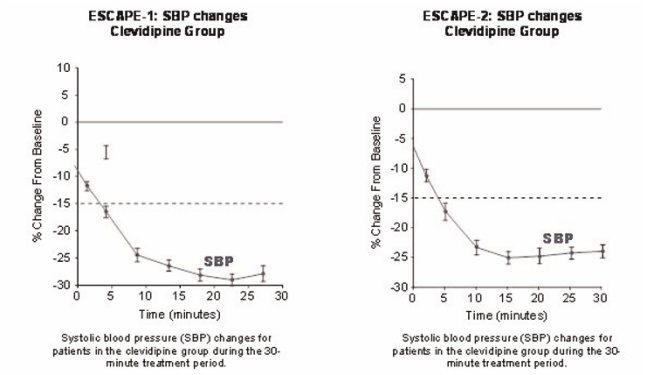
Introduction Precise, rapid control of blood pressure (BP) is important in emergency and critical care settings as uncontrolled hypertension is associated with morbidity and mortality in high-risk

Figure 1 (abstract P242)



Systolic blood pressure (SBP) changes for patients in the clevidipine group during the 30-minute treatment period.

Systolic blood pressure (SBP) changes for patients in the clevidipine group during the 30-minute treatment period.

surgery patients as well as severely hypertensive patients. Clevidipine is an ultrashort-acting, vascular and arterial-selective calcium antagonist currently under development for treating acute hypertension.

Methods We analyzed data from two double-blinded, placebo-controlled trials (ESCAPE-1 and ESCAPE-2) that evaluated the ability of clevidipine to control BP in high-risk cardiovascular surgery patients. In addition, we evaluated the design of a recently initiated trial that analyzes clevidipine in severe hypertension (VELOCITY trial).

Results In both ESCAPE-1 and ESCAPE-2, clevidipine demonstrated a statistically significant decrease in mean arterial pressure from baseline ($P < 0.0001$) compared with placebo at the 5-minute time point. A BP lowering effect was observed within 1–2 minutes with clevidipine, with the median time to achieve target systolic blood pressure (SBP) of 6 and 5.3 minutes, respectively (see Figure 1). In the patients with acute severe hypertension, the VELOCITY trial studies the percentage of patients in whom the SBP falls below the lower limit of a patient-specific predetermined target range at the initial dose of 2.0 mg/hour within 3 minutes of initiating the infusion, as well as the percentage of patients who reach the prespecified target SBP range within 30 minutes of the beginning of the study drug.

Conclusion In both the ESCAPE-1 and ESCAPE-2 studies, clevidipine demonstrated the ability to precisely achieve target blood pressure reductions in a short period of time, in a high-risk patient population. Further analysis of the rapid decreases noted with clevidipine is being conducted in patients with acute severe hypertension in the VELOCITY trial.

P243

Clinical meaning and prognosis of the elevation degree of cardiac Troponin I in pericarditis of the adult: short-term and mid-term follow-up results

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Introduction The inflammatory process of acute pericarditis (Pc) may involve the epicardium and cause myocardial damage, as reflected by cardiac Troponin I (TnI) release. Studies performed with TnI demonstrated that the temporal pattern of this release is similar to that of an acute myocardial infarction (AMI); however, the true prognostic significance of TnI remains unknown in this setting.

Objective To investigate the clinical and prognostic value of TnI release in adult with acute Pc.

Methods From January 2000 to March 2006 we retrospectively studied 89 patients with the final diagnosis of acute myocarditis (Mc), of which 66 (74%) fulfilled at least two criteria of acute Pc (typical chest pain, pericardial friction rub, and/or alterations in the ECG). We only included those diagnosed with idiopathic or viral Pc with elevation of TnI over the level of cut for AMI in our hospital (≥0.6 ng/dl). We divided patients into tertiles according to the value of TnI (22 in each group). An echocardiographic (Echoc) study and a ECG monitorization was performed at admission in all. The coronariography was done in 24 (36%), which did not show lesions. The average follow-up was 24 ± 18 months and included Echoc in 61 (92%).

Results Age 28 ± 9 years, 87% men; two (3%) patients had antecedents of idiopathic Pc and only one of Mc. The average of the peak of TnI was 17 ± 11 ng/dl, being the average of the values of TnI in each group of 6 ± 3 (first tertile), 15 ± 2 (second tertile) and 30 ± 11 ng/dl (third tertile). LVEF% was ≥55 in 61 (92%) and there were no differences in the age and sex between the three groups. The elevation of TnI did not correlate with the LVEF% (62 ± 5 vs 61 ± 4 vs 60 ± 7; $P = 0.60$). Only the values of TnI in the third tertile were associated with the elevation of the ST segment in ≥5 derivations ($P = 0.001$), and with abnormal ventricular wall motion ($P = 0.046$). There was no association with the presence of pericardial effusion, arrhythmias nor cardiac failure. During follow-up, two (3%) patients presented Mc, and three Pc without elevation of TnI. The remaining patients (92%) were asymptomatic and without cardiac dysfunction. The average LVEF% was >55% in all of them

Conclusion In adults with acute Pc, the elevation degree of TnI is associated with the degree of elevation of the ST segment but it is not a negative prognosis indicator.

P244

Emergency electrocardiography-guided pericardiocentesis in cardiac tamponade

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Introduction Pericardiocentesis (PC) and pericardial fluid drainage is the method of choice in cardiac tamponade (CT). It is usually performed under echocardiography control. The objective of the study was the description of CT etiology, symptoms and clinical findings and the evaluation of the electrocardiography (ECG)-guided PC procedure.

Methods Thirty-nine consecutive patients (nine females) with CT, mean age 56 years, underwent 41 emergency PC between November 1998 and November 2006. There was full data registry for 31 patients and 33 PC. We used a subxiphoidal approach in 31 and an apical approach in two cases. Catheters used were Cordigan (Braun) and C-PCS-830-LOCK (Cook). A full transthoracic echocardiography (TTE) study preceded and PC was performed under ECG monitoring (intrapericardial ECG recording).

Results Patients with CT had the following symptoms or clinical findings: dyspnea (77%), pleural effusion (68%), chest pain (48%), weight loss (29%), fever (23%), cough (19%), peripheral edema (12%), abdominal pain (12%), hoarseness (12%), jugular vein distension (6%). Forty-five percent of patients were hemodynamically stable, while 26% had high BP. The mean heart rate on admission was 94/minute. Seventy-one percent of patients exhibited hypoxemia (half of them mild). Deep heart sounds were

recognized in 39% and pulsus paradoxus was present in 29% of cases. Only 12% had pericardial knock and pericardial friction rub was absent in all patients. On ECG there was sinus rhythm in 71%, the rest being atrial fibrillation. Sixty-five percent of patients showed repolarization changes, and only 16% had low voltage. On TTE, 3/4 of patients had right atrium/right ventricle collapse and the intapericardial space measured 1.8–3.8 cm. Only 39% of patients exhibited cardiac enzyme increase (cardiac troponin I, CK-MB), while the majority had elevated CRP. The underlying diagnosis for CT in 35% of cases was lung adenocarcinoma/nonsmall cell carcinoma or breast carcinoma. In 35% the final diagnosis was that of idiopathic pericarditis. Seventy percent of pericardial fluid samples were exudates and 74% were sanguineous/serosanguineous. Four patients had pericardial fluid under pressure. The mean volume drained was 1,540 ml (850–3,010), the mean period of drainage was 56 hours (3 hours–14 days). No major complications occurred; 23% patients had nonmalignant arrhythmias (AF, NSVT).

Conclusions 'Classical' symptoms and signs (low BP, pulsus paradoxus, deep heart sounds or low voltage) can be absent in CT. Emergency PC with ECG intrapericardial ECG recording, after meticulous TTE, can be safe. Appearance of nonmalignant arrhythmias could be a rare complication.

P245

Diagnostic accuracy of automated computerised electrocardiogram interpretation compared with a panel of experienced cardiologists

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Introduction Computerised electrocardiogram (ECG) interpretation is widely applied, especially within the clinical settings of primary care and surgical preadmission. Concerns have been raised over the accuracy of computerised ECG interpretation. Our aim was to compare the performance of computer-based ECG interpretation with that of a panel of experienced cardiologists.

Methods All consecutive ECGs performed in a hospital cardiology department over a 1-week period were analysed. Two cohorts were assessed, open access patients from primary care and surgical preoperative assessment patients. Cardiologists were blinded to clinical details and the computerised ECG interpretation. ECGs were analysed by a panel of cardiologists with the consensus view taken as the reference standard. ECGs were interpreted in relation to 'rhythm' and 'other abnormalities' and were classified as normal or abnormal.

Results Seventy consecutive ECGs were analysed, 47 from open access and 23 from surgical preassessment. The cohort's median age was 60 years (range 27–87 years, male $n = 30$). Twenty-four ECGs were normal. There was complete disagreement over the computerised ECG interpretation of one ECG, which was deemed of major clinical significance. Partial disagreement occurred in the remainder. The greatest level of disagreement related to the interpretation of left ventricular hypertrophy and ECG evidence of myocardial ischaemia/infarction. Likelihood ratios (LR) were not calculated for negative results as there were no false negative results. LR for abnormal ECG 'rhythm' were 18.3 (6.7–53.4) and for abnormal ECG 'other abnormalities' were 3.15 (2.13–5.11) (Table 1).

Conclusions Need exists to improve the diagnostic algorithms used by computerised ECG interpretation. It is essential that all automated computerised ECG interpretations be over read by a physician.

P246

Cystatin C in the prognostic stratification of patients with an acute coronary syndrome

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Introduction Early risk stratification is essential in the management of patients with an acute coronary syndrome (ACS). Measurements of renal function such as serum creatinine and estimation of creatinine clearance carry independent prognostic information in this population. Cystatin C is a new and better marker of renal function than creatinine. The aim was therefore to evaluate the prognostic value of cystatin C in this population.

Methods Four hundred and twenty-eight patients with an ACS, admitted to our coronary care unit (CCU), were studied prospectively. Sixty-three per cent presented a non-ST-segment elevation myocardial infarction (NSTEMI) and 37% a ST-segment elevation myocardial infarction (STEMI). During their hospitalization we registered cardiovascular risk factors: we determined the presence of microalbuminuria (>3 mg/dl) in a 24-hour urine sample. We also took blood samples during the first 24 hours of their admittance to the CCU for a complete hemogram, levels of total cholesterol, HDL cholesterol, LDL cholesterol, triglycerides, creatinine, creatinine clearance (Cockroft–Gault equation), glucose, HbAc1, high-sensibility C-reactive protein, Cystatin C and a follow-up of levels of Troponin, CK and CK-MB. All patients were submitted to a coronary angiography in the first 72 hours to give a clinical score to their coronary artery disease (disease of one, two or three arteries).

Results We determined the Cystatin C level in 59 patients (16 females and 43 males). In 36% (21 patients) we found normal levels (<0.95; 0.80 ± 0.9), called group 1. In the other group (group 2) we found higher levels of Cystatin C (>0.95; 1.63 ± 0.77). Patients in group 2 presented a higher age, a higher frequency of high blood pressure, worse Killip class score at the moment of admittance, higher inflammatory activity (leucocytosis, $P = 0.001$ and higher levels of C reactive protein, $P = 0.005$), higher grade of renal dysfunction ($P = 0.001$) and anaemia ($P = 0.06$). Patients in group 2 presented a worse intrahospital prognosis with a higher incidence of cardiac insufficiency (45% to 14%, $P = 0.01$), ventricular arrhythmias (29% to 5%, $P = 0.05$), pericardial effusion (18% to 0%, $P = 0.05$) and a higher mortality (21% to 5%, $P = 0.08$). In the multivariant analysis, Cystatin C was an independent predictor of cardiac insufficiency (OR = 4.5, 95% CI 1.1–20.8, $P = 0.05$).

Table 1 (abstract P245)

Abnormality	Kappa	Sensitivity	Specificity	NPV	PPV
Rhythm	0.92 (0.84–1)	1 (0.88–1)	0.95 (0.85–0.98)	1 (0.93–1)	0.9 (0.76–0.97)
Other	0.68 (0.52–0.84)	1 (0.91–1)	0.68 (0.68–0.53)	1 (0.88–1)	0.75 (0.62–0.85)

Conclusion Higher levels of Cystatin C (>0.95) in patients with an ACS indicate a worse intrahospital prognosis and also a higher inflammatory activity and renal dysfunction.

P247

The reduction of the glomerular filtration rate and the presence of microalbuminuria at the moment of admittance reduce the prognostics of patients with an acute coronary syndrome

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Critical Care 2007, **11(Suppl 2):**P247 (doi: 10.1186/cc5407)

Introduction Determination of the glomerular filtration rate (GFR) in patients with an acute coronary syndrome (ACS) has an important prognostic value. The presence of microalbuminuria (MA) is a known risk factor in patients with hypertension and diabetes. We know less about the effect of reduction of the GFR on patients with an ACS.
Method Four hundred and twenty-eight patients with an ACS, admitted to our coronary care unit (CCU), were studied prospectively. Sixty-three percent presented a non-ST-segment elevation myocardial infarction and 37% a ST-segment elevation myocardial infarction. During their hospitalization we registered cardiovascular risk factors; we determined the presence of MA (>3 mg/dl) in a 24-hour urine sample. We also took blood samples during the first 24 hours of their admittance to the CCU for a complete hemogram, levels of total cholesterol, HDL cholesterol, LDL cholesterol, triglycerides, creatinine, creatinine clearance (Cockroft–Gault equation), glucose, HbAc1, high-sensibility C-reactive protein and a follow-up of levels of Troponin, CK and CK-MB.
Results Thirty-nine percent of the patients with an ACS presented a GFR less than 60 ml/minute, and 36% presented MA at the moment of admittance to the CCU. Forty-four percent of the patients with a GFR less than 60 ml/minute also presented MA; on the contrary, only 32% of the patients with a GFR more than 60 ml/minute did so ($P = 0.01$). This group contains significantly more women ($P = 0.001$), more history of ischemic brain events and peripheral artery disease ($P = 0.03$), worse Killip score at the moment of admittance ($P = 0.001$), more development of cardiac insufficiency ($P = 0.003$) and a higher mortality during hospital stay ($P = 0.03$).
The intrahospital survival of patients with GFR less than 60 ml/minute and MA was 79%, to 96% in patients without MA and a GFR more than 60 ml/minute ($P = 0.01$; Log-rank test = 6). Patients with a GFR less than 60 ml/minute but without MA presented an intrahospital survival of 85%. In the multivariant analysis a GFR less than 60 ml/minute (OR = 2.0; 95% CI 1.13–3.53) and the presence of MA (OR = 2.30; 95% CI 1.37–3.86) were independent predictive factors of cardiac insufficiency and mortality.
Conclusions The presence of a GFR less than 60 ml/minute and MA at the moment of admittance of a patient with an ACS identifies a group of patients with a bad prognosis. Future studies can reveal whether an improvement of the renal function can be beneficial for this group of patients.

P248

Circulating levels of tumor necrosis factor alpha, brain natriuretic peptide and cardiac Troponin I upon admission and 31-day mortality in patients with acute decompensated chronic heart failure

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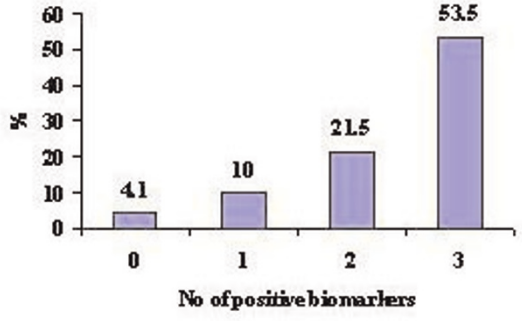
Critical Care 2007, **11(Suppl 2):**P248 (doi: 10.1186/cc5408)

Background Elevated circulating levels of TNFα, brain natriuretic peptide (BNP) and cardiac Troponin I (cTnI) have been connected with adverse prognosis in patients with chronic heart failure (CHF). However, there are scant data about the predictive value of these biomarkers in combination.
Methods A total of 577 consecutive patients (mean age: 73 ± 9 years), who were hospitalized for acute decompensation of NYHA class III/IV (65.3% of ischemic etiology) low-output (mean LVEF: 22 ± 5) CHF, were studied. Biochemical markers were measured upon admission. The incidence of 31-day death was the prespecified primary endpoint.
Results The incidence of the primary endpoint was 17.7%. By multivariate Cox analysis, including baseline characteristics and the study biomarkers, elevated circulating levels of TNFα (RR = 2.1; $P < 0.001$), BNP (RR = 3.5; $P < 0.001$) and cTnI (RR = 3.8; $P < 0.001$) were independently associated with the primary endpoint. When the patients were divided according to the number of positive biomarkers (estimated by ROC analysis) there was a significant gradual increase in the rate of the primary endpoint with increasing of the number of the positive biomarkers (4.1%, 10%, 21.5% and 53.5% 31-day mortality rate for patients with zero, one, two and three positive biomarkers, respectively; $P < 0.001$) (Figure 1).

Figure 1 (abstract P248)



Conclusions The present results suggest that in patients hospitalized due to acutely decompensated severe low-output CHF, serum levels of TNFα, BNP and cTnI can be used in combination for enhanced early risk stratification.

P249

Secondary prevention following surgical revascularisation: continuing under-use of angiotensin-converting enzyme inhibitors

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Critical Care 2007, **11(Suppl 2):**P249 (doi: 10.1186/cc5409)

Introduction Over the past decade, coronary revascularisation has helped reduce mortality and morbidity rates from coronary artery disease. In addition to revascularisation, long-term prognosis is dependent on successful implementation of secondary prevention, in particular the use of aspirin, statins, angiotensin-converting enzyme (ACE) inhibitors and, in many, β-blockers. Previous studies have highlighted the under-utilisation of secondary preventative strategies in this patient population. A focused review of secondary preventative medication at the time of revascularisation provides an excellent opportunity to ensure optimal use of these agents. Our aim was to identify the proportion of patients undergoing nonemergency surgical revascularisation discharged on these four secondary preventative medications.
Methods A retrospective analysis of our inhouse cardiothoracic surgical database was performed. All patients had undergone surgical revascularisation between January 2003 and November 2006. Only patients undergoing coronary artery bypass grafting were included.
Results A total of 2,749 consecutive patients were included in the analysis, mean age 65.5 years (±9.2). In total, 2,302 isolated coronary artery bypass grafting procedures and 447 combined procedures were performed. See Table 1.

Table 1 (abstract P249)

	2003	2004	2005	2006
Total	522	758	767	702
Previous myocardial infarction	296 (56.7%)	364 (48%)	353 (46%)	347 (49.4%)
Left ventricular systolic dysfunction	113 (21.6%)	145 (19.1%)	175 (22.8%)	186 (26.5%)
EuroSCORE	3.8 (2.7)	3.9 (3)	3.9 (2.8)	4.3 (2.9)
Aspirin	490 (93.9%)	694 (91.6%)	700 (91.3%)	652 (92.9%)
ACE inhibitor/ angiotensin receptor blocker	285/34 (61%)	421/43 (61%)	430/53 (63%)	382/49 (61%)
β-Blocker	412 (78.9%)	632 (83.4%)	587 (76.5%)	540 (76.9%)
Statin	470 (90%)	700 (92.3%)	710 (92.6%)	638 (90.9%)

Conclusion Although the utilisation of these preventive therapies has improved compared with previous studies, additional improvements could be made and in particular there is a continuing under-utilisation of ACE inhibitors. There are several reasons why ACE inhibitors might not be used in the early postoperative phase (hypotension, temporary renal dysfunction, etc.). These results reinforce the need to review these patients following recovery from surgery with a view to optimising secondary preventive treatment. This may best be done in community secondary prevention clinics with agreed guidelines.

P250

Cardiopulmonary exercise testing as a screening test for perioperative management of major cancer surgery: a pilot study

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Critical Care 2007, **11(Suppl 2):**P250 (doi: 10.1186/cc5410)

Introduction Cardiopulmonary exercise testing is an important screening test to evaluate cardiorespiratory function before major body cavity surgery.
Objective To develop a clinical strategy for the identification and management of high-risk major cancer surgical patients in order to reduce perioperative morbidity and mortality.
Methods Forty-one major cancer surgery patients underwent a cardiopulmonary exercise test (CPX) as part of their preoperative assessment. Their cardiac and pulmonary risk factors were analysed. Depending on the anaerobic threshold (AT) values, patients are considered poor risk, moderate risk or very low risk for surgery.
Results Three patients did not complete the test. Two of them had very poor cardiopulmonary reserve and one had leg fatigue with good pulmonary function. Seven patients were considered high risk with AT < 10. The remaining 31 patients had AT > 11 and underwent major cancer surgery. In total, 10 surgical procedures were cancelled based on poor CPX performance. Two patients with low AT underwent surgery after preoptimisation with no complications. There are no deaths related to cardiopulmonary complications in any patient deemed fit for major cancer surgery and intensive care management, as determined by CPX testing. The average intensive care stay was 8.9 days (range 1–19 days). The surgical procedure was altered in two patients based on CPX results.
Discussion CPX testing is an important screening test for major surgery to determine the cardiorespiratory risk factors. It is useful in reducing surgical perioperative mortality and avoids unnecessary intensive care admissions after major body cavity surgeries. The CPX test is also useful in perioperative anaesthetic management. It may not predict morbidity and the average intensive care stay. It is very useful in selecting patients for preoptimisation before major cancer surgery.
Conclusion Preoperative screening using CPX testing is useful in identification of high-risk cancer surgical patients and the appropriate selection of perioperative management.

P251

Low-dose dobutamine after surgery in high-risk patients: effects on postoperative complications

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Critical Care 2007, **11(Suppl 2):**P251 (doi: 10.1186/cc5411)

Introduction Dobutamine may have a role in increasing splanchnic perfusion, thereby protecting this area from further injury. We aimed to investigate the effects of low-dose dobutamine (5 μg/kg/min) on tissue perfusion and postoperative complications in high-risk patients.
Methods A prospective, randomized, blinded and placebo-controlled study. One hundred surgical patients admitted to a step-down unit were evaluated and 82 patients were enrolled, 42 for the control group (saline) and 40 for the dobutamine group (5 μg/kg/hour during 24 hours). The same therapeutic goals were

applied for both groups. The presence of tachycardia or hypotension in response to study drug infusion was considered a signal of occult hypoperfusion and deemed a need for fluid replacement, which was given according to an algorithm.
Results Complications occurred in 35% and 50% of the patients in the dobutamine and control groups, respectively (RR 0.70, 95% CI 0.41–1.17; not significant). The patients in whom dobutamine was interrupted due to persistent tachycardia despite fluid replacement had more complications (75% vs 40.6%; RR 1.85, 95% CI 1.03–3.29, $P < 0.05$), higher mortality (62.5% vs 12.5%; RR 5.0, 95% CI 1.72–14.46, $P < 0.05$) and lower central venous oxygen saturation (55% ± 15% vs 70% ± 16%; $P = 0.021$) in comparison with patients tolerant to dobutamine infusion.
Conclusion Low-dose dobutamine after surgical trauma has no effects on the prevalence of postoperative complications in high-risk surgical patients. Morbimortality was significantly higher in patients with severe occult hypoperfusion.

P252

Intestinal complications associated with cardiovascular surgical procedures

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Introduction Intestinal complications after cardiopulmonary bypass procedures are infrequent but they carry a significant incidence of morbidity and mortality. Predictors of these complications are not well developed, and the role of fundamental variables remains controversial. The purpose of this study was to ascertain the frequency of intestinal complications following open heart surgery, to assess preoperative predisposing factors and to elucidate that prompt diagnosis and institution of therapy are the most common factors to improve the outcome.
Methods A prospective survey was conducted among 4,588 patients undergoing cardiac surgery and attending the surgical ICU from 1 January 2002 to 31 December 2004. All case histories of patients were objected to meticulous analysis searching for complications involving gastrointestinal tract and requiring surgical consultation. Patients with minor disorders were excluded from the study. We performed a multivariable logistic regression analysis to identify the risk factors for development of postoperative intestinal complications.
Results Gastrointestinal complications occurred in 63 patients, while in 35 patients appeared transient episodes of gut mucosal ischemia. Sixteen patients presented mesenteric ischemia, six paralytic ileus, six colonic obstruction, two lower gastrointestinal bleeding, two upper gastrointestinal bleeding, two perforated duodenal ulcer and one rectal perforation. Intestinal complications correlated with advanced age (67.5 ± 12 years), preoperative congestive heart failure and peripheral vascular disease, prolonged bypass time (156 ± 91.7 min) and aortic cross-clump time (97.6 ± 44.45 min), the number of blood and plasma transfusions, re-exploration of the chest, the administration of inotrops (70%) and the usage of a intra-aortic balloon pump (42%). The mean EuroSCORE value was 12.72 ± 3.8. The majority of patients presented at the end of the first postoperative week. Fifteen patients died (48%).
Conclusions Intestinal complications after cardiac surgery are uncommon but life-threatening and may result from ischemic mucosal injury, which increases mucosal permeability and promotes the translocation of bacterial toxins and the release of mediators. Clinical features are often subtle and a high index of suspicion is necessary for an early diagnosis and the institution of appropriate treatment.

P253

Combined metabolic parameters and gas exchange to predict morbidity after extracorporeal circulation

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Critical Care 2007, **11(Suppl 2):**P253 (doi: 10.1186/cc5413)

Introduction Under normal resting conditions, the oxygen delivery (DO_2) matches the overall metabolic demands of the organs, the oxygen consumption (VO_2) is about 25% of the DO_2, and energy is produced basically through the aerobic mechanism. In cardiac surgery with extracorporeal circulation (ECC), several factors (for example, hemodilutional anemia, myocardial stunning resulting in a low cardiac output (CO)) can determine an imbalance between O_2 demand and DO_2 and may affect the outcome. Below the critical DO_2 there is a linear decrease of both VO_2 and CO_2 production (VCO_2), but due to the anaerobic VCO_2 the respiratory quotient increases. This study is aimed to evaluate the role of O_2 and CO_2 derived parameters to predict postoperative morbidity in cardiac surgery.
Methods Eight hundred and twenty-seven consecutive adult patients who underwent coronary surgery were studied. We selected 38 intraoperative and postoperative O_2 and CO_2 derived parameters, which could be associated with postoperative morbidity. Postoperative data were collected in the first 3 hours after admission to the ICU. The influence of each predictor on outcome was analyzed. Morbidity was defined as one or more of the following events: cardiovascular, respiratory, neurological, renal, infectious, and hemorrhagic complications. Univariate and multivariate analyses were performed. ROC curve analysis was also used to define the best predictive variables.
Results Intraoperative predictors of morbidity were ECC and aortic cross-clamp times, and lowest hematocrit during ECC. The area under the ROC curve (AUC) was 0.74 for the lowest hematocrit on ECC, and its cutoff value was 24%. Among the postoperative variables, DO_2, oxygen extraction ratio (O_2ER), DO_2/VCO_2 ratio, and VCO_2/CO ratio were related to morbidity. The AUCs for oxygen and CO_2 derived parameters were 0.80, 0.76, 0.75, and 0.70 (DO_2, O_2ER, DO_2/VCO_2 ratio, and VCO_2/CO ratio, respectively). The best predictive cutoff values were 590 ml/minute, 38%, 3.9, and 40, for DO_2, O_2ER, DO_2/VCO_2 ratio, and VCO_2/CO ratio, respectively.
Conclusion Various predictors of hypoperfusion have been tested in critically ill patients and correlations have been found for O_2 and CO_2 derived parameters. Long ECC time plays a major role in the balance between VO_2 and DO_2; O_2 and CO_2 derived parameters could be useful markers to detect anaerobic metabolism in cardiac surgical patients.

P254

Vasoplegic syndrome after cardiopulmonary bypass surgery – associated factors and clinical outcomes: a nested case–control study

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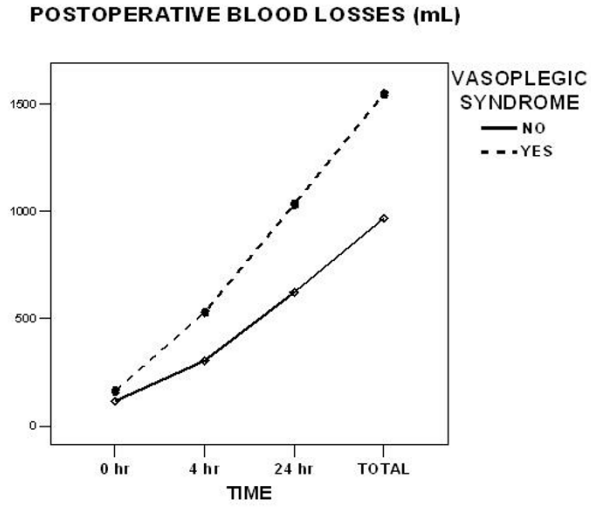
Introduction Vasoplegic syndrome (VS) following heart surgery using cardiopulmonary bypass (CPB) has been recently recognized and implicated in life-threatening complications. The

aim of this study was to identify associated factors for the development of VS after CPB.

Methods We performed a nested case–control study of 50 patients undergoing CPB, 27 (54%) men and 23 (46) women, mean age 66.5 (SD 9.6) years. VS was defined as systemic vascular resistance index <1,600 dyn•seg/cm^5/m^2 and cardiac index >2.5 l/min/m^2 within the first postoperative 4 hours. Vasoplegic shock was defined as vasoplegic patients that needed norepinephrine for at least 4 hours, after failure to respond to appropriate volume expansion. Excessive bleeding was defined as blood loss >1 l/24 hours, while total bleeding was considered as blood loss until chest tube withdrawal. Demographic variables, surgical procedures and postoperative variables were collected. We recorded data related to coagulation, fibrinolysis, complement, inflammation, blood loss at different time points, preoperative, at 0, 4 and 24 hours after surgery, and hemoderivative requirements. We used the Pearson chi-squared test, the Fisher exact test, the Student *t* test and the Mann–Whitney U test for nonparametric variables. SPSS version 12.1 was used.

Results Seventeen (34%) patients had VS, 11 (65%) men and six (35%) women. Longer aortic clamping time ($P = 0.007$) and CPB time ($P = 0.013$) were associated with VS. These patients showed a higher cardiac index at 4 hours ($P < 0.001$) and lactic acid within the first 24 hours. Seven of these patients (41%) fulfilled vasoplegic shock criteria ($P < 0.001$). We found higher levels of IL-6 at 0 hours ($P = 0.02$) and 4 hours ($P = 0.001$), and soluble TNF receptor at 0 hours ($P = 0.044$). At ICU admission (0 hours) there was a higher coagulation activation: INR ($P = 0.005$), fibrinogen ($P = 0.001$), antithrombin ($P = 0.007$); lower levels of plasminogen activator inhibitor-1 ($P = 0.023$) as well as lower plasminogen activator inhibitor-1/tissue-plasminogen activator ratio ($P = 0.021$), and higher levels of D-dimer ($P = 0.041$); lower levels of C3 ($P = 0.023$), B factor ($P = 0.013$), C4 ($P = 0.015$) as well as a significantly higher decrease between preoperative and 0-hour levels of C1-inhibitor, C4, C3 and B factor. Lower levels of leptins at 0, 4 and 24 hours were found. Vasoplegic patients showed higher blood losses along all time points (Figure 1), higher incidence of excessive bleeding (60% vs 40%; $P = 0.011$) and required more hemoderivatives during the ICU stay, plasma ($P = 0.016$) and platelets ($P = 0.002$).

Figure 1 (abstract P254)



Conclusions VS post-CPB was associated with activation of serin protease systems, which leads to higher blood loss and excessive bleeding.

P255

Role of plasminogen activator inhibitor-1 polymorphism on the development of vasoplegic syndrome associated with cardiopulmonary bypass

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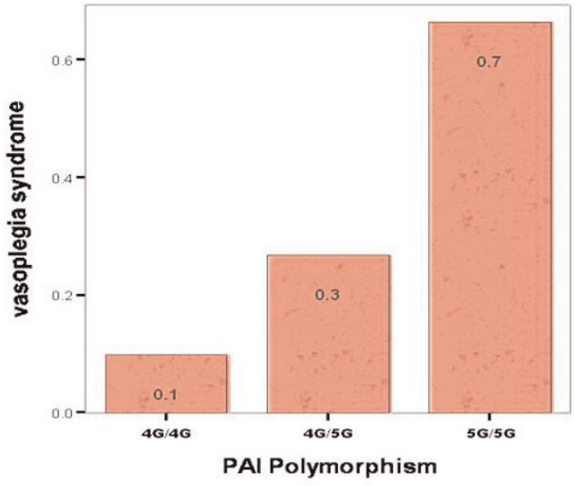
Critical Care 2007, **11(Suppl 2):**P255 (doi: 10.1186/cc5415)

Introduction Vasoplegic syndrome (VS) after cardiac surgery with cardiopulmonary bypass (CPB) can vary from mild to severe complication and it appears with an incidence ranging between 5% and 15%. The etiology is not completely elucidated but risk factors such as temperature and duration of cardiopulmonary bypass and preoperative treatment with angiotensin-converting enzyme (ACE) inhibitors have been associated [1]. We wanted to investigate the possible role of several genetic polymorphisms in patients with VS after elective CPB.

Methods We performed a nested case–control study of 50 patients undergoing CPB, 27 (54%) men and 23 (46) women, mean age 66.5 (SD 9.6) years. VS was defined as systemic vascular resistance index lower than 1,600 dyn•seg/cm^5/m^2 and a cardiac index greater than 2.5 l/min/m^2 within the first 4 hours after surgery. We recorded data related to hemodynamic parameters at different postoperative time points, at ICU admission (0 hours), 4 and 24 hours after surgery, and the polymorphism of the following genes: plasminogen activator inhibitor-1 (PAI-1) and β-TNF + 250. In addition, 23 neutral markers were genotyped to follow genomic control strategies that would detect spurious associations due to population substructure. We used the Pearson chi-squared test and binary logistic regression. SPSS version 12.1 was used.

Results We observed 17 (34%) patients with vasoplegia criteria, 11 (65%) men and six (35%) women, age 67 (61–72) years. The only one associated with VS was the PAI-1 polymorphism, and its distribution in the study population was: 4G/G genotype in 10 (20%) patients, 4G/5G in 26 (52%) patients, and 5G/G in 14

Figure 1 (abstract P255)



(28%) patients. According to the PAI-1 polymorphism, vasoplegia criteria were found in one (5.5%) 4G/G carrier, in seven (39%) 4G/5G carriers and in 10 (55.5%) 5G/G carriers ($P = 0.012$) (Figure 1). The post-hoc power for PAI-1 polymorphism and vasoplegia was 0.85. After controlling for temperature, clamping time, antifibrinolytics, body mass index and ACE inhibitors, the 5G/G genotype was independently associated with vasoplegia ($P = 0.017$); OR: 24.6 (95% CI: 1.8–342).

Conclusions The PAI-1 polymorphism (homozygous 5G/G) was independently associated with the onset of VS.

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P256

Complement activation and excessive bleeding in cardiopulmonary bypass surgery

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Critical Care 2007, **11(Suppl 2):**P256 (doi: 10.1186/cc5416)

Introduction Complement activation has been associated with postoperative bleeding. We investigated the association between complement activation, coagulation and fibrinolysis systems, and postoperative excessive bleeding in cardiopulmonary bypass (CPB) surgery.

Methods We performed a nested case–control study of 50 patients undergoing CPB, 27 (54%) men and 23 (46) women, mean age 66.5 (SD 9.6) years. Excessive bleeding (EB) was defined as blood loss higher than 1 l over the 24 hours. Demographic variables, comorbid conditions, surgical procedures and postoperative variables were collected. We recorded data related to coagulation, fibrinolysis, complement, and blood loss at different time points, preoperative, at ICU admission (0 hours) and 4 and 24 hours after surgery. We used the Pearson chi-squared test, the Fisher exact test, the Student *t* test and the Mann–Whitney U test for nonparametric variables and Spearman's rho for nonparametric correlations.

Results EB patients had higher activation of classical, alternative and final pathways of complement at 0 and 4 hours. Also we found a significantly higher decreasing of several components of complement from preoperative values to postoperative values (0 and 4 hours) associated with EB. This decrease of complement was correlated with a similar decrease of platelets and anti-thrombin levels between the preoperative period and 0 hours, and an increase of D-dimer levels in the first 4 hours.

Conclusions Complement activation was associated with EB due, in part, to a greater activation of platelets, coagulation and fibrinolysis.

P257

Impact of body mass index on postoperative bleeding in cardiopulmonary bypass

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Critical Care 2007, **11(Suppl 2):**P257 (doi: 10.1186/cc5417)

Introduction Body mass index (BMI) has been described as a risk factor for coronary artery disease, but association with postoperative bleeding after cardiopulmonary bypass (CPB) has been found in several studies recently. Nevertheless the strong relationship between a low BMI and excessive bleeding remains unexplained. We sought to investigate the BMI role on postoperative bleeding and its relationship with leptin levels, coagulation, fibrinolysis and complement parameters.

Methods We performed a nested case–control study of 26 patients, who did not receive antifibrinolytic prophylaxis. We used Bray's classification for BMI: lower than 27 kg/m^2; 27–30 kg/m^2; higher than 30 kg/m^2. Variables were collected preoperatively, at ICU admission (0 hours), and at 4 and 24 hours after surgery. Excessive bleeding was defined as blood loss higher than 1 l in the first 24 hours after intervention. The associations of BMI with demographic factors, leptin levels, coagulation, fibrinolysis and complement parameters were analyzed. Pearson's chi-squared test and Fisher's exact test were used, the Student *t* test for independent groups and the Mann–Whitney U test for nonparametric variables.

Results In total, 61.5% of patients showed BMI >27 kg/m^2 (median 28 kg/m^2, range 25.2–30.7 kg/m^2). Patients with BMI lower than 26.4 kg/m^2 (25–28 kg/m^2) presented excessive bleeding ($P = 0.026$). Leptin levels after adjusting by BMI were significantly associated with excessive bleeding at all postoperative time points ($P < 0.001$, $P < 0.001$ and $P = 0.004$, respectively) (Figure 1). BMI presented a direct correlation with leptins, fibrinogen and plasminogen activator inhibitor-1 (PAI-1) on arrival, meanwhile 24-hour bleeding showed an inverse correlation with the same parameters and BMI (Table 1). Patients with BMI < 27 kg/m^2 had significantly greater coagulation, fibrinolysis and complement activation. Therefore these patients required significantly greater hemoderivatives.

Figure 1 (abstract P257)

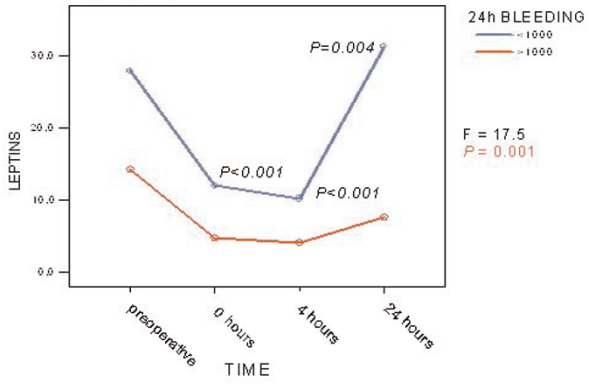

Table 1 (abstract P257)

ICU arrival	BMI		24-hour bleeding	
	Rho	*P*	Rho	*P*
Leptins	0.46	0.02	–0.57	0.02
Fibrinogen	0.51	<0.01	–0.49	<0.01
PAI-1	0.40	0.04	–0.64	<0.01

Conclusions Lower BMI was associated with higher postoperative bleeding and lower procoagulant factor levels.

P258

Muscle versus liver mitochondrial respiration in experimental three-hit endotoxemia

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Critical Care 2007, **11(Suppl 2):**P258 (doi: 10.1186/cc5418)

Introduction Endotoxemia and hemorrhage may both affect mitochondrial function. We aimed to characterize the impact of a short-term, three-hit hemorrhage/endotoxemia model on liver and skeletal muscle mitochondrial respiration.

Methods Seven anesthetized pigs were bled (blood loss 20%) and retransfused to euvolemia before and after endotoxin infusion (0.4 μg/kg/hour for 2 hours). The cardiac index (CI) (thermodilution) and systemic mean arterial pressure (MAP) were recorded. State 3/4 respiration (nanoatom O_2/min/mg protein for glutamate) was assayed from tissue samples at baseline (muscle) and the end of the experiment (muscle and liver). Hepatic mitochondrial respiration was compared with controls ($n = 6$).

Results One pig died earlier (not included). Data are presented as the median (range). $P < 0.05$, Friedman test. Muscle mitochondrial respiration was similar at baseline and the end of experiment; state 3 (317 (222–594) vs 409 (295–468)), state 4 (29 (22–58) vs 40 (31–49)), respiratory control ratio (11 (7–15) vs 10 (9–11)) (not significant). Hepatic mitochondrial state 4 was higher (27 (16–31) vs 19 (13–22)) and respiratory control ratio lower (3 (3–4) vs 5 (4–6)) in the hemorrhage/endotoxemia group, compared with controls.

Table 1 (abstract P258)

	Baseline	After bleeding	After endotoxin	End of experiment
MAP (mmHg)	69 (52–70)	36 (30–46)	67 (49–84)	47 (19–109)
CI (ml/kg/min)	85 (62–95)	55 (42–76)	95 (78–113)	69 (16–151)
PAP (mmHg)	14 (10–17)	12 (9–13)	45 (40–51)	32 (17–38)
SvO_2 (%)	49 (41–56)	33 (25–37)	54 (47–68)	46 (14–66)

PAP, pulmonary artery pressure. $P < 0.05$, Friedman test.

Conclusions Repeated ischemia/reperfusion episodes plus short-term endotoxemia decreased the efficiency of hepatic but not muscle mitochondrial respiration. Mitochondrial dysfunction under these experimental circumstances seems to be organ specific.

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P259

Hepatic mitochondrial dysfunction in fluid-resuscitated porcine septic shock

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Background Sepsis-induced multiple organ failure may crucially depend on the development of mitochondrial dysfunction and consequent cellular energetic failure. We investigated whether hepatic mitochondrial dysfunction was present in a clinically relevant porcine model of fluid-resuscitated septic shock.

Methods Anesthetized and ventilated pigs (40 ± 3 kg) were randomly assigned to septic shock by fecal peritonitis (F, $n = 3$) or control (C, $n = 3$) after placement of portal/hepatic vein catheters and portal vein and hepatic artery flow probes. F and C received 8 ± 13 ml/kg/hour and 5 ± 7 ml/kg/hour ringer lactate + starch, respectively. The mean arterial pressure (MAP), total liver flow (TLF), hepatic O_2 delivery ($DO_{2,h}$) and hepatic O_2 consumption ($VO_{2,h}$) were recorded at baseline (BL), 12 and 24 hours (ml/kg/min). Activities of mitochondrial respiratory chain enzymes (complex I–IV) were assessed by spectrophotometry in snap-frozen liver samples. Data are presented as the mean ± SD.

Results Hyperdynamic circulation developed in F with increasing $DO_{2,h}$ and decreasing $VO_{2,h}$ (Table 1). Complex II activity significantly decreased from 19.3 ± 4.2 to 9.5 ± 2.6 ($P < 0.05$ vs BL and between groups) in F compared with C. Complex I–III–IV function decreased in parallel in F.

Table 1 (abstract P259)

	BL	12 hours	24 hours
MAP F	78 ± 22	98 ± 25	81 ± 19
MAP C	91 ± 4	101 ± 12	94 ± 6
TLF F	17 ± 1	46 ± 11*	50 ± 5*
TLF C	23 ± 7	35 ± 4	39 ± 7†
$DO_{2,h}$ F	2.0 ± 0.6	3.8 ± 0.2	5.4 ± 1†
$DO_{2,h}$ C	1.9 ± 0.4	3.2 ± 0.4	3.5 ± 0.4
$VO_{2,h}$ F	0.8 ± 0.2	0.6 ± 0.1	0.5 ± 0.1
$VO_{2,h}$ C	1.5 ± 0.7	1.1 ± 0.1	0.9 ± 0.4

*$P < 0.05$ vs BL and between groups. †$P < 0.05$ vs BL.

Conclusion While increasing $DO_{2,h}$ far exceeded decreasing $VO_{2,h}$ in the setting of hyperdynamic fluid-resuscitated septic shock, hepatic mitochondrial function was significantly impaired compared with control.

P260

Real-time monitoring of mitochondrial function in the urethral wall

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Monitoring of the mitochondrial NADH redox state (an indicator of intracellular oxygen levels) together with microcirculatory blood flow (TBF) and with oxygenation (HbO_2) could serve as a preferred approach to evaluate tissue O_2 balance or viability. We hypothesize that in the presence of reduced oxygen delivery and extraction, blood flow will be redistributed in order to protect the most vital organs by increasing their regional blood flow, while O_2 delivery to the less vital organs will diminish. Thus, the NADH redox state of less vital organs could serve as an indicator of overall O_2 imbalance as well as an endpoint of resuscitation. We have therefore developed an optical device embedded in a Foley catheter to provide real-time data on the NADH redox state, TBF and HbO_2 in critically ill patients.

The CritiView is a computerized optical device that integrates hardware and software in order to provide real-time information of

tissue viability [1]. A modified three-way Foley catheter that contains a fiberoptic probe connects the CritiView to the mucosal side of the urethral wall. We have used this device in five female pigs that underwent graded hemorrhage, and in four patients who were monitored during aortic abdominal aneurysm operations.
These preliminary swine model and human studies confirm the feasibility of collecting information about mitochondrial function from the urethral wall. The main effects of graded hemorrhage started when the blood volume decreased by 30%. At 40% blood loss, minimal levels of TBF and HbO_2 were correlated to the maximal NADH levels. The values of the three parameters returned to baseline after retransfusion of the shed blood. Aortic clamping in patients led to a significant decrease in TBF and HbO_2 while NADH levels increased. After aortic declamping, the parameters recovered to normal values.
Our preliminary results show that the CritiView may be a useful tool for the detection of O_2 imbalance and the development of an emergency metabolic state in nonvital tissues.

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P261

Cytokines monitored by microdialysis detect rejection earlier than current methods in liver transplantation

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Critical Care 2007, **11(Suppl 2):**P261 (doi: 10.1186/cc5421)

Introduction The outcome of liver transplantation is steadily improving. There is still need for earlier detection of complications such as hepatic artery thrombosis and rejection. In an earlier *in vitro* study we showed that the CMA microdialysis system with a 100 kDa pore size membrane can be used to measure the selected cytokines and complement. We monitored patients undergoing liver transplantation with microdialysis continuously for a week postoperatively, and analyzed both parameters to detect ischemia, and cytokines and anaphylatoxins to explore whether rejection was detected earlier than with the standard methods.
Methods Twenty patients undergoing 22 liver transplantations were included. Two microdialysis catheter were introduced in the liver and one in subcutaneous tissue. We analyzed metabolic parameters (glucose, pyruvate, glycerol and lactate), and IL-6, IL-8, MCP-1, IP-10, and C5a.
Results Fourteen patients had an uneventful course postoperatively, judged clinically and by routine biochemical markers and ultrasound Doppler. These patients had a median lactate starting at 3.5 mM (2 hours after reperfusion) falling to below 2 mM during the first 24 hours, and thereafter staying low. The L/P ratio (a specific measure of ischemia) dropped from about 20 to below 10. These patients had a steady rise in IP-10 from 200 to 3,000 pg/ml, and also a slight raise in IL-6 initially. *Case 1.* The male patient had a steadily increasing L/P ratio during the 7 days of microdialysis measurements, indicating an insufficient blood supply. He underwent surgery 5 days later and a hepatic artery thrombosis was found. A biopsy was done during the operation showing an acute rejection. There was a significant rise in IP-10 to 13,000 pg/ml 7 days before the diagnosis of rejection. *Case 2.* The female patient had an acute rejection verified by biopsies on day 10 postoperatively. Her IL-8, IP-10 and C5a increased 10-fold to 100-fold in the liver 3 days earlier than an increase in liver enzymes and 5 days before the rejection was verified by biopsy.
Conclusion We have described the normal course of the four cytokines IL-6, IL-8, MCP-1 and IP-10 and complement C5a after liver transplantation, as well as metabolic parameters to detect ischemia. In two patients with rejection we found a large increase in IP-10, IL-8 and complement split-product C5a in the liver but not in the subcutis 3–5 days before any other parameter of liver injury.

P262

Microcirculatory hemodynamic alterations during cardiac luxation in off-pump coronary artery bypass grafting surgery

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Critical Care 2007, **11(Suppl 2):**P262 (doi: 10.1186/cc5422)

Introduction During luxation of the beating heart in off-pump coronary artery bypass grafting surgery the cardiac output drops and causes hypotension (<60 mmHg). It is expected that this state of obstructive shock is detrimental for adequate perfusion and oxygenation of organ tissue. However, it is unknown whether these luxations cause microcirculatory dysfunction. In this study we have explored the hemodynamics of the sublingual microcirculation during mechanical manipulations of the beating heart.
Methods During cardiac luxations, in 12 patients reflectance spectrophotometry (O_2C®; Lea Medizintechnik, Germany) was used to measure oxygen availability and in 12 other patients sidestream dark field imaging (MicroScan®; MicroVision Medical, The Netherlands) was used to directly visualize the sublingual microcirculatory hemodynamics in a single network of microvessels. Microvascular analysis software (MAS®; MicroVision Medical) was used to analyze the vessel density and blood flow. Synchronously, systemic hemodynamics were recorded and the cardiac output was calculated by pulse contour analysis of arterial pressure (PulseCO®; LiDCO, UK) in all patients.
Results During cardiac luxations, the oxygen availability in the sublingual microcirculation decreased (μHbO_2 64.2 ± 9.1 to 48.6 ± 8.7%; $P < 0.01$) while the functional capillary density did not change (15.9 ± 1.1 to 15.6 ± 1.3 mm/mm²; $P = 0.65$). Although the small vessels (0–20 μm) did not fall out they did show hypoperfusion (V_{max} 895 ± 209 to 396 ± 178 μm/s; $P < 0.01$), whereas in the medium vessels (20–50 μm) there was no significant change in blood velocity (V_{max} 751 ± 239 to 596 ± 192 μm/s; $P = 0.18$) as observed with sidestream dark field imaging and calculated with microvascular analysis software.
Conclusion Alterations in sublingual microcirculation hemodynamics reflect the direct effects of obstructive shock and elucidate the microcirculatory autoregulation.

P263

Muscle microcirculation alterations increase with disease severity in chronic heart failure patients

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Critical Care 2007, **11(Suppl 2):**P263 (doi: 10.1186/cc5423)

Objective To evaluate skeletal muscle microcirculation by near-infrared spectroscopy (NIRS) in patients with chronic heart failure (CHF).
Background Skeletal muscle microcirculation is impaired in patients with CHF, and this impairment seems to correlate with disease severity.
Methods We evaluated 49 patients with CHF (mean age: 58 ± 12 years) and 12 healthy volunteers. Of the CHF patients, 14 had

end-stage heart failure (ESCHF) and were undergoing treatment with intermittent inotropic agent infusion during the period of the study protocol. The thenar muscle tissue oxygen saturation (StO_2%) was measured noninvasively by NIRS before, during and after 3-minute occlusion of the brachial artery (occlusion technique).
Results Patients with ESCHF ($n = 14$) and CHF ($n = 35$) presented a significantly lower tissue oxygen saturation (StO_2) than healthy subjects (75 ± 6%, 77 ± 8% and 85 ± 5%, $P = 0.001$ respectively). The oxygen consumption rate during the occlusion of the brachial artery differed significantly between patients with ESCHF, CHF and healthy subjects (22.4 ± 9%/min, 29 ± 10%/min and 38.1 ± 11.1%/min, $P = 0.001$ respectively). The reperfusion rate differed significantly between patients with ESCHF, CHF and healthy subjects (302 ± 136%/min, 393 ± 134%/min and 480 ± 133%/min, $P = 0.002$ respectively).
Conclusions Peripheral muscle microcirculation assessed by NIRS is impaired in CHF patients. The degree of dysfunction is associated with disease severity and is acutely partially reversed with inotropic agent infusion.

P264

Sublingual microcirculation is impaired during cardiopulmonary bypass in cardiac surgery

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Introduction Cardiac surgery patients are at low risk for postoperative complications, but these may involve multiple organ failure with a high mortality rate. These complications may be related to occurrence of organ ischemia and reperfusion during and just after surgery. We investigated whether microcirculatory flow alterations occur during cardiac surgery.
Methods We observed 10 consecutive patients who underwent cardiac surgery with cardiopulmonary bypass (CPB). The microcirculation was studied using sidestream dark field (SDF) imaging. The sublingual capillary flow was estimated using a semiquantitative microvascular flow index (MFI) in small (diameter 10–25 μm), medium (25–50 μm), and large (50–100 μm) sized microvessels (0 = none, 1 = intermittent, 2 = sluggish, 3 = continuous flow). SDF imaging was performed at least three times per time period (that is, at baseline, after starting CPB and after surgery) in each patient. Data are presented as the median and interquartile range.
Results The MFI decreased in all sizes of microvessels <15 minutes after starting CPB in comparison with baseline ($P < 0.05$, Table 1). After starting CPB, the mean arterial pressure (MAP) was lower (61 mmHg (53–65 mmHg)) than at baseline (100 mmHg (92–118 mmHg); $P = 0.01$). After return to the ICU, the MFI increased ($P < 0.05$) and returned to baseline values in all microvessels.
Conclusions SDF imaging can be used as a bedside tool to evaluate sublingual microcirculatory changes during cardiac surgery. Despite maintaining common circulatory parameters during CPB, the nonpulsatile status, hypothermia, and the temporary drop in MAP after starting CPB were associated with decreased sublingual MFI, which normalized after surgery. Further studies should reveal whether these changes are related to outcome.

Table 1 (abstract P264)

	Baseline	CPB	Postsurgery
MFI small	3 (3–3)	2 (0.4–3)	3 (2.9–3)
MFI medium	3 (2.2–3)	1.9 (0.8–3)	3 (2.9–3)
MFI large	3 (3–3)	2.4 (0.9–3)	3 (3–3)
MAP	100 (92–118)	61 (53–65)	79 (71–85)

P265

Sublingual microcirculation is impaired on the first day postoperatively in patients undergoing gastric tube reconstruction

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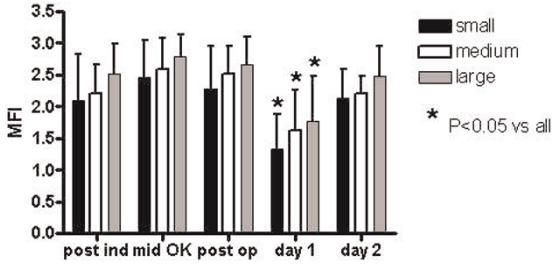
Introduction Complications of oesophagectomy with gastric tube reconstruction include leakage and stenosis. This can be explained by compromised local perfusion, although it is unclear to which extent local and systemic factors contribute to this process. The aim of this study was to observe the microvascular blood flow in an unaffected, distant tissue during the perioperative period.
Methods Twelve patients were included. Anesthesia consisted of thoracic epidural analgesia, restrictive peroperative fluid therapy (net peroperative fluid balance below 4 l) and early extubation. In the ICU, fluid infusion was adjusted in order to maintain hourly urine production of 0.5 ml/kg. The mean arterial pressure was maintained at or above 60 mmHg with administration of noradrenalin if necessary. Microcirculation was visualized in the sublingual tissue with the MicroScan, a sidestream dark field imager. Data were collected at five time points: immediately after induction, after gastric tube reconstruction, directly postoperative, and days 1 and 2 postoperatively. Video data collected with the MicroScan were analysed according to semiquantitative analysis described by Boerma and colleagues [1]. We divided the vessels into three categories: small (5–10 μm), medium (10–15 μm) and large (>15 μm). By dividing the images into four quadrants and categorizing the flow per vessel-size per quadrant, we calculated the microvascular flow index (MFI)
Results See Figure 1.

Figure 1 (abstract P265)



Sublingual microvascular perfusion.

Conclusion The sublingual microcirculation is decreased on the first day postoperatively in patients undergoing gastric tube reconstruction.

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P266

Oscillation frequency of skin microvascular blood flow is associated with mortality in critically ill patients

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Introduction Microcirculatory dysfunction has been hypothesized to play a key role in the pathophysiology of multiple organ failure, and consequently to patient outcome. The objective of the present study was to investigate differences in reactive hyperemia response and oscillation frequencies in survivors and nonsurvivors of patients with multiple organ dysfunction syndrome (MODS).
Methods Twenty-nine patients (15 survivors; 14 nonsurvivors) with two or more organ failures were eligible for study entry. All patients were hemodynamically stabilized, and demographic and clinical data were recorded. A laser Doppler flowmeter was used to measure the cutaneous microcirculatory response. Reactive hyperemia and oscillatory changes in the Doppler signal were measured during 3 minutes before and after a 5-minute period of forearm ischemia during hyperemia.
Results Nonsurvivors demonstrated a significantly higher MODS score when compared with survivors ($P = 0.004$). Norepinephrine requirements were higher in nonsurvivors ($P = 0.018$). Nonsurvivors had higher arterial lactate levels ($P = 0.046$), decreased arterial pH levels ($P = 0.001$), and decreased arterial PO_2 values ($P = 0.013$) when compared with survivors. A higher oscillation frequency of skin microvasculature at rest ($P = 0.033$) and after an ischemic stimulus ($P = 0.009$) was observed in nonsurvivors. No differences were observed in reactive hyperemia response between groups. The flowmotion frequency observed in reactive hyperemia was associated with the severity of the MODS ($P = 0.009$), and – although not statistically significant – arterial lactate concentration ($P = 0.052$).
Conclusion An increased skin microvascular oscillation frequency during rest and after an ischemic stimulus is associated with increased mortality in patients suffering from MODS. We suggest that the underlying mechanism of the increased flowmotion could be a response of the skin microvasculature to hypoxia or to an impaired oxygen utilization of the skin tissue.

P267

Effect of intermittent positive pressure ventilation on the skeletal muscle and small intestine microcirculation in rats

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Critical Care 2007, **11(Suppl 2):**P267 (doi: 10.1186/cc5427)

Introduction Intermittent positive pressure ventilation (IPPV) may be accompanied by alteration of microcirculation [1,2]; however, the effect of IPPV is not mentioned in the interpretation of the results of studies evaluating microcirculation using orthogonal polarization spectral or sidestream dark-field imaging. This study aimed to evaluate the effect of IPPV on microcirculation in the skeleton muscles and in the serosa of the small intestine in rats.
Methods Ten animals were tracheostomized and prepared for microcirculation study; after tissue preparation, five rats were allowed to breath spontaneously (Group SB = spontaneous breathing), and five rats (Group IPPV) were connected to a small animal ventilator (IPPV: FiO_2 0.21, respiratory rate 60/min, tidal volume 10 ml/kg, inspiratory time 50% of respiratory cycle, and 2 cmH_2O PEEP). Sidestream dark-field images were obtained from the quadriceps femoris muscle (QFM) and serosa surface of the ileum. The arterial blood pressure and rectal temperature were also recorded. The functional capillary density (FCD) and small and medium vessels rate were analysed offline using AVA V1.0 software (AMC, University of Amsterdam, The Netherlands), $P \leq 0.05$.
Results The FCD was decreased significantly in QFM in rats with IPPV with respect to Group SB (184 ± 27 resp. 197 ± 61 cm/cm^2), but the FCD of the intestinal serosa was not affected by IPPV (265 ± 46 resp. 267 ± 25 cm/cm^2). There were no differences in mean blood pressure and temperature between groups (128 ± 7 Torr and 36.6 ± 0.1°C in Group SB, or 128 ± 10 Torr and 36.5 ± 0.1°C in Group IPPV).
Conclusion The use of IPPV should be taken into account in the interpretation of the studies examining the changes in microcirculation in rats.
Acknowledgement Research project MZO 00179906.
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P268

Changes in sublingual microvascular flow during experimental human endotoxemia

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Introduction We examined sublingual microvascular changes in experimental human endotoxemia. Changes in microcirculation and mitochondrial dysfunction appear to be key mechanisms in sepsis, since they can lead to regional mismatch of oxygen supply and demand. Lipopolysaccharide (LPS) can be used to induce endotoxemia as a model of sepsis, but the effects on microcirculatory perfusion have not been tested before, particularly after tolerance induction during repeated challenges of LPS.
Methods Six healthy volunteers received an intravenous injection of 2 ng/kg *Escherichia coli* LPS to induce endotoxemia on five consecutive days. Microvascular perfusion was sublingually measured using sidestream darkfield imaging just before, and 2 and 4 hours after LPS injection on day 1. All measurements were repeated on day 5 of LPS administration. Sublingual capillary flow was estimated using a semiquantative microvascular flow index (MFI) in small (10–25 μm), medium (25–50 μm) and large-sized (50–100 μm) microvessels (no flow, 0; intermittent flow, 1; sluggish flow, 2; and continuous flow, 3). Changes were evaluated with the paired Wilcoxon test and sign test. $P < 0.05$ was judged to indicate a significant difference. Values are expressed as the median (P25–P75).
Results Two hours after the induction of endotoxemia ($n = 6$), sublingual flow in small (2 (1.7–2.3)), medium-sized (1.5 (1.2–1.9)), and large microvessels (2.5 (1.2–2.7)) did not differ from baseline values (2.3 (1.5–2.8), 2.3 (1.4–2.5), and 2.3 (1.3–2.5), respectively, all $P =$ not significant). Microvascular flow did not change in the subsequent 2 hours. In addition, no difference in microvascular flow could be demonstrated between timepoints on day 1 and day 5 of intermittent endotoxemia.
Conclusion In this small pilot study in experimental human endotoxemia, no significant effect of LPS administration on microcirculatory perfusion could be observed, nor any sign of tolerance. Further studies should reveal whether microvascular impairment does not occur in early human experimental

endotoxemia, or that sidestream darkfield imaging is not useful in this specific setting.

P269

Biochemical changes detected by microdialysis in subcutaneous tissue during experimental endotoxemia in rat

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Introduction Shock is defined currently as tissue oxygen metabolic disorders. It is most important to understand oxygen metabolic disorders in individual tissue. Microdialysis allows the determination of the metabolic condition in regional tissue and it appears ideal to determine the regional metabolic tissue conditions during endotoxemia.
Objective This study was designed to assess the regional metabolic tissue conditions on markers of tissue metabolism (lactate in regional tissue: tissue lactate (TL)) and tissue partial oxygen pressure (PtO_2) during severe endotoxemia and to compare them with variables determined by standard monitoring (hemodynamics, blood gas analysis, blood lactate (BL)).
Materials and methods Male Wister rats (body weight 270–300 g) were used for this study. The rats in the control group ($n = 6$) were injected with saline of 2 ml intraperitoneally, and the rats in the experimental group ($n = 6$) were treated with intraperitoneal injection of lipopolysaccharide (LPS) of 40 mg/kg. The hemodynamic parameters, arterial blood gas analysis, BL and PtO_2 were measured in both groups. TL and pyruvate in subcutaneous tissue were measured using microdialysis. These parameters were measured every 50 minutes until 400 minutes after LPS was administered.
Results In the control group, all parameters were not changed during the observation period of 400 minutes. In the experimental group, the mean arterial pressure (MAP) remained fairly stable until 300 minutes after injection of LPS, and the MAP gradually decreased subsequently. While the MAP was maintained, the PtO_2 gradually decreased linearly (Figure 1). TL increased with time linearly. Meanwhile, BL did not change from 150 to 250 minutes; after 300 minutes it increased abruptly in the experimental group (Figure 2).
Conclusions In our experimental endotoxemia model it has been shown that partial pressure of oxygen in subcutaneous tissue decreased even if systemic blood pressure was maintained. Boekstegers and colleagues [1] revealed that mean skeletal muscle PO_2 was increased in patients with sepsis compared with patients with limited infection. We obtained conflicting results to those of Boekstegers and colleagues. The reason for this is unknown. BL abruptly increased during 50–150 minutes, probably from abnormal metabolism induced by LPS in whole-body organs. It is considered that BL did not show a rise during 150–250 minutes due to metabolization of lactate in liver and muscle. TL, which is insusceptible of lactate metabolism by other organs, may reflect abnormality of tissue metabolism precisely.

Figure 1 (abstract P269)

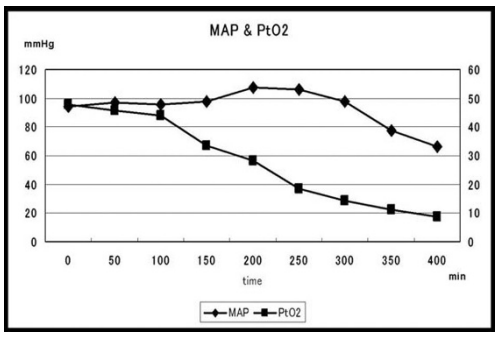
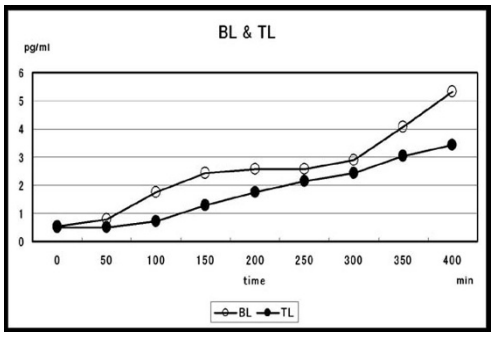


Figure 2 (abstract P269)



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P270

Occurrence and functional consequences of shunting of the microcirculation after mesenteric ischemia

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Shunting of the microcirculation contributes to the pathology of sepsis and septic shock. In this study, we hypothesize that shunting of the microcirculation occurs after superior mesenteric artery (SMA) ischemia (occlusion) and reperfusion, and we explore functional consequences using intravital microscopy.
Spontaneously breathing animals (rats) ($n = 30$) underwent occlusion of the SMA for 0 (controls), 30 or 60 minutes followed by reperfusion (4 hours) with normal saline. Leukocyte–endothelial interactions in mesenteric venules were quantified in an exteriorized ileal loop using intravital microscopy. Abdominal blood flow was recorded continuously, and arterial blood gases were analyzed at intervals. Continuous SMA blood flow measurements were performed in comparable groups without exteriorizing an ileal loop.
Adherent leukocytes increased shortly after reperfusion in ischemia groups, and plateaued in these groups. The centerline velocity and shear rate in the recorded venules were significantly reduced after reperfusion down to low-flow/no-flow in animals undergoing 60 minutes of mesenteric artery occlusion compared with animals with 30 minutes occlusion and controls, whereas perfusion of the SMA and ileal vessels persisted. The microcirculatory changes in animals with 60 minutes occlusion were accompanied by progressive metabolic acidosis, substantially larger volumes of intravenous fluids needed to support arterial blood pressure and significantly reduced survival (30%). In the groups with continuous SMA blood flow measurements, SMA blood flow increased in

relation to abdominal blood flow after reperfusion in animals with 60 minutes occlusion, and remained constant in animals undergoing 30 minutes occlusion and controls. Survival was 80% in animals with 60 minutes occlusion without an exteriorized ileal loop. SMA occlusion for 60 minutes and subsequent reperfusion causes perfusion abnormalities in the mesenteric microcirculation as often seen in sepsis and septic shock with increased microcirculation shunting, progressive metabolic acidosis and increased mortality. To detect these significant changes requires prolonged observation periods and might help to find new treatments to improve the poor prognosis of mesenteric ischemia.

P271

Changes in tissue oxygen saturation reflect changes in targeted oxygen delivery in postoperatively optimised patients

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Introduction Targeting oxygen delivery in the postoperative period has been shown to reduce hospital length of stay and complications [1]. Using a near-infrared spectroscopy device such as the Inspectra™ 325 allows the measurement of tissue oxygen saturation (STO_2) noninvasively as well as a rudimentary measure of blood flow beneath the probe. It is plausible, then, that changes in oxygen delivery (DO_2) during postoperative optimisation may be reflected in changes in STO_2 and provide a noninvasive surrogate of DO_2.
Methods All adult patients admitted to the ICU after surgery who underwent protocolised haemodynamic optimisation were included. All patients had STO_2 recorded over the thenar eminence using an Inspectra™ 325 for the first 8 hours of their stay.
Results We found a significant correlation between the changes in STO_2 and oxygen delivery index (DO_2I) over the first 8 hours of intensive care stay (n = 40, correlation coefficient of 0.947, $P = 0.0001$, Figure 1). We classified patients who achieved $DO_2I > 600$ ml/min/m^2 as responders. These responders had higher STO_2 values by 3 hours of optimisation, a change that remained significant throughout the duration of the study (Figure 2).
Conclusion Changes in STO_2 during postoperative optimisation appear to mirror changes in DO_2I and may allow more widespread use of noninvasive tissue oxygenation devices in surgical optimisation.

Figure 1 (abstract P271)

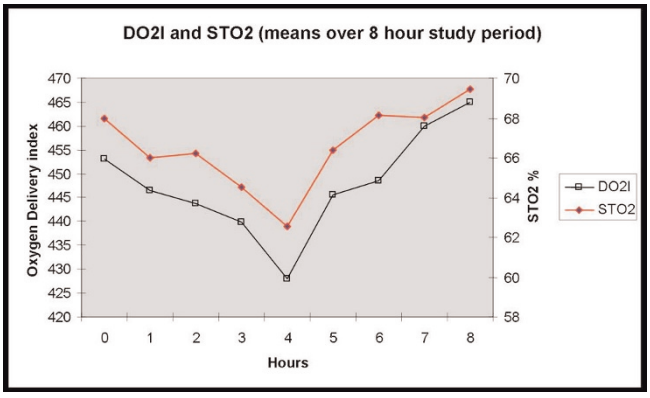
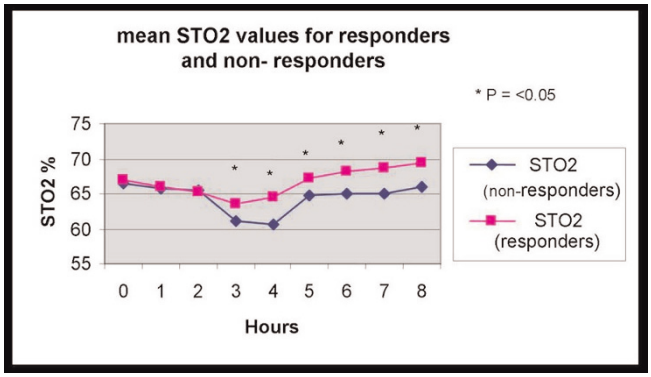


Figure 2 (abstract P271)



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P272

General anesthesia impairs muscle microvascular compliance

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Introduction Drugs used to induce and maintain general anesthesia have deep effects on the cardiovascular system. To our knowledge there are no studies investigating microvascular compliance during general anesthesia with a noninvasive approach based on near-infrared spectroscopy (NIRS) technology.
Methods We randomized 36 healthy subjects undergoing maxillofacial surgery to receive general anesthesia with a sevofluorane–remifentanil (Group S) or a propofol–remifentanil association (Group P). We collected noninvasive measures of hemoglobin concentration from the gastrocnemius muscle of the subjects using a NIRS device (NIMO, NIROX srl, Italy), which performs quantitative assessments of the [HbO_2] and [Hb] exploiting precise absorption measurements close to the absorption peak of the water. Data were collected during a series of venous occlusions at different cuff pressures, before and after 30 minutes from induction of general anesthesia. The muscle blood volume and microvascular compliance were obtained with a process previously described elsewhere [1]. Data were analyzed with a one-way analysis of variance test.
Results Demographic data of the 36 subjects were similar in both Groups S and P. General anesthesia reduced the heart rate and mean arterial pressure and increased the total muscle blood volume in both groups (Group S: from 2.4 ± 0.9 to 3.2 ± 1.2 ml/100 ml; Group P: from 2.4 ± 1.2 to 3.5 ± 1.8 ml/100 ml; $P < 0.05$). During general anesthesia, despite no differences in muscle blood volume between the two groups, sevofluorane–remifentanil significantly decreased microvascular compliance (from 0.15 ± 0.08 to 0.09 ± 0.04 ml/mmHg/100 ml; $P = 0.001$) whereas propofol–remifentanil did not (from 0.15 ± 0.08 to 0.16 ± 0.11 ml/mmHg/100 ml; $P = 0.39$).

Conclusion General anesthesia affects the microvascular bed of skeletal muscle. An association between opioid and ipnotic agents increases the muscle blood volume, whereas microvascular compliance is reduced only by the sevofluorane–remifentanil association.

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P273

Skeletal muscle oxygen saturation estimates mixed venous oxygen saturation in patients with severe left heart failure

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Introduction Low cardiac output states, such as left heart failure, are characterized by a preserved oxygen extraction ratio compared with severe sepsis. Near-infrared spectroscopy (NIRS) allows noninvasive estimation of skeletal muscle tissue oxygenation (StO_2). The aim of study was to determine relationship between StO_2 and mixed venous oxygen saturation (SvO_2) in patients with severe left heart failure with or without additional severe sepsis or septic shock.
Methods Sixty-five patients with severe left heart failure due to primary heart disease were divided into two groups: Group A were patients without ($n = 24$) and Group B were patients with ($n = 41$) additional severe sepsis/septic shock. The thenar muscle StO_2 was measured using NIRS.
Results In Group A StO_2 was lower compared with Group B and healthy volunteers (58 ± 13% vs 90 ± 7% vs 84 ± 4%, $P < 0.001$). StO_2 was higher in Group B compared with healthy volunteers ($P = 0.02$). In Group A StO_2 correlated with SvO_2 ($r = 0.689$, $P = 0.002$), and StO_2 overestimated SvO_2 (bias: −2.3%, precision: 4.6%). In Group A changes of StO_2 correlated to changes of SvO_2 ($r = 0.836$, $P < 0.001$; $\Delta SvO_2 = 0.84 \times \Delta StO_2 - 0.67$). In Group B important disagreement between these variables was present. Plasma lactate concentrations negatively correlated with StO_2 values only in group A ($r = -0.522$, $P = 0.009$; lactate = $-0.104 \times StO_2 + 10.25$).
Conclusions Exact numerical values of StO_2 are not equivalent to those of SvO_2. However, for clinical purpose, StO_2 values could be used for fast noninvasive SvO_2 estimation; and the trend of StO_2 may be substituted for the trend of SvO_2 in severe left heart failure without additional severe sepsis or septic shock.

P274

Tissue oxygen saturation and the rate of tissue deoxygenation during stagnant ischemia in the medical emergency department

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Hypothesis Tissue oxygen saturation (StO_2) and the rate of tissue deoxygenation during stagnant ischemia can early and reliably detect inadequate tissue oxygenation and assess prognosis in medical emergency room patients.
Introduction Early recognition of patients with inadequate tissue oxygenation facilitates early diagnostic evaluation and treatment that was correlated with improved outcome. Near-infrared spectroscopy is noninvasive and in the emergency setting is a rapidly appliable method for measuring StO_2.
Methods In a prospective observational study we included 340 consecutive medical emergency room patients. On admission, StO_2 and the rate of tissue deoxygenation during stagnant ischemia were measured by the near-infrared spectroscopy method (InSpectra tissue spectrometer; Hutchinson Technology Inc., The Netherlands) and correlated with clinical signs of shock, lactate and outcome.
Results Three hundred and forty patients were included. Of 137 patients admitted, 16 (11.7%) were admitted to the ICU and 14 (10.2%) died in the hospital. The StO_2 was higher in patients who were not admitted compared with patients with LOS > 7 days (80.2 ± 8.7% vs 76.9 ± 9.2%, $P = 0.009$). Tissue deoxygenation was faster (16.7 ± 7.0%/min vs 12.9 ± 5.6%/min, $P = 0.014$) in survivors. Tissue deoxygenation was slower in the group of patients with clinical signs of shock compared with all patients (11.8 ± 6.0%/min vs 16.5 ± 7.0%/min, $P < 0,05$). Age, lactate and rate of tissue deoxygenation but not StO_2 were significant predictors of death (Table 1). There was weak but significant correlation between StO_2 and age ($P < 0.0001$, $r = -0.28$), StO_2 and lactate ($P = 0.035$, $r = -0.12$) and StO_2 and systolic blood pressure ($P < 0.0001$, $r = 0.26$).

Table 1 (abstract P274)

Predictors of survival

Predictor	Odds ratio	*P* value
Age	1.083	0.004
Lactate	1.798	<0.001
Deoxygenation rate	0.895	0.046

Conclusions StO_2 and the rate of tissue deoxygenation during stagnant ischemia are promising additional variables, which can be measured rapidly and noninvasively in the emergency room setting. The rate of deoxygenation rather than StO_2 may be helpful for early detection of patients with inadequate tissue perfusion and worse prognosis.

P275

Near-infrared spectroscopy during resuscitation of trauma patients predicts development of multiple organ dysfunction: a prospective cohort study

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Critical Care 2007, **11(Suppl 2):**P275 (doi: 10.1186/cc5435)

Introduction Near-infrared spectroscopy (NIRS) noninvasively monitors muscle tissue oxygen saturation (StO_2). It may provide a continuous measurement to identify occult hypoperfusion, guide resuscitation, and predict the development of multiple organ dysfunction (MOD) after severe trauma. We evaluated the correlation between initial StO_2 and the development of MOD in multitrauma patients.
Methods Patients presenting to our urban, academic, Level I Trauma Center/Emergency Department (TC/ED) and meeting standardized trauma-team activation criteria were enrolled. NIRS monitoring with collection of StO_2 at the thenar eminence was initiated immediately on arrival at the ED and continued up to 24 hours for those admitted to the trauma ICU. Standardized resuscitation assessment laboratory measures and clinical evaluation tools were collected. The primary outcome in this prospective

study was the association between StO_2 and the development of MOD within the first 24 hours based on a MOD score of 6 or greater. Clinicians were blinded from the StO_2 values.
Results Over a 14-month period, 78 patients were enrolled. Of the 78 patients, 26 (33.3%) developed MOD within the first 24 hours. The MOD patients had mean (SD) initial StO_2 values of 53.3 (±10.3), significantly lower than those of non-MOD patients (61.1 (±10.0); $P = 0.002$). The MOD patient mean shock index of 0.92 (±0.28) was also significantly higher than those of non-MODS patients (0.73 (±0.19); $P = 0.0007$). Lactate values were not significantly different.
Conclusions Noninvasive, continuous StO_2 NIRS on initial arrival in the TC/ED correlates with the shock index and with the development of MOD.

P276

Buccal visible light spectroscopy and laser Doppler flowmetry: reliability analysis

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Background There are insatiable demands for new technologies to advance basic biological investigation at the microcirculatory level. Oxygen to see (O_2C)® is a newly developed system that combines laser Doppler flow (LDF) and visible light spectroscopy (VLS) technology. The aim of our study was to assess the reliability of O_2C® measurements applied to the buccal mucosa and to the thenar eminence in healthy volunteers.
Methods Microcirculatory hemoglobin oxygen saturation (μHbO_2, %) and blood flow (flow, AU) were measured using an O_2C® (Lea Medizintechnik GmbH, Giessen, Germany) probe applied to the buccal mucosa and to the thenar eminence. Measurements were obtained simultaneously at two depths, superficial (2 mm) and deep (6 mm), every 2 seconds for 5 minutes and were recorded for later analysis. The procedure was repeated on another occasion at least 1 week apart.
Results We studied 20 healthy subjects; 10 males and 10 females (mean age = 38 ± 18 years, range 21–74 years). Both μHbO_2 and flow measurements were consistently higher when measured from the deep tissue layers (6 mm) than those measured from the superficial layers, regardless of the site of measurement. Buccal mucosal μHbO_2 ranged from 78% to 96% and varied only minimally (CV: 4–7.5%), whereas there was a marked variability in flow measurements (CV: 29–63.9%). The reproducibility of buccal mucosal μHbO_2 and flow measurements were moderate to good (that is, intra-individual reliability, ICC: range 0.7–0.87, $P < 0.05$). However, only measurements from the superficial mucosal layers showed a moderate to good degree of inter-individual agreement (that is, inter-individual reliability, ICC: range 0.68–85, $P < 0.001$). LDF and VLS values measured on the thenar eminence were highly variable, were not reproducible, and the inter-individual agreement was poor.
Conclusion O_2C® provides reliable measurement of buccal μHbO_2 and microvascular flow. Skin measurements on the thenar eminence are highly variable and unreliable.

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Central venous pressure in a femoral access: a true evaluation?

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Introduction In patients with bad vascular access, the evaluation of central venous pressure (CVP) obtained in a femoral vein could be an alternative to the evaluation in central venous catheters (CVCs) located in internal jugular or subclavian veins.
Objective To compare CVP measurement obtained in two different locations (jugular or subclavian veins and femoral veins).
Setting A 16-bed medical–surgical ICU.
Materials and methods This study began about 2 years ago, and the CVP of 41 patients in our ICU were evaluated and compared. Each one of those 41 patients had a CVC in two different locations, one placed in the internal jugular or subclavian veins, and a second in a femoral vein. Simultaneous measurements of CVP were undertaken by two different operators, with a pressure transducer zero referenced at the mid-chest. Standard CVCs with similar features (20 cm length) were used. The patients with an intra-abdominal pressure (IAP) > 15 mmHg were excluded. The IAP was previously evaluated in all patients, using the method described by Sugrue and Hillman. A linear correlation analysis was performed, considering significance $P < 0.05$ and a correlation coefficient > 0.85.
Results Forty-one patients were studied, and four patients were excluded due to an IAP > 15 mmHg. The mean age was 63.7 ± 16.2 years, the ICU stay was 10.4 ± 3.5 days, the APACHE II score was 27.8 ± 6.7, and SAPS II was 55.8 ± 11.2. The mean CVP measured with jugular/subclavian access was 11.3 ± 4.5 mmHg, and in the femoral access was 11.8 ± 4.4 mmHg. The linear correlation between those measurements was 0.96, and $P < 0.007$.
Conclusion The CVP can be accurately measured in a femoral vein, using standard CVC, in patients with an IAP < 15 mmHg.

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Left ventricular volumes but not filling pressure are determinants of mortality in critically ill patients

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Introduction Transthoracic echocardiography (TTE) is gaining acceptance as a powerful diagnostic tool in critical illness. It can assess left ventricular (LV) volumes, as well as indices of ventricular filling pressure (including the ratio of mitral E velocity/mitral annular velocity [*E*/*E*′]). TTE evidence of raised filling pressure is associated with mortality following myocardial infarction but its prognostic value in critical illness is undefined. The aim of this study was to evaluate the prognostic significance of echocardiographic LV volumes and filling pressure in the critically ill.
Methods A consecutive group of 94 patients (66 males, mean ± SD age 61 ± 15 years) who had standard TTE supplemented by measurement of *E*/*E*′ in a tertiary referral ICU were enrolled. TTE was performed 5 ± 6 days after ICU admission. Severity of critical illness was assessed using APACHE III. Cox proportional hazards regression analysis was based on 28-day mortality from the date of echo with survivors censored on hospital discharge.
Results The mean APACHE III score was 72 ± 25. Hospital mortality was 33% ($n = 31$). Table 1 summarises correlates of 28-

day mortality. The independent predictors of mortality were APACHE III risk of hospital death (HR 1.3 (1.1–1.5), $P = 0.003$), and increased LV end systolic volume (HR 2.1 (1.2–3.7), $P = 0.007$). Indices of ventricular filling pressure (*E*/*E*′, left atrial area/volume) were not predictors of mortality.

Table 1 (abstract P278)

Variable	OR (95% CI)	*P*
APACHE III score (/10)	1.2 (1–1.4)	0.017
E/*E*′ (/10)	1.3 (0.6–2.8)	0.5
LV end diastolic volume (/100 ml)	2.0 (1.2–3.3)	0.0059
LV end systolic volume (/100 ml)	2.2 (1.3–3.8)	0.0047

Conclusion In this cohort of critically ill patients, increased echocardiographic LV end systolic volume, but not filling pressure, is a highly significant predictor of mortality that adds incremental value to APACHE III prediction.

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Prehospital echocardiography in pulseless electrical activity victims using portable, handheld ultrasound

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Objective Potentially treatable causes of sudden cardiac arrest, such as pericardial tamponade, myocardial insufficiency or hypovolemia, should be identified as soon as possible (that is, at the scene). Although these diagnoses are mainly made by echocardiography, old and new ERC or ILCOR guidelines only recommend pauses of ventilation or chest compressions as 'brief interruptions' at a maximum of 10 seconds, thereby potentially limiting transthoracic ultrasound examinations. We introduced an ALS-based algorithm of focused echocardiographic evaluation during resuscitation (FEER) to be performed in a time-sensitive manner.
Methods We tested both the capability of FEER to differentiate states of pulseless electrical activity, and its feasibility in the out-of-hospital setting using mobile, battery-powered ultrasound systems. Trained emergency physicians (EP) applied FEER to assessing basic ventricular function by 'eye-balling' in less than 10 seconds in prehospital cardiac arrest victims who were being resuscitated. True pulseless electrical activity (PEA) was defined according to the ERC as 'clinical absence of cardiac output despite electrical activity'. In contrast, any PEA was classified as a 'pseudo-PEA' when cardiac output was visualized by echocardiography.
Results Seventy-eight CPR cases (age 66 ± 19 years) were included. On arrival of the EP on the scene, a true PEA was suspected in 31/78 cases. However, in 20/31 PEA cases cardiac wall movement was detected (pseudo-PEA) and correctable causes such as pericardial tamponade (four cases), poor ventricular function (14 cases) and hypovolemia (two cases) were treated. Fourteen out of 20 pseudo-PEA cases survived to hospital admission. In 11/30 PEA cases, no cardiac wall movement was visible (true PEA). All such patients died on the scene. FEER-based changes in therapy were induced in 25/31 cases.
Conclusions Application of FEER was feasible within a 10-second time-frame of CPR interruptions. While differentiating PEA states, FEER has the ability to identify a pseudo-PEA state, allowing further treatment of the underlying disorder on the scene to improve outcome.

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The effectiveness of transthoracic echocardiography as a screening examination in a noncoronary intensive care unit

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Introduction The authors tested the feasibility of transthoracic echocardiography (TTE) as a routine technique in a medical/surgical ICU.
Methods The study was carried out in a 16-bed noncoronary ICU during 18 months. For this purpose, a TTE was performed within the first 24 hours of admission. The issues addressed were: data acquisition possibilities, quantification of selected echocardiographic parameters (cardiac chamber dimensions, left ventricular function, cardiac output, and Doppler examination), detection of any structural echocardiographic alteration, as well as new severe conditions.
Results In this study 704 consecutive patients were enrolled, with a mean age of 61.5 ± 17.5 years, an ICU stay of 10.6 ± 17.1 days, APACHE II score of 22.6 ± 8.9, and SAPS II of 52.7 ± 20.4. In four patients TTE could not be performed. The data are presented in Table 1. At least an echocardiographic alteration was detected in 234 (33%) patients. The most common alterations were left atrial enlargement ($n = 163$), and left ventricular dysfunction ($n = 132$). Patients with these alterations were older (66 ± 16.5 vs 58.1 ± 17.4 years, $P < 0.001$), presented a higher APACHE II score (24.4 ± 8.7 vs 21.1 ± 8.9, $P < 0.001$) and a higher mortality (40.1 vs 25.4%, $P < 0.001$). Severe previously unknown echocardiographic diagnoses were detected in 53 (7.5%) patients. The most frequent condition was severe left ventricular dysfunction. By multivariate logistic regression analysis, TTE parameters did not correlate with mortality or ICU stay. Mortality was related to ICU stay (CI 1.0–1.019, $P < 0.001$).

Table 1 (abstract P280)

Chamber	689
Left ventricular function	670
Inferior vena cava	571
Mitral E/A	399
Isovolumetric relaxation time	569
Tricuspid regurgitation	291
Cardiac output	610
All patients	704

Conclusion We conclude that TTE is feasible in a noncoronary ICU, most parameters being obtained. A routine utilization of TTE detected 53 (7.5%) patients with severe unsuspected diseases.

P281

Identification of contractility abnormalities in intensive care unit patients with sepsis using tissue Doppler imaging

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Introduction Tissue Doppler imaging (TDI), as a more recent ultrasound technique, is a precious diagnostic tool revealing earlier

left ventricular (LV) contractility abnormalities as compared with the conventional echocardiography. This study aimed at assessing the contribution of TDI to the early diagnosis of LV systolic dysfunction in ICU septic patients maintaining a normal ejection fraction (EF).
Methods Twenty-two ICU patients of average age 57.6 ± 7.3 years (13 males) (Group A) and 20 seemingly healthy individuals (Group B) were studied. The ICU patients met the sepsis criteria (infection by Gram-negative bacterium and, at least, two of the SIRS criteria). The APACHE II score mean value was 21.2 ± 4.9. All the patients of the study were subjected to the same session in a 2D echocardiogram. The EF of the left ventricle was calculated according to Simpson's method. The systolic velocities on the long axis were measured by TDI, placing the sample volume 0.5 cm distance from the mitral annular in the basic posterior interventricular septum (Sm) and on the lateral wall (Sl). Patients with ischemic, dilated, hypertrophic cardiomyopathy, severe valvular disease, uncontrolled blood pressure and chronic atrial fibrillation were excluded.
Results No differences were observed in the LV systolic performance by use of the conventional 2D echocardiography between the two groups (EF: 63.8 ± 3.7% in Group A as compared with 64 ± 4.8% in Group B, P = not significant). Nevertheless, differences were ascertained in the maximum systolic velocities on the long axis using TDI. Sm: 8.2 ± 1.1 m/s in Group A, 9.7 ± 1 m/s in Group B ($P = 0.04$), Sl: 10.6 ± 1.3 m/s in Group A, 13.6 ± 1.4 m/s in Group B ($P = 0.02$).
Conclusion TDI echocardiography identifies LV contractility abnormalities in ICU septic patients that appear to have a normal EF in the conventional echocardiogram, so it provides earlier recognition and treatment of LV dysfunction related to sepsis.

P282

Determination of intravascular volume status in critically ill patients using portable chest X-rays: measurement of the vascular pedicle width

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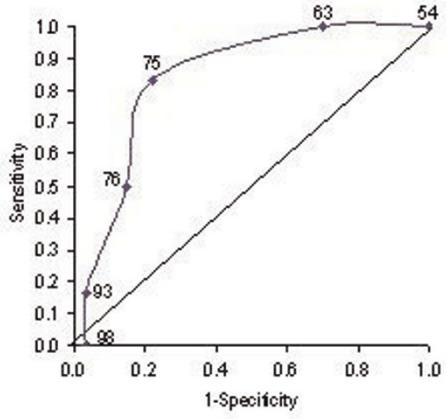
Introduction Traditionally invasive haemodynamic measurements of pulmonary artery occlusion pressures have been used to assess the volume status in critically ill patients. The vascular pedicle, as seen on chest X-ray scan, is the mediastinal silhouette of the great vessels. We hypothesized that the vascular pedicle width (VPW) on supine, portable chest X-ray scans could be used to predict intravascular volume overloaded status in critically ill patients.
Methods We conducted a prospective, blinded observational trial where both pulmonary artery occlusion pressures (PAOP) and VPWs were measured in patients admitted to the ICU. We used measurements of PAOP ≥ 18 mmHg as indicative of a fluid overloaded state, and measurements of PAOP < 18 mmHg as normal or low volume states. Standardized, portable chest X-ray scans in the supine position were obtained within 1 hour of PAOP measurement. Receiver-operating characteristics (ROC) curves were constructed using different cutoffs of the VPW measurement to identify sensitivities and specificities for each value (see Figure 1).
Results Measurements were obtained from 50 patients. Using ROC-derived cutoffs, a VPW measurement of 74.5 mm was found to have a sensitivity of 83% and a specificity of 78% for correctly predicting a fluid overloaded state.
Conclusions These results suggest that serial measurements of the VPW can reliably be used to predict intravascular volume overload in the ICU.

Figure 1 (abstract P282)



Receiver-operating characteristics curve for vascular pedicle width. The curve shows the ability of the vascular pedicle width to differentiate between fluid overload and euvolemia at different cutoff points. The area under the curve is 0.724. Increased vascular volume is defined as pulmonary artery occlusion pressure ≥ 18 mmHg.

P283

The role of clinical examination, chest X-ray and central venous pressure in volume assessment in critically ill patients: a comparison with PiCCO-derived data

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Background Assessment of preload and goal-directed resuscitation are crucial parts of ICU therapy. To assess preload, clinical parameters such as filling of the jugular veins, edema and pleural effusions as well as X-ray are used. In addition, haemodynamic parameters such as the central venous pressure (CVP), pulmonary arterial wedge pressure and PiCCO-derived global end-diastolic volume index (GEDVI) are determined. The GEDVI has been shown to be superior to pressure-based parameters with regard to volume responsiveness in several studies. However, PiCCO data are not available in all patients, and frequently clinical examination, CVP and chest X-ray are the first tools for preload assessment. It was the aim of our study to evaluate clinical assessment, X-ray and CVP with regard to the GEDVI and extravascular lung water index (ELWI).
Methods In 86 patients of an internal ICU, clinical examination was independently determined by a physician and investigator not working in the ICU. Subsequently, chest X-ray (analysed by an experienced radiologist), CVP and PiCCO (Pulsion Company, Munich, Germany) measurements were performed and these data were correlated to clinical findings.
Results Patients (n = 86; 34 females, 52 males) included 25 patients with cirrhosis, 18 patients with pancreatitis, 19 patients with sepsis; age 63.0 ± 15.5 years; APACHE II score 23.3 ± 8.4. Leg edema significantly correlated to CVP ($r = 0.247$; $P = 0.038$) and (negatively) to GEDVI ($r = -0.258$; $P = 0.032$). CVP and GEDVI were not associated: $r = 0.035$; $P = 0.784$. The ELWI significantly correlated to the degree of rales ($r = 0.258$; $P = 0.016$) and GEDVI ($r = 0.557$; $P < 0.001$). The ELWI and CVP did not correlate ($r = 0.030$; $P = 0.785$). Global clinical preload assess-

ment (scale 1–10) was not predictive for GEDVI. Radiological assessment significantly overestimated the GEDVI (901.41 ± 139.76 vs 782.56 ± 183.80 ml/m^2; $P < 0.001$) and underestimated the ELWI (7.22 ± 1.38 vs 9.77 ± 4.51 ml/kg; $P < 0.001$).

Conclusions (1) Leg edema and increased CVP do not exclude preload deficiency determined by the GEDVI, which was overestimated by X-ray. (2) CVP and leg edema are poor predictors of the ELWI, which was significantly associated with audible rales but underestimated by X-ray.

P284

Clinicians' prediction of advanced cardiopulmonary variables in critically ill patients: a multicenter study

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Introduction Lack of evidence that more advanced monitoring techniques improve outcome may have led to insufficient monitoring of critically ill patients. However, clinical judgment and conventional hemodynamic monitoring alone were shown to be inadequate for a reliable estimate of hemodynamic status. We have therefore compared clinicians' prediction of advanced cardiopulmonary parameters with actual measurements.

Methods Cardiopulmonary assessment was done in critically ill patients from 12 European ICUs just before the use of the PiCCO monitor (Pulsion, Germany). Independent prediction of cardiac output (CO), systemic vascular resistance (SVR), indexed global end-diastolic volume (GEDVi), stroke volume variation (SVV), and indexed extravascular lung water (EVLWi) was done by one to four physicians per patient. Following the first set of PiCCO measurements each physician self-rated the accuracy of his pre-PiCCO predictions.

Results A total of 257 questionnaires of 165 patients (67 females and 98 males, age 59.8 ± 16.7 (range 16–93) years) were completed by 135 residents and 122 specialists. The main reasons for using the PiCCO included unclear fluid status (109 cases), sepsis/septic shock (70 cases), respiratory failure (42 cases), cardiogenic shock (19 cases), renal failure (27 cases), and other (18 cases). Only 30–50% of the predicted values were correct (±20% of measured values) (Table 1). Ranges of errors were: CO (–77/+100%), SVR (–94/+303%), GEDVi (–88/+135%), SVV (–91/+367%), EVLWi (–76/+650%). There was a significant underestimation of CO ($P < 0.00001$) and GEDVi ($P < 0.0003$), and overestimation of SVR ($P < 0.003$) and SVV ($P < 0.0002$).

The 240 self-ratings (scale of 1–5, [1] = excellent; [5] = poor) of predictions accuracy included – [1] 1.6%, [2] 40%, [3] 38.8%, [4] 15.1%, [5] 4.5%. The mean self-rate was 2.8 ± 0.9, with that of residents (2.8 ± 0.9, $n = 129$) being similar to that of specialists (2.7 ± 0.8, $n = 111$), $P < 0.31$.

Conclusions The ability of physicians to predict advanced cardiopulmonary parameters based on clinical evaluation and conventional monitoring alone has considerable limitations and is not improved by experience.

Acknowledgement The authors of this unsupported study are members of Pulsion's medical advisory board.

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Change of therapeutic plan following advanced cardiopulmonary monitoring in critically ill patients: a multicenter study

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Introduction Many therapeutic decisions are made in the ICU on the basis of clinical judgment and conventional monitoring alone, although these may be inadequate for a reliable estimate of hemodynamic status. We therefore measured the effects of more advanced cardiopulmonary parameters (ACP) on major therapeutic decisions.

Methods Cardiopulmonary assessment was done in critically ill patients from 12 European ICUs independently by one to four physicians per patient just before the use of the PiCCO monitor (Pulsion, Germany). Following cardiopulmonary evaluation and prediction of ACP (reported elsewhere), each physician suggested a therapeutic plan before and after the first set of PiCCO measurements (cardiac output, systemic vascular resistance, global end-diastolic volume, stroke volume variation, and extravascular lung water), and then self-rated the accuracy of his original therapeutic plan.

Results A total of 257 questionnaires of 165 patients (67 females and 98 males, age ± SD 59.8 ± 16.7 (range 16–93) years) were completed by 135 residents and 122 specialists. The main reasons for using the PiCCO included unclear fluid status (109 cases), sepsis/septic shock (70 cases), respiratory failure (42 cases), cardiogenic shock (19 cases), renal failure (27 cases), other (18 cases). Changes (plan-and-not-give and no-plan-and-give) made in the pre-PiCCO therapeutic plans included: fluid, 31.8%; inotropes, 23.3%; vasoconstrictors, 23.5%; diuretics, 15% (Table 1). The 240 overall self-ratings of the original plan (scale of 1–5, [1] = not different; [5] = very different) included – [1] 33.7%, [2] 23.5%, [3] 25.9%, [4] 11.5%, [5] 5.3%. The mean self-rate was 2.3 ± 1.2, with that of residents (2.3 ± 1.3, $n = 129$) being similar to that of specialists (2.3 ± 1.1, $n = 111$), $P < 0.88$.

Table 1 (abstract P284)

	EVLWi	%	CO	%	SVR	%	GEDVi	%	SVV	%
Under	69	29.4	127*	49.6	46	18.1	72	28	85	39.7
Correct	93	39.6	99	38.6	90	35.4	93	50.2	64	29.9
Over	73	31.1	30	11.7	116	45.7	73	21	65	30.4

*Number of predictions.

Table 1 (abstract P285)

	Given	%	Not given	%
Fluid P	109	43	53	21
Fluid NP	28	11	65	25
Inotropes P	33	13	46	18
Inotropes NP	14	5	164	64
Vasoconstrictors P	50	20	36	14
Vasoconstrictors NP	24	9	143	57
Diuretics P	19	7	20	8
Diuretics NP	18	7	197	78

P = planned; NP = not planned.

Conclusions The measurement of advanced cardiopulmonary parameters caused both specialists and residents to make considerable changes in therapeutic decisions that were previously made based on clinical judgment and conventional monitoring alone.

Acknowledgement The authors of this unsupported study are members of Pulsion's medical advisory board.

P286

Assessment of extravascular lung water and pulmonary vascular permeability evaluated by the pulse contour cardiac output in systemic inflammatory response syndrome patients

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Introduction Pulse contour cardiac output (PiCCO) provides an estimate of the intrathoracic blood volume (ITBV), extravascular lung water (EVLW), and pulmonary vascular permeability index (PVPI). Few investigations have prospectively examined EVLW in patients with severe sepsis or ARDS.

Objective The aim of this study was compare measurements of ITBV, EVLW, and PVPI in systemic inflammatory response syndrome (SIRS) patients.

Materials and methods Twenty-eight adult patients with SIRS admitted to our ICU were studied in three groups. Group A, nine patients with pneumonia; group B, nine patients with extrathoracic infection; group C, 10 patients without infection were enrolled. In each patient, PiCCO was used to measure the ITBV and EVLW for 3 days of meeting criteria for SIRS. The PVPI was calculated as the ratio of EVLW to ITBV. EVLW values were indexed by the predicted body weight and ITBV values were indexed by the predicted body surface. All data are presented as mean ± standard deviation. The Kruskal–Wallis H test was performed for statistical analysis and $P < 0.05$ was considered statistically significant.

Results See Table 1. One hundred and forty samples of data were collected. The mean PVPI value was within the normal range. The EVLWI and PVPI were significantly higher in group A than in group B. The EVLWI and PVPI were significantly higher in group B than in group C too.

Table 1 (abstract P286)

	Group A	Group B	Group C
ITBVI	933 ± 256	977 ± 197	996 ± 407
EVLWI	12 ± 5	10 ± 4*	8 ± 3*,**
PVPI	2.3 ± 1.1	1.8 ± 0.8*	1.6 ± 0.7*,**

*$P < 0.05$ vs group A. **$P < 0.05$ vs group A and group B.

Conclusion Our data indicate that the permeability of pulmonary vessels is increased more with infection than without infection, and is also higher with pneumonia than with extrathoracic infection in SIRS patients.

P287

Fluid status assessment in mechanically ventilated septic patients

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Background Early optimization of fluid status is of major importance in the treatment of critically ill patients. It is unclear whether sonographic measurement of the inferior vena cava (IVC) diameter is valuable in the evaluation of fluid status in mechanically ventilated septic patients.

Methods Thirty mechanically ventilated patients with severe sepsis or septic shock (age 59.9 ± 15.4 years; APACHE II score 30.6 ± 7.7; 18 males) requiring advanced invasive hemodynamic monitoring due to cardiovascular instability were included in a prospective observational study in a university hospital setting with a 24-bed medical ICU and a 14-bed anaesthesiological ICU. Volume-based hemodynamic parameters were determined using the thermal-dye transpulmonary dilution technique. Simultaneously, the IVC diameter was measured throughout the respiratory cycle by trans-abdominal ultrasonography.

Results We found a statistically significant correlation of both inspiratory and expiratory IVC diameter with central venous pressure ($P = 0.004$ and $P = 0.001$), extravascular lung water index ($P = 0.001$ and $P < 0.001$), intrathoracic blood volume index ($P = 0.026$ and $P = 0.05$), the intrathoracic thermal volume (both $P < 0.001$), and the paO_2/FiO_2 oxygenation index ($P = 0.007$ and $P = 0.008$, respectively).

Conclusions Sonographic determination of the IVC diameter is useful in the assessment of volume status in mechanically ventilated septic patients. This approach is rapidly available, noninvasive, inexpensive, easy to learn and applicable in almost any clinical situation without doing harm. IVC sonography may contribute to a faster, more goal-oriented optimization of fluid status and may help to identify patients in whom deleterious volume expansion should be avoided. It remains to be elucidated whether this approach influences the outcome of septic patients.

P288

Noninvasive cardiac output: accuracy between the ultrasound cardiac output monitor and the esophageal Doppler monitor

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Introduction The hypothesis is that measurement of the cardiac index (CI) is accurate between the ultrasound cardiac output monitor (USCOM) and the esophageal Doppler monitor (EDM). The EDM is a minimally invasive device that has demonstrated strong correlation with cardiac output measurements obtained by thermodilution. A disadvantage of the EDM is the need for probe placement in the esophagus, effectively limiting its use to

mechanically ventilated patients. The USCOM, in contrast, can measure cardiac hemodynamics by use of a CW Doppler probe placed on the skin to measure blood flow across either the aortic or pulmonic valve.

Methods A prospective study of adult ED patients who were intubated and managed concurrently with an EDM. Setting: urban tertiary care center with >90,000 annual visits. Exclusion criteria: ESRD, ascites, known valvular heart disease and pre-existing tracheotomy. IRB approval was obtained with waiver of informed consent. USCOM measurements of CI were obtained, blinded to EDM values measured concurrently. Repeated pairs were obtained every 30–60 minutes, in a similar manner. Statistical analysis: correlation and Bland–Altman plots using SPSS 9.0.

Results A total of 95 paired measures were obtained from 20 patients with an average age of 60.1 years, 60% male and 70% African American. The mean CI was 5.2 with a range of 1.4–6.6 l/min/m^2. For the aggregate, $r = 0.81$ ($P < 0.001$) and bias was 0.14 with limits of agreement (LOA) of −1.48 to 1.76. Excess scatter was noted at CI > 4.0 CI. For CI < 4.0, correlation was 0.80 ($P < 0.001$) with bias and LOA of −0.15 and −1.01 to 0.71. At CI < 2.5, greater accuracy was noted with bias of 0.01 and LOA of 0.73 to 0.75.

Conclusions CI measurement with the USCOM has a high degree of agreement with the EDM, most notably when CI is below 4.0. Of particular interest is the high degree of accuracy seen at low CI values (<2.5). These findings support the use of the USCOM for CI measurement in mechanically ventilated patients and a wider range of patients in which the EDM would be impractical or difficult to use.

P289

Noninvasive cardiac output monitoring: a clinical validation

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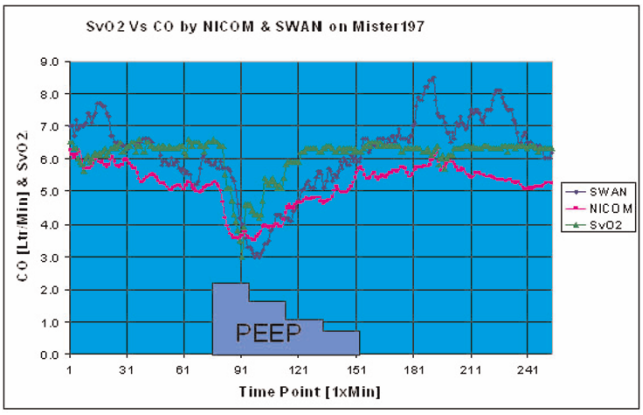
Introduction Our objective was to evaluate the clinical utility of noninvasive cardiac output monitoring (NICOM), a new tool for automatic continuous cardiac output (CO) monitoring based on chest bioreactance, using continuous thermodilution as reference (PAC-CCO).

Method We included 110 consecutive adult patients immediately after cardiac surgery in a prospective, single-center study taking place in the ICU. CO measurements obtained from NICOM and PAC-CCO were simultaneously recorded minute by minute (Figure 1). We evaluated the accuracy, precision, responsiveness, and reliability of NICOM for detecting CO changes. Tolerance for each of these parameters was specified prospectively.

Results A total of 65,888 pairs of CO measurements were collected. Mean reference values for PAC-CCO ranged from 2.79 to 9.27 l/min. During periods of stable PAC-CCO (slope < ±10%, 2SD/mean <20%), the correlation between NICOM and PAC-CCO was $R = 0.82$; bias was +0.16 ± 0.52 l/min (+4.0 ± 11.3%), and the relative error was 9.1 ± 7.8%. In 85% of patients the relative error was <20%. During periods of increasing CO, slopes were similar with the two methods in 96% of patients and intraclass correlation was positive in 96%. Corresponding values during periods of decreasing CO were 90% and 84%, respectively. Precision was always better with NICOM than with PAC-CCO. During hemodynamic challenges, changes were 3.1 ± 3.8 minutes faster with NICOM ($P < 0.01$) and amplitude of changes were not different (not significant). Finally, sensitivity of the NICOM for detecting significant directional changes was 93% and specificity was 93%.

Figure 1 (abstract P289)



Mixed venous hemoglobin oxygen saturation (SvO_2) vs cardiac output (CO) by noninvasive cardiac output monitoring and Swan on Mister197.

Conclusion CO measured by NICOM had most often acceptable accuracy, precision, and responsiveness in a wide range of circulatory situations.

P290

Method comparison – a new approach to implementing the Bland–Altman analysis to estimate the precision of a new method: tested on 30 critically ill patients monitored with pulse pressure analysis and continuous cardiac output vs intermittent thermodilution

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Introduction The Bland–Altman plot is the standard way of determining agreement between two methods of measuring the same variable. Following work by Critchley and Critchley [1], ±30% is now accepted as the cutoff point when calculating the percentage error. This study estimates the coefficient of variation (CV) of three different cardiac output (CO) techniques with the aim of assessing the relative contributions to the percentage error.

Materials and methods Thirty critically ill patients had their CO measured every hour with continuous cardiac output by Vigilance (CCO), pulse pressure analysis by LiDCO™plus (PulseCO) and intermittent thermodilution (ITD) (average of four ITD curves). Data were analysed with Bland–Altman plots, calculation of the percentage error, determination of the CV of ITD, and calculation of the overall CV for CCO and PulseCO.

Results Two hundred and forty (eight per patient) measurements of CO were obtained. CCO vs ITD had an overall bias (±2SD) of 0.2 ± 2.4 l/min (error 31%), mean CO (ITD + CCO) 7.7 l/min. PulseCO vs ITD had an overall bias of −0.1 ± 2.4 l/min, mean CO (PulseCO + ITD) 7.5 l/min (error 33%). According to the above criteria (without measuring the CV for ITD), CCO performed well when compared with ITD (31%) but PulseCO (33%) was outside clinically acceptable levels of agreement. The CV for a single ITD CO measurement was 15%, and this decreased to 7.5% when averaging four thermodilution curves. Using the CV for ITD of 7.5%, the relative CVs for the CCO and PulseCO were

determined. The CV for CCO was 13.6% and for PulseCO was 14.7%.

Conclusions In trying to understand the relative contributions of error when testing two techniques to measure the same variable it is vital to understand the CV of the reference technique. Using this approach, both the PulseCO and Vigilance perform in a clinically acceptable fashion.

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P291

Comparison of vascular pedicle width and PiCCO-derived haemodynamic measurements in patients in a general intensive care unit

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Introduction Assessing clinically the intravascular volume status of critically ill patients can be exceedingly difficult. Due to concerns about the efficacy and safety (possible increase in mortality) of using invasive haemodynamic monitoring, noninvasive diagnostic testing has gained increasing importance.

Objective To compare the reliability of vascular pedicle width (VPW) as an indicator of overload, in patients of a general ICU, with a method of invasive haemodynamic monitoring that has proved its efficacy in the literature and in everyday practice.

Patients and methods The VPW, which represents the mediastinal silhouette of the great vessels, was compared with the haemodynamic measurements, which were obtained with the method of transpulmonary thermodilution (PiCCO Plus; Pulsion, Munich, Germany). We measured the VPW in anteroposterior chest X-rays in the supine position, with standard parameters, in 100 patients without prior cardiac surgery, prior mediastinal irradiation, obesity, severe acute respiratory distress syndrome and positive end-expiratory pressure > 7.5 cmH_2O. In every patient we performed invasive haemodynamic monitoring with the PiCCO Plus. An intrathoracic blood volume index (ITBI) > 1,000 ml/m^2, global end-diastolic index (GEDI) > 800 ml/m^2, and extravascular lung water index (ELWI) > 7.0 ml/kg were considered the markers of significant volume overload. After further refinement, 27 patients fulfilled the above criteria and were considered eligible to be included in the study.

Results The mean VPW in overloaded patients was 75.14 mm compared with a mean of 64.71 mm for the rest. The results were subsequently analyzed using Spearman's nonparametric test and we found correlation (0.785, 0.710, and 0.510) between VPW and the GEDI, ITBI, and ELWI, respectively. The results were considered statistically significant ($P < 0.000$, $P < 0.000$, and $P < 0.005$, respectively).

Conclusion The VPW, when appropriately assessed at the bedside by the same physician and therefore avoiding the possible bias, using portable chest X-rays, might give very useful information regarding the volume status of the patients, results that are comparable in their efficacy with those obtained with invasive and more expensive methods.

P292

Reliability of the continuous cardiac index measurement using the pulse contour analysis of the PiCCO system

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Critical Care 2007, **11(Suppl 2):**P292 (doi: 10.1186/cc5452)

Introduction Reliable continuous hemodynamic monitoring of critically ill patients is essential for effective volume management and adequate administration of vasoactive drugs. The PiCCO system allows continuous measurement of the cardiac index using arterial pulse contour analysis. Calibration of this system by transpulmonary thermodilution is recommended every 8 hours. In this study we compared the difference of the continuous measurement of the cardiac index using the arterial pulse contour analysis (CIpc) with the cardiac index acquired by the transpulmonary thermodilution (CItd) when calibrating the system.

Methods Our study includes 140 measurements in 10 critically ill patients (eight males, two females, age 37–84 years, mean 64.1 ± 13.0 years) requiring hemodynamic monitoring with the PiCCO system. Five patients had septic shock, three hepatorenal syndrome and two acute heart failure. First the CIpc was recorded immediately before the next calibration and afterwards the CItd was measured three times, which resulted in a simultaneous calibration of the pulse contour algorithm of the PiCCO system. We performed a mean of 14 ± 9.4 measurements per patient. The time-lag between the measurements was 12 hours 54 minutes ± 7 hours 47 minutes.

Results The comparison of the CIpc immediately before calibration and the calibration-derived CItd resulted in a correlation coefficient of 0.84 with a P value of 0.02. In the Bland–Altman analysis the CIpc was a mean 0.14 l/min/m^2 lower than the CItd. The standard deviation was 0.72 l/min/m^2. There was no correlation of the time-lag between the calibrations and the difference of CIpc and CItd ($r = -0.03$; $P = 0.13$).

Conclusion The PiCCO system allows a reliable continuous measurement of the cardiac index using the pulse contour analysis. In our study we could not find an increased difference of CIpc and CItd even with longer time periods between the calibrations using transpulmonary thermodilution. Because calibration is easy to achieve and additional data for the intrathoracic blood volume and the extravascular lung water are obtained, a 12-hour period between the calibrations is reasonable.

P293

PiCCO monitoring – are two injections enough?

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Critical Care 2007, **11(Suppl 2):**P293 (doi: 10.1186/cc5453)

Introduction PiCCO monitoring using the thermodilution technique has become an alternative method of invasive haemodynamic monitoring for the critically ill patient. Usually the results of an arbitrarily chosen number (one to five) of thermal indicator injections are averaged to increase the reliability of the measurement. The number of injections needed to achieve a given level of precision has, however, not previously been systematically investigated. We tried in this study to validate the accuracy of two injections instead of three injections.

Methods We analysed retrospectively all data (triplate measurements) obtained during the past 2 years by PiCCO monitoring: injection of 10 ml saline solution three times by the same operator.

We compared the cardiac index (CI) obtained at each bolus, the average of the CI obtained at the first two injections (M1) and then the triplate (M2).
Results Two hundred and forty-nine triplates were collected in 25 patients with septic shock, under mechanical ventilation. There were no significant differences in CI at each bolus. The average of the first two iced injections M1 = 3.28 ± 1.07 l/min/m^2. The average of the triplate M2 = 5.74 ± 1.07.
Discussion Normally, we consider that 10–15% of variation in the CI signifies a change in the haemodynamic state. The difference between M1 and M2 exceeds 15%. In the literature, Nilsson and colleagues [1] demonstrated concerning the pulmonary arterial catheter that we need an average of at least four injections to be 95% confident.
Conclusion With PiCCO monitoring, certainly two injections are not enough to have reliable measurement of the CI.
Reference
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P294

Lithium dilution cardiac output measurement in the critically ill patient: determination of precision of the technique

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Introduction Pulmonary intermittent thermodilution (from the pulmonary artery catheter), transpulmonary thermodilution (PiCCOplus; Pulsion, Munich, Germany) and transpulmonary lithium dilution (LiDCO™plus; LiDCO, Cambridge, UK) are all well-validated techniques in common use in intensive care for cardiac output estimation. The precision has been looked into previously and strategies to improve it have been made (that is, averaging three or four measurements over the respiratory cycle) yet not much is known about the precision of transpulmonary techniques in terms of repeatability. This study aims to look into the coefficient of variation (CV) of the lithium dilution technique in a mixed (medical/surgical) intensive care population and propose a method to improve its precision.
Materials and methods We performed four consecutive lithium dilution cardiac output determinations on 70 critically ill patients requiring haemodynamic monitoring. The heart rate (HR), central venous pressure (CVP) and mean arterial pressure (mAP) were documented in conjunction with cardiac output estimation. Data were excluded if a ±5% change in HR, CVP or mAP occurred during the sequential measurements. The CV ((SD/mean cardiac output) x 100) was calculated for single measurements and for the average of repeated measurements. In order to clinically accept the precision of the technique, we aimed to obtain a CV below 10%.
Results Sixty-five series were suitable for analysis. The CV showed a normal distribution and no correlation with the magnitude of the mean cardiac output. The mean CV for single lithium dilution was 12.3%. The CV for the average of *n* lithium dilutions was 8.6% for *n* = 2, 7.1% for *n* = 3, 6.1% for *n* = 4.
Conclusions The CV for one lithium dilution was higher than clinically acceptable (12.3 > 10%). The average of two lithium dilution measurements improves the precision by 30% and shows an excellent CV (that is, 8.6%). When measuring cardiac output with LiDCO an average of two lithium dilution curves provide an excellent precision, and we suggest that in this population (medical/surgical) this approach should always be used when calibrating the pulse pressure algorithm (PulseCO) at the baseline.

P295

Transpulmonary lithium indicator dilution: a new method of intrathoracic blood volume measurement

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Introduction Extravascular lung water (EVLW) measurement may improve outcome. Double indicator dilution, which is the most accurate method of EVLW measurement, is no longer commercially available. Lithium indicator dilution could be used to measure the intrathoracic blood volume index (ITBVI) and therefore EVLW.
Method A single-centre, observational study. Consent was sought from patients aged over 50 years undergoing elective cardiac surgery with cardiopulmonary bypass (CPB). Exclusion criteria included significant valvular regurgitation and lithium therapy. Anaesthetic, CPB, blood transfusion, ventilation and sedation practices were standardised. Indicator dilution measurements were performed following induction of anaesthesia, after CPB and then 2, 4 and 24 hours following surgery, using existing technology (LiDCO Ltd, London, UK). Data are presented as the median (IQR).
Results Twenty patients were recruited (age 70 years (64–75 years); Parsonnet score 10 (1–14)). No difficulties were encountered with the new method of ITBVI measurement. Absolute values and the changes in the ITBVI were close to those anticipated. Linear regression analysis did not indicate mathematical coupling between the cardiac index (CI) and the ITBVI (R^2 = 0.22; $P < 0.001$). The relationship between the pulmonary blood volume index (PBVI) and the ITBVI was not constant.
Conclusion Lithium indicator dilution may be a valuable new method of ITBVI measurement, and therefore EVLW measurement.

Table 1 (abstract P295)

	Time				
	Preoperative	Post-CPB	2 hours postoperatively	4 hours postoperatively	24 hours postoperatively
ITBVI (ml/m^2) (*n* = 20)	739 (612–969)	1,078 (815–1,262)	1,266 (1,031–1,433)	1,188 (947–1,343)	1,008 (738–1,257)
PBVI (ml/m^2) (*n* = 16)	213 (201–279)	343 (307–371)	338 (288–449)	394 (305–545)	407 (267–464)
CI (l/min/m^2) (*n* = 20)	1.92 (0.45)	1.81 (0.42)	2.03 (0.56)	2.20 (0.58)	2.28 (0.94)

P296

Comparison between uncalibrated cardiac output using the femoral and radial arterial pressure waveform in critically ill patients

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Introduction Cardiac output (CO) monitoring is often required to manage critically ill patients. Nominal values can be determined from analysis of arterial pressure waveforms. It is assumed that arterial waveforms from different arterial sites give similar CO values. The aim of this study was to compare the values of uncalibrated CO derived from simultaneous radial (COr) and femoral (COf) blood pressures.
Methods We enrolled 17 medical and surgical ICU patients, requiring haemodynamic monitoring and vasoactive drugs. Simultaneous recordings of the arterial radial and femoral waveforms were made from arterial pressure monitors via an A–D converter and analysed to obtain CO values using the PulseCO® algorithm of the LiDCOplus (LiDCO, London, UK). Paired CO values were selected at several points on each recording. Calibrations were not done at each time point so the comparison required examination of the ratio of uncalibrated COr and COf.
Results The median value of the CO ratio was 0.95 (IQR 0.88–1.02), with a high variability across the patients, ranging from 0.3 to 1.41, whereas intrapatient variability was low, with a median CV of 3.26% (IQR 1.1–5.3%). Although the ratio in COs between the two sites varied greatly, the difference between the median (range) arterial pressures was 2 mmHg (–3 to 8 mmHg). However, the pulse pressure difference between the two sites was generally large with a median (range) of 2 mmHg (–26 to 44 mmHg).
Conclusions CO derived from blood pressure records at radial and femoral sites can appear similar when a patient population as a whole is considered. However, in individual patients, the difference between the two sites is large enough to be clinically unacceptable without a site-specific recalibration.

P297

Measurement of intrathoracic blood volume by lithium dilution: comparison with thermodilution

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Introduction The intrathoracic blood volume is usually measured clinically by transpulmonary thermodilution (PiCCO system; Pulsion Ltd). New software also allows measurement at the bedside by lithium dilution (LiDCO system; LiDCO Ltd). We sought to compare the new lithium dilution method with the existing method.
Methods Ethics approval was obtained. Nonpregnant adult patients on the ICU with PiCCO monitoring were recruited. Consent was given by patients' representatives. Simultaneous calibration of PiCCO and LiDCO systems with one lithium dilution curve and the average of three thermal dilution curves allowed comparison of results.
Results Six patients were studied (five males, one female). All were intubated but none were receiving muscle relaxation. Mean age was 60.6 ± 21.8 years. The mean APACHE II score was 20.8 ± 2.3. Ten paired results were obtained (see Table 1). The mean difference of LiDCO from PiCCO overall was –5.49 ± 21.3%. The correlation coefficient $r = 0.73$ ($P = 0.0166$).
Conclusion There was general agreement between LiDCO and PiCCO. There were significant differences (>30%) in only three out of 10 measurements. Combining the results of >1 lithium calibration may improve accuracy. These results are promising but a larger trial will be required.

Table 1 (abstract P297)

Patient	ItbiP	ItbiL	Difference (%)
1	894	960	7.4
2a	1,517	1,990	31
2b	1,572	1,078	–31.4
3	1,069	724	–32.3
4	1,280	1,318	3.0
5a	1,478	1,213	–17.9
5b	1,324	1,058	–20.1
5c	1,429	1,797	25.8
6a	732	731	–0.01
6b	787	627	–20.3

P298

Impedance cardiography to assess hemodynamic status: a comparison with transpulmonary thermodilution

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Critical Care 2007, **11(Suppl 2):**P298 (doi: 10.1186/cc5458)

Introduction Measurement of extravascular lung water (EVLW) obtained with transpulmonary thermodilution (PiCCO system) can help the physician to guide fluid management of critically ill patients [1]. The thoracic fluid content (TFC) is a parameter deriving from the electric conductivity of the thorax, determined from intravascular, alveolar and interstitial fluids [2,3]. To the author's knowledge, there is no clinical study comparing PiCCO EVLW and the TFC provided by the impedance cardiac output (ICG) system. The aim of the study was to compare measurements of cardiac index (CI) obtained with PiCCO (P) and ICG before and after fluid challenge (FC), to evaluate whether the TFC can provide a noninvasive estimate of lung fluid balance, compared with PiCCO EVLW, in 10 critically ill patients.
Methods We studied 10 patients (eight males), aged 16-76 years (mean 22 ± SD 38), admitted to our ICU for head injury (three patients), septic shock (four patients), ARDS (one patient), and postsurgical (two patients).
The APACHE II score was 26-36 (30 ± 5). They were all monitored with the P system (PiCCO, V4.12; Pulsion Medical Systems AG) and the ICG system (Solar ICG module; GE Medical Systems Technology, Milwaukee, USA, 2001), to evaluate the CI. All patients received FC to optimize the haemodynamic status. Haemodynamic measurements were made before and after FC with colloids (5 ml/kg in 30 min). Statistical analysis was performed with Spearman nonparametric correlation and the Bland–Altman test.
Results Twenty samples of data were collected. The CI P mean ± SD was 3.91 ± 0.83 l/min/m^2 before FC and 3.32–8.52 l/min/m^2 after FC. The mean CI ICG value before FC was 3.44 ± 0.99 l/min/m^2 (2.10–5.50) and was 4.56 ± 1.37 l/min/m^2 after FC. The correlation coefficient found was 0.526 ($P < 0.05$) and 0.588 after. The 95% CI was 0.149–0.804. The overall mean CI P – CI ICG difference

was 0.70 l/min/m^2, with ±1.96 SD of −2.53 and 3.23, respectively. One measurement (5%) extended beyond the lower SD limit. The EVLW index ranges from 3.3 to 13.7 (7.86 ± 3.27) ml/kg before FC and 3.4 to 15.1 (8.58 ± 3.52) ml/kg after FC ($P = 0.015$). The TFC before FC was 34–60 (43 ± 10) ml/kg and 32–64 (46 ± 10) ml/kg after FC ($P = 0.011$). The correlation coefficient found before FC is 0.798 ($P = 0.007$) with 95% CI 0.656–0.940. The correlation coefficient found after FC is 0.802 ($P = 0.005$) with 95% CI 0.661–0.943.

Conclusions The main findings in this study are the great discrepancy between the two methods. CI measurements obtained with the ICG system underestimated CI when compared with the P system, particularly after FC. The TFC and EVLW index trends derived from FC appear similar; TFC measurements obtained with the ICG system show good correlation when compared with the EVLW index of the P system and it may be a useful index of pulmonary overloading, if supported by further randomized clinical trials.

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P299

Clinical evaluation of the FloTrac/Vigileo system and two established methods for continuous cardiac output monitoring in patients undergoing cardiac surgery

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Critical Care 2007, **11(Suppl 2):**P299 (doi: 10.1186/cc5459)

Introduction A new arterial pressure waveform analysis device, which does not need external calibration (FloTrac/Vigileo; Edwards Lifesciences, Irvine, CA, USA), became recently available for cardiac output (CO) measurement. However, only limited validation data for this technique are so far available [1,2].

Objective The aim of this study was to compare cardiac output assessed by the FloTrac/Vigileo system (FCO), the PiCCOplus system (PCO) [1] (Pulsion Medical Systems; Munich, Germany) and continuous cardiac output (CCO) monitoring using a pulmonary artery catheter (Vigilance; Edwards Lifesciences) with intermittent pulmonary artery thermodilution (ICO) in cardiac surgery patients.

Methods With ethics committee approval and written patient informed consent, patients undergoing elective cardiac surgery were studied. The CCO, FCO and PCO were recorded in the perioperative period after induction of anaesthesia (= study initiation) and 1, 4, 8, 12 and 24 hours post initiation. At each measurement point the ICO was assessed as mean of three repeated bolus injections. Statistical analysis was done using Bland–Altman analysis of absolute CO values and of percentage changes (δ) between consecutive CO measurements (= trend analysis).

Results One hundred and eighty-five matched sets of data were available for statistical analysis from 31 patients (ASA III, male/female ratio = 26/5, mean ± SD age = 66.58 ± 0.53 years (range: 45–84 years), mean ± SD body mass index = 28.2 ± 5.3 kg/m^2 (range: 19.5–48.0 kg/m^2)). CO values during the observation time ranged from 2.4 to 9.3 l/min. Bland–Altman analysis revealed a mean bias ± 2SD (limits of agreement) of 0.20 ± 2.3 l/min for FCO–ICO, 0.3 ± 2.7 l/min for PCO–ICO and 0.3 ± 2.5 l/min for CCO–ICO. Mean bias ± 2SD was −3.6 ± 59.2% for δ FCO–δ ICO, −1.6 ± 67.1% for δ PCO–δ ICO and 2.5 ± 58.8% for δ ICO–δ CCO.

Conclusion These results indicate that the FloTrac/Vigileo system is a reliable alternative to PiCCO and the pulmonary artery catheter for CO measurement in cardiac surgery patients.

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P300

Flow Trac™ cardiac output determination correlates with echocardiography

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Critical Care 2007, **11(Suppl 2):**P300 (doi: 10.1186/cc5460)

Introduction A new device may be used in intensive care to measure the cardiac output (CO) by arterial pulse pressure waveform analysis, but few studies have evaluated the reliability of this method and the correlation with other methods of CO determination. The aims of this study were to evaluate the CO obtained using the Flow Trac™ Vigileo™ and the correlation with CO obtained by transthoracic echocardiography (TTE).

Materials and methods Ten critical care patients admitted to a general ICU were enrolled in the study. All patients were mechanically ventilated (tidal volume 6–8 ml/kg, plateau pressure < 30 cmH_2O) and connected to an integrated monitoring system (Flow Trac™/Vigileo™; Ewdards Lifescience, Irvine, CA, USA) that attaches to an arterial cannula. After haemodynamic stabilization the CO was calculated from an arterial pressure-based algorithm that utilises the relationship between pulse pressure and stroke volume. At the same time a TTE examination was performed (Hewlett Packard, SONO 1000) and the CO was calculated by Doppler measurement of the left ventricular outflow area (LVOT) and the velocity–time integral (VTI LVOT), assuming stroke volume = cross-sectional area x VTI. Every patient had two CO determinations by TTE during Flow Trac™ measurement. A regression analysis and Bland–Altman analysis were used to compare the two methods of CO determination.

Results A total of 40 CO determinations were performed in 10 patients. Table 1 reports the main results.

Table 1 (abstract P300)

	R^2	P	Bias	SD of bias
CO Flow Trac™/CO TTE	0.85	<0.0001	0.24	0.45

Conclusion CO measurements obtained by Flow Trac™ show agreement with CO TTE with no clear bias, but comparative studies with thermodilution are warranted.

P301

A survey of cardiac output monitoring in intensive care units

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Critical Care 2007, **11(Suppl 2):**P301 (doi: 10.1186/cc5461)

Introduction We surveyed adult ICUs, looking at cardiac output monitor use with a view to demonstrating a practice change over the last 3 years.
Method The senior physicians on ICUs in the South of England were surveyed via telephone. Information was collected as to which cardiac output monitors were available for use, which was their first choice and how often they measured cardiac output in severe sepsis.
Results Forty-nine out of 52 ICUs units contacted completed the survey. Monitor availability can be seen in Figure 1 and use in severe sepsis compared with 2003 can be seen in Table 1.

Figure 1 (abstract P301)

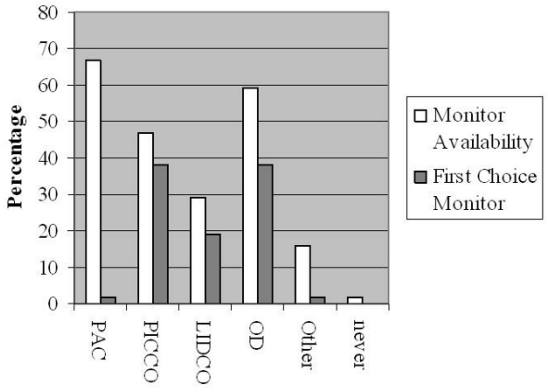

Table 1 (abstract P301)

	Rarely (<5%)	Sometimes (<50%)	Routinely (>50%)	Always
Severe sepsis (%)	0	30	45	25
Severe sepsis 2003 (%)	11	36	37	14

Conclusion Less invasive forms of cardiac output monitor are now used as the first line. A survey in 2005 showed 20% of units still used the PAC as their first-line monitor. This change has been associated with a lower threshold for use in severe sepsis.

P302

CeVOX for continuous central venous oxygenation measurement in patients undergoing off-pump coronary artery bypass grafting

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Critical Care 2007, **11(Suppl 2):**P302 (doi: 10.1186/cc5462)

Objective The aim of this study was to compare central venous O_2 saturation ($ScvO_2$) [1] measured continuously by the CeVOX (Pulsion Medical System, Munich, Germany) device ($CScvO_2$) with $ScvO_2$ determined by blood gas co-oximetry ($BScvO_2$).
Methods Twenty-five patients undergoing elective off-pump coronary artery bypass grafting were studied during operation (OP) and during their ICU stay (ICU). OP/ICU measurement started after *in vivo* calibration of CeVOX. $BScvO_2$ and $CScvO_2$ readings were recorded at intervals of 30 minutes during OP and 120 minutes during ICU. Bland–Altman analysis and Pearson correlation was performed for overall OP, overall ICU, consecutive measurements during OP ≤1 hour, 1–2 hours and 2–3 hours after initial calibration (OP1–OP3, respectively) as well as during ICU ≤4 hours, 4–8 hours, 8–12 hours and 12–16 hours after re-calibration (ICU1–ICU4, respectively).
Results Five hundred and nine matched sets of data were obtained; the $BScvO_2/CScvO_2$ range was 36–98.9%/46.5–99.0%, respectively. Overall mean bias ± 2SD was −1.2 ± 13.8% for $CScvO_2$–$BScvO_2$ during OP and −2.6 ± 16.2% during ICU. The correlation coefficient (r^2) for $CScvO_2$ vs $BScvO_2$ was 0.614 (OP) and 0.174 (ICU). Statistics for OP1–OP3 were comparable, whereas mean bias ± 2SD increased and r^2 decreased during ICU1–ICU4 (Table 1).
Conclusions The results indicate that $ScvO_2$ can be reliably assessed by CeVOX. In order to maintain accurate measurements, scheduled re-calibrations at intervals <12 hours are mandatory.
Reference
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P303

Incidence of low central venous oxygen saturation after standard postoperative intensive care management

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Introduction Targeted early postoperative management of high-risk surgical patients has been reported to be associated with a lower rate of complications and shorter hospital length of stay (HLOS) compared with conventional management. A low postoperative central venous oxygen saturation ($ScVO_2$) has also been shown to be associated with higher rates of complications and of HLOS for high-risk surgical patients. Benefit from early goal-directed therapy would be unlikely if 'standard' postoperative management resulted in a low incidence of patients with a low $ScVO_2$ in the early postoperative period.

Table 1 (abstract P302)

	OP1	OP2	OP3	ICU1	ICU2	ICU3	ICU4
Mean bias ± 2SD (%)	−0.2 ± 13.9	+1.3 ± 9.6	+1.8 ± 16.6	−0.1 ± 12.0	−0.6 ± 15.4	−0.5 ± 13.8	−4.6 ± 16.9
r^2 (*P* value)	0.580 (<0.001)	0.616 (<0.001)	0.513 (<0.001)	0.416 (<0.001)	0.514 (<0.001)	0.310 (0.001)	0.030 (0.247)

Methods Arterial and central venous blood gas analysis was done on admission (T1) and after 8 hours (T2) of admission to the ICU. The HLOS and the incidence of complications were determined for patients with low (<70%) or normal (≥70%) $ScVO_2$.
Results Sixty-three postoperative patients were screened and 23 patients were analysed. Patients were excluded if they did not have a central line positioned in the superior vena cava or blood had not been sampled at both time points. Patients with pre-ICU HLOS >5 days ($n = 10$), acute spinal cord injury ($n = 3$), or admitted for postoperative airway management ($n = 4$) were omitted. $ScVO_2$ was low in 7/23 patients at T2 and six of these had lower gastrointestinal surgery. The HLOS (median (IQR)) was longer in those with low $ScVO_2$ at T2 (17 (37.8) v 9.5 (5.0) days, $P = 0.04$). The incidence of complications was not different. There were no differences between the $ScVO_2$ groups at T2 with respect to age, gender, standard base excess, lactate, haemoglobin, mean arterial pressure or central venous pressure. The volume of colloid the two groups received in the 8-hour observation period was not different although there was a trend for the low group to receive more crystalloid ($P = 0.08$).
Conclusion A significant proportion of patients had a low $ScVO_2$, which was associated with increased HLOS. The results provide a basis for the trial of postoperative early goal-directed therapy for high-risk surgical patients admitted to our ICU.

P304

Relative influence of hypoxemia and anemia on the measurement of central venous oxygen saturation

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Introduction Central venous oxygen saturation ($ScvO_2$) is frequently used as a surrogate measurement of adequacy of perfusion. However, $ScvO_2$ is also affected by arterial oxygen saturation (SpO_2), oxygen consumption, and hemoglobin (Hb) according to the formula: $ScvO_2 = SpO_2 - (VO_2 / Q*1/Hb)$. The aim of this study was to investigate the relative influence of hypoxemia and anemia on the measurement of $ScvO_2$.
Methods A database of 700 pairs of arterial and central venous blood gases drawn from 300 patients admitted to the ICU of a university hospital was considered. After assessing for the technical adequacy of sampling (defined as a discrepancy of hematocrit and blood glucose between arterial and venous samples lower than 5%), 462 couples were selected for analysis. Samples were then clustered according to $ScvO_2$: <70% (low), ≥70% (high). SpO_2, partial pressure of oxygen (PaO_2) and Hb were considered. Venous to arterial difference of partial pressure of CO_2 ($DpCO_2$), arterial to venous difference of oxygen content ($DavO_2$) and the oxygen extraction ratio (ER) were also considered as measures of perfusion adequacy. Differences between low and high $ScvO_2$ samples were estimated by Mann–Whitney rank sum test (Sigma Stat, SPSS), accepting $P < 0.05$ as significant. Data are presented as median (25th–75th percentile).
Results $ScvO_2$ was 62.5% (56.3–66.2) in the low group ($n = 180$), 76.7% (73.6–80.7) in the high group ($n = 282$). In the low group values were: SpO_2 95.0% (95.1–98.3), PaO_2 72.0 mmHg (59.5–112.5), $DpCO_2$ 8 mmHg (6–9), $DavO_2$ 4.3 ml/100 ml (3.4–5.2), ER 0.346 (0.310–0.399), Hb 9.9 g/dl (8.9–11.1). In the high group values were: SpO_2 98.3% (96.2–99.5), PaO_2 106.5 mmHg (81.0–167.0), $DpCO_2$ 6 mmHg (4–7), $DavO_2$ 2.9 ml/100 ml (2.3–3.6), ER 0.215 (0.185–0.250), Hb 9.9 g/dl (8.7–11.1). As expected, $DpCO_2$, $DavO_2$ and ER were different between high and low $ScvO_2$ groups ($P < 0.001$). However, while Hb was similar ($P = 0.670$), SpO_2 and PaO_2 were significantly lower when $ScvO_2$ was below 70% ($P < 0.001$). Normalization of $ScvO_2$ to SpO_2 ($ScvO_2/SpO_2$) allowed one to overcome the effects of hypoxemia. Values were: 0.662 (0.603–0.693) in the low group and 0.794 (0.757–0.828) in the high group ($P < 0.001$).
Conclusions When considering $ScvO_2$ as a surrogate measure of perfusion adequacy, it is mandatory to consider the relative effect of hypoxemia. Anemia was less relevant in our case mix.

P305

Oxygen delivery optimization using lithium indicator dilution and pulse power analysis during major surgery in high-risk patients

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Introduction Increasing oxygen delivery in high-risk surgical patients led to a dramatic reduction in both mortality and morbidity. Yet, it is still not widely practised due to logistical difficulties associated with its use. We aimed to evaluate whether pulse power analysis calibrated by the lithium dilution technique, a pragmatic minimally invasive technique, can be used to optimize the oxygen delivery index (DO_2I) in high-risk patients during major surgery.
Methods Lithium indicator dilution and pulse power analysis were used to measure cardiac output and to calculate DO_2I (LiDCOplus system). We prospectively evaluated the oxygen delivery pattern and perfusion variables of 26 high-risk patients (LiDCO group) submitted to major surgeries and goal-directed therapy during surgery and 8 hours postoperatively, aiming to maximize the DO_2I to levels higher than 600 ml/min/m^2 using dobutamine and either 'restrictive' (4 ml/kg/min) or 'liberal' (12 ml/kg/min) strategies of intraoperative fluid management (partial results). Postoperatively both groups received 1.5 ml/kg/min lactated ringer. Fluid challenge with 250 ml colloid was done in the presence of signs of hypovolemia and additional fluids were given if necessary. Patients were considered responders if they achieved the therapeutic goal. A historical group of 42 high-risk surgical patients in whom the therapeutic goals were to keep a mean arterial pressure between 80 and 110 mmHg, a central venous pressure between 6 and 12 cmH_2O, hematocrit > 30% and urine output > 0.5 ml/kg/hour in the first 24 hours after ICU admission was used as control.

Figure 1 (abstract P305)

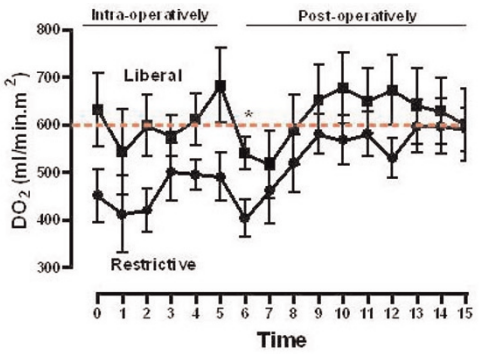

Table 1 (abstract P305)

	Control	LiDCO
Age	60 ± 17	68 ± 10
Lact1	3.5 ± 1	2.6 ± 1
Lact2	2.7 ± 1	1.9 ± 1
$ScvO_2$-1	64 ± 18	75 ± 10
$ScvO_2$-2	68 ± 13	72 ± 14
Complications (%)	50	15
Deaths (%)	26	7.7

Results Median doses of 10 μg/kg/min and 7.5 μg/kg/min dobutamine were used intraoperatively and postoperatively, respectively. A total of 75% and 84% of the patients were responders during surgery and postoperatively. However, a much better pattern of DO_2I during surgery was seen in the liberal group than in the restrictive group (Figure 1). The values for arterial lactate and central venous oxygen saturation ($ScvO_2$) on ICU admission and 24 hours later for both groups are shown in Table 1. Significantly lower arterial lactate and higher $ScvO_2$ were seen in optimized patients ($P < 0.05$ vs control group). Major complications occurred in 50% of the patients in the historical control group (21/42) and in 15% of the LiDCO group (4/26) (RR 0.15, 95% CI 0.037–0.600, $P < 0.05$).
Conclusion The use of a therapeutic approach guided by DO_2I calculated by the LiDCO plus system, intraoperatively and postoperatively, seems to be a feasible and practical approach to guide oxygen delivery optimization therapy during major surgery in high-risk patients. Better perfusion and a much lower rate of complications were seen in optimized patients.

P306

Oxygen delivery to carbon dioxide production ratio for continuously detecting anaerobic metabolism in trauma patients

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Introduction Lactate levels have been shown to correlate with tissue hypoxia. Unfortunately, due to their slow clearance, lactate levels may not reflect the actual metabolic condition. Under tissue hypoxia the carbon dioxide production (VCO_2) should be less reduced than the oxygen consumption, and the respiratory quotient (RQ) should increase. The oxygen delivery (DO_2)/VCO_2 ratio could be used as an indicator of anaerobic metabolism (AM) since it reflects the oxygen demand and delivery, and the tissue oxygenation. We tested the DO_2/VCO_2 ratio as a potential predictor of AM in trauma patients.
Methods Eighty consecutive adult trauma patients were prospectively studied. The DO_2, VCO_2, RQ, DO_2/VCO_2 ratio, SvO_2, and arterial lactate (Lac) values were collected at ICU admission. The DO_2 was calculated using the cardiac index measured by a pulse contour system (Hemoscan). The VCO_2 was measured under steady-state conditions using a CO_2 analyzer (930 Siemens Elema). The presence of AM (for example, hyperlactatemia, Lac+) was defined by an increase in Lac >2 mmol/l. Correlation analysis and the ROC test were applied.
Results For a threshold value of $DO_2 > 9$ ml/kg, Lac showed an inverse relationship with SvO_2 ($R = -0.84$; $P < 0.01$) and DO_2/VCO_2 ratio ($R = -0.73$; $P < 0.01$). Conversely, a direct correlation between Lac and RQ ($R = 0.66$; $P < 0.01$) was found. For a $DO_2 < 9$ ml/kg, SvO_2 did not correlate with Lac. Opposite, a direct correlation between Lac and RQ ($R = 0.81$; $P < 0.01$) was found. The DO_2/VCO_2 ratio showed an inverse relationship with Lac ($R = -0.75$; $P < 0.01$). ROC curves to predict Lac+ were constructed. The areas under the ROC curves were 0.40, 0.74, and 0.81 for SvO2, RQ, and DO2/VCO2 ratio, respectively. An optimal cutoff value of 3.1 (sensitivity = 0.70, specificity = 0.77) was determined for the DO_2/VCO_2 ratio predicting the presence of Lac+.
Conclusions Our findings showed that, for a $DO_2 > 9$ ml/kg, the SVO_2, RQ, and DO_2/VCO_2 ratio may be used interchangeably. For a $DO_2 < 9$ ml/kg, the DO_2/VCO_2 ratio seems a more reliable predictor of AM than SvO_2 and RQ. The DO_2/VCO_2 ratio can be simply and quickly calculated at the bedside because pulse wave analysis allows the DO_2 to be frequently calculated, and because the CO_2 analyzer provides VCO_2 values continuously. Combined gas exchange and pulse wave monitoring might be a valuable and a useful approach to detect AM in trauma patients.

P307

Passive leg raising-induced changes in mean radial artery pressure can be used to assess preload dependence

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Introduction We evaluated whether changes in, routinely measured, mean radial artery pressure (MAP) due to passive leg raising (PLR) can be used to assess preload dependence in nonspontaneous breathing patients. We therefore compared the changes in cardiac output (CO) with changes in MAP, pulse pressure (PP) and systolic pressure (SP) as well as the stroke volume variation (SVV) before PLR.
Methods In this prospective, intervention and response study, 30° PLR of both legs was performed in 20 supine patients receiving mechanical ventilation after elective cardiothoracic surgery. The thermodilution cardiac output (COtd), heart rate, central venous pressure (CVP), MAP, PP, SP and SVV measurements were performed before, during and after PLR.
Results The COtd, MAP, CVP, PP and SP increased after PLR. No change in heart rate and systemic vascular resistance was observed. We found a significant correlation between PLR-induced changes in COtd versus SVV during baseline (slope = 0.902, $P = 0.003$), changes in MAP (slope = 0.499, $P = 0.003$), PP (slope = 0.190, $P = 0.024$) and SP (slope = 0.276, $P = 0.021$). Changes in CVP were not correlated to changes in COtd. The area under the receiver operating curves was larger than 0.7 but not different for MAP, PP, SP and SVV.
Conclusion Not only baseline SVV but also PLR-induced changes in MAP, PP and SP are reliable parameters to assess preload dependence in cardiac surgery patients. In the clinical setting we prefer the MAP approach, based on simplicity, availability and robustness.

P308

Pulse pressure variation and adrenal insufficiency in septic shock

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Introduction It is known that corticosteroid therapy improves the hemodynamic state in patients with septic shock and relative

adrenal insufficiency. This effect is partially due to a direct action on vascular tone in the more vasoplegic patient, so they may be more hypovolemic. We tried in this study to determine whether pulse pressure variation measured just before the adrenocorticotropin test can predict the adrenal state.

Methods During a period of 3 years (January 2001–December 2003) we realized a prospective observational study. All patients having septic shock were enrolled. Patients with arrhythmia were excluded. We measured hemodynamic data (mean arterial pressure (MAP), pulse pressure variation (ΔPP)), then we realized an ACTH short test (injection of 250 mg ACTH with dosage of the cortisol level before the injection, at 30 and 60 minutes).

Results One hundred and one patients were enrolled. Age was 48 ± 17 years. SAPS II = 45 ± 16, APACHE II score = 18 ± 8, MAP = 52 ± 12 mmHg, lactate = 3.5 ± 2 mmol/l, and basal cortisol level (BCL) = 278 ± 143 μg/l. We divided all patients into two groups using the ΔPP cutoff: <12% (n = 30) and ≥12% (n = 71). There is no difference in the two groups in age, SAPS II, and MAP. Patients with low ΔPP (<12%) have a significantly (P = 0.01) low BCL: 204 ± 127 μg/l vs 291 ± 133 μg/l, a low increase of cortisol level in response to ACTH: 264 ± 144 μg/l vs 369 ± 142 μg/l (P = 0.02), and a low maximum variation after the ACTH test: 59 ± 52 μg/l vs 79 ± 63 μg/l (not significant). The relative adrenal deficiency (Δmax < 90 μg/l) is more frequent in patients with low ΔPP: 80% vs 60%. Survival is lower in the low ΔPP group, 13% vs 40%.

Discussion Patients with low ΔPP seem to be of poor prognosis because they have a low BCL, a low maximum cortisol increase after the ACTH test, and a high death rate. Annane and colleagues [1] found that nonsurvivors have low MAP, high lactate level, high basal cortisol level and low maximum cortisol level increase after the test compared with survivors. This finding is in contrast to our patients.

Conclusion Patients with low ΔPP before realizing the ACTH test tend to have more probability of adrenal deficiency, have more probability to receive corticosteroid and have poor prognosis.

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P309

Changes in stroke volume and intrathoracic blood volume induced by a sequential leg compression in critically ill patients.

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Introduction The new sequential leg compression device (SCD) (Tyco, Mansfield, MA, USA) pneumatically applies sequential compression to the lower limb, while maintaining a pressure gradient throughout the compression cycle [1,2]. We hypothesized that the SCD Response System could shift blood volume toward the thoracic compartment comparable with a volume challenge, with an increase in preload index such as the intrathoracic blood volume index (ITBVI) and stroke volume index (SVI). The aim of the study was to evaluate the relationships between changes in SVI (ΔSVI) induced by SCD and ΔSVI induced by rapid fluid loading (RFL) in critically ill patients.

Methods Twenty-seven patients (mean age 60 ± 9.1 years) admitted to the ICU were studied. Each patient received conventional monitoring plus hemodynamic–volumetric monitoring (PiCCO System; Pulsion Medical Systems, Munich, Germany). The heart rate, mean arterial pressure, central venous pressure, cardiac index, ITBVI, and SVI were recorded in the supine position before and after treatment with the SCD Express Compression System®. The same data where collected before and after a RFL performed with 3 ml/kg hydroxyethyl starch 6%. The relationships between ΔSVI induced by SCD and ΔSVI induced by RFL were analyzed by linear regression analysis. Statistical significance was considered to be at P <0.05.

Figure 1 (abstract P309)

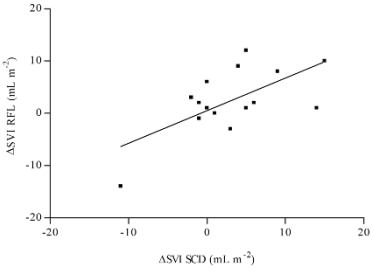
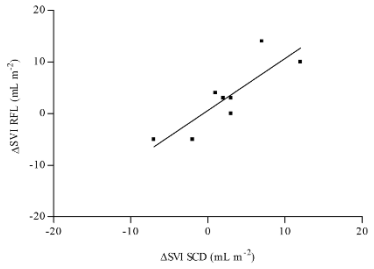


Figure 2 (abstract P309)



Results Linear regression analysis between ΔSVI induced by SCD (ΔSCD) and ΔSVI induced by RFL (ΔRFL) showed r^2 = 0.50 (P = 0.0002). When analyzed in a subgroup of spontaneously breathing versus mechanically ventilated patients, the relationships observed were respectively r^2 = 0.41 (P < 0.01) (Figure 1) and r^2 = 0.73 (P < 0.007) (Figure 2).

Conclusions The SCD Response System could shift blood volume toward the thoracic compartment comparable with RFL better in mechanically ventilated than in spontaneously breathing patients. Larger population studies are needed to confirm these preliminary data.

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P310

Respiratory pulse oximetry plethysmographic waveform amplitude correlates with arterial pulse pressure variations

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Introduction Arterial pulse pressure (PP) respiratory variation is a good predictor of fluid responsiveness in ventilated patients. Recently, it has been shown that variation in PP may correlate with variation in pulse oximetry plethysmographic (POP) waveform

amplitude, as they both depend on the stroke volume. We designed a prospective study to evaluate the correlation between respiratory arterial PP variation and POP waveform amplitude variations in ventilated patients and the influence of acute lung injury (ALI) in this relationship.

Methods Sixty patients were included in the study. Thirty-nine (65%) had diagnosis of ALI and 21 (35%) had normal gas exchange, defined as a relation of PaO_2 to FiO_2 (P/F) below and above 300, respectively. Respiratory variation in arterial PP and POP waveform amplitude were recorded simultaneously on a beat-to-beat basis, and mean values of two measures for each parameter were compared for correlation and agreement.

Results Respiratory variation in POP waveform amplitude could accurately predict variation in arterial PP with a sensibility of 83.3%, specificity of 85.7%, positive predictive value (PPV) of 71.4 and negative predictive value (NPV) of 92.3. The area under the ROC curve was 0.88 (0.79–0.97) with a best cutoff value of 14% to predict a variation in arterial PP of 13%. The kappa index of agreement was 0.65 ($P < 0.001$). Eighteen (30%) patients had variations in arterial PP above 13%, and 21 (35%) showed variations in POP waveform amplitude above 14%. In patients without ALI (P/F > 300) the sensibility was 100%, specificity was 93.3%, NPV was 100% and PPV was 80%. In the group with ALI (P/F < 300) the kappa index measure of agreement was 0.55, and in the group without ALI the kappa index was 0.85. PEEP levels were not different between the groups.

Conclusion Respiratory variation in arterial PP above 13% can be accurately predicted by a variation in POP waveform amplitude of 14% with good correlation and agreement. Our results confirm the findings of a recent trial and suggest that the correlation is even stronger when ALI is absent. These findings raise potential clinical applications of respiratory variation in POP waveform amplitude for haemodynamic management of patients without an arterial catheter.

P311

Assessing fluid responsiveness in patients undergoing abdominal major surgery: a comparison of the respiratory systolic variation test and other indices

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Critical Care 2007, **11(Suppl 2):**P311 (doi: 10.1186/cc5471)

Introduction Fluid responsiveness can be predicted by respiratory-induced changes in arterial blood pressure. In this study we compare the predictive performance of various haemodynamic parameters, including the respiratory systolic variation test (RSVT), pulse pressure variation (DPP) and stroke volume variation (SVV), in 18 patients undergoing abdominal major surgery.

Methods Eighteen patients, ASA I–II, were undergoing pancreatic surgery (whipple resection). The heart rate (HR) central venous pressure (CVP), arterial pressure (AP), cardiac output (CO), cardiac index (CI), stroke volume (SV), stroke volume index (SVI), SVV, DPP and RSVT were measured before and after a volume load of 7 ml/kg hydroxyethylstarch. (CO, CI, SV, SVI and SVV were displayed by the Edwards Vigileo monitor with FloTrac sensor.) Receiving-operating characteristic (ROC) curves were plotted for each parameter to evaluate its predicting value. In addition, correlation between the baseline value of haemodynamic parameters RSVT, DPP, SVV and change in SVI after volume administration was made.

Results DPP, SVV and RSVT demonstrate a good predicting value (ROC area 0.870, 0.877 and 0.943 with $P = 0.010$, 0.009 and 0.002, respectively). A statistically significant correlation was found between preoperative values of DPP, SVV and RSVT and percentage changes in SVI after volume load (better than the values of HR, AP, CVP).

Conclusion Functional parameters are superior to static indicators of cardiac preload in predicting the response to fluid administration. DPP and SVV, with their suggested threshold value, can predict fluid responsiveness in patients undergoing major abdominal surgery. The RSVT may be a more accurate predictor of fluid responsiveness although its performance demands a complex respiratory manoeuvre and is dependent on offline measurement and calculations, which limits its clinical use.

P312

Goal-directed intraoperative fluid therapy improved postoperative renal functions in aortic surgical patients

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Critical Care 2007, **11(Suppl 2):**P312 (doi: 10.1186/cc5472)

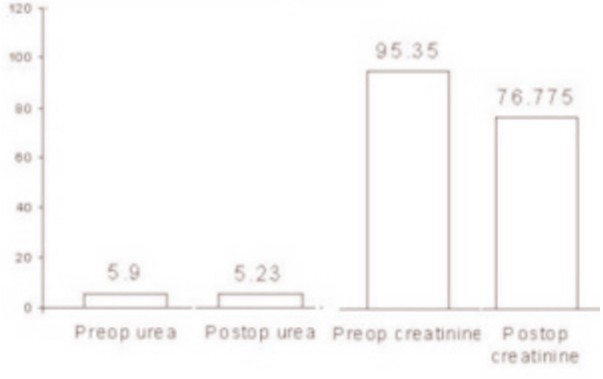
Introduction Goal-directed intraoperative fluid therapy reduced the hospital stay after major surgery [1]. Aortic vascular surgery is associated with excessive blood loss and massive fluid shift [2]. We found that postoperative urea and creatinine improved when intravascular fluid volume was maintained using transoesophageal Doppler.

Methods We randomly selected 40 patients who underwent elective infrarenal aortic surgery (aortic aneurysm repair/aorto-bifemoral grafting). All patients' cardiac output was continuously monitored using a transoesophageal Doppler probe (EDM™; Deltex Medical, Inc., Irving, TX, USA). The corrected flow time (FTc) was recorded immediately after induction as a baseline and recorded again pre-extubation. A target FTc of 375–425 ms was aimed for. The estimated total blood loss was calculated for each patient at the end of surgery. Preoperative and 24-hour postoperative urea and creatinine were recorded for comparison.

Results The mean baseline FTc was 278 ms, and the mean target FTc was 405 ms. The mean average blood loss was 3.77 l/patient. The mean preoperative urea and creatinine were 5.9 mmol/l and 95.3mmol/l, respectively. The mean 24-hour postoperative urea and creatinine were 5.23 mmol/l and 76.77 mmol/l, respectively. See Figure 1.

Conclusion Goal-directed intraoperative fluid therapy aiming for FTc of 375–425 ms as a target improved the 24-hour

Figure 1 (abstract P312)



postoperative urea urea and creatinine in 40 aortic surgical patients in spite of the excessive blood loss.

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P313

Analysis of physiological functions of different human serum albumin pharmaceutical preparations

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Introduction New information is emerging as a basis for reconsidering albumin as a key homeostatic molecule in the critically ill. We are only beginning to understand the full spectrum of albumin properties and action in healthy individuals and hypoalbuminaemic patients. Besides its function in the regulation of colloidal osmotic pressure, albumin has an important antioxidant capacity and a role in the transport of a wide range of drugs, hormones, ions, amino acids, and fatty acids. Few comparative studies have as yet been performed, and they address only a restricted number of parameters mostly defined by the European Pharmacopeia.
Objective To study and compare the main albumin functions of eight preparations of pharmaceutical-grade albumin, using a battery of different techniques. Two additional albumin preparations, a preparation without stabilisers and a recombinant albumin from Pichia pastoris, were also included in the study.
Methods The following biochemical and physicochemical parameters were investigated: total protein concentration (Biuret assay) and albumin antigen (nephelometry); quantitative analysis of contaminating proteins by nephelometry, levels of polymers and fragments by gel filtration chromatography on Superose 6, the binding affinity of exogenous ligands for Sudlow's site I (warfarin) or site II (dansylsarcosine) by steady-state spectrofluorimetry, the reactivity of Cys34 with Ellman's reagent, and the esterase-like activity using *p*-nitrophenyl acetate as substrate by spectrophotometry.
Results All pharmaceutical-grade products show a purity ranging from 95% to 108%. The main contaminant proteins are prealbumin, transferrin, α-1 acid glycoprotein, haptoglobulin, and retinol-binding protein. All of them are in conformity with the European Pharmacopeia specifications. The warfarin-binding capacity of the 10 albumin preparations was studied. An average binding constant of 2.6 (±0.3) x 10^5 M^{-1} ($n = 1$) was found. The presence of stabilisers reduced the binding of dansylsarcosine significantly (by 27–40%). The esterase-like activity toward *p*-nitrophenyl acetate and the reactivity of Cys34 differed from product to product. Interesting is the absence of free Cys34 in the recombinant albumin.
Conclusion Significant differences were observed between the 10 different human albumin preparations, recombinant or not. We confirm that the presence of stabilisers such as tryptophan derivatives significantly reduces the binding capacity of Sudlow's site II. Two important physiological properties of albumin, the esterase-like and antioxidant activities, were also found to be modified to different extents in all pharmaceutical-grade products in comparison with the albumin without stabiliser. The benefits of albumin administration should be considered carefully, taking into account the different functions and properties of albumin.

P314

Saline-induced hyperchloraemic metabolic acidosis: an unrecognised phenomenon among medical staff?

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Introduction Hyperchloraemic acidosis is well recognised within critical care, is implicated in the development of organ dysfunction and is an important consequence of administration of large volumes of chloride-containing intravenous (i.v.) fluid, such as normal (0.9%) saline [1,2]. Within most hospitals, junior medical staff with differing levels of experience prescribe the majority of i.v. fluid therapy.
Aims and methods A clinical scenario was used to assess current knowledge among medical staff regarding i.v. fluid therapy. 'An 85-year-old lady is brought into A&E semiconscious. Temperature 32°C, blood pressure 90/50 mmHg and BM 6.5 mmol/l. Arterial blood gases (ABG) on room air: pH 7.12 pO_2 10.8 kPa, pCO_2 2.6 kPa, HCO_3^- 12 mmol/l, O_2 saturation 94% and base excess −19'. Medical staff were asked to complete a questionnaire relating to the case under supervised conditions.
Results Eighty-seven questionnaires were completed by seven SpR/consultants, 48 F2/senior house officers, 13 F1 and 19 final-year medical students. ABG interpretation was correct in 80/87 (92%). Only 52/87 (59.8%) could calculate the anion gap and only 1/87 listed fluid as a cause of a metabolic acidosis. Eighty-three staff (93.4%) knew that a metabolic acidosis caused an increased respiratory rate. Normal saline was the first-choice fluid for resuscitation in almost 60% (52/87) cases. The chloride concentration of normal saline was known by 12/87 staff (13.8%). The serum chloride concentration was known by 28/87 staff (32%).
Conclusion The majority of medical staff prescribe normal saline as their first-choice intravenous fluid. Many medical staff are unaware of the electrolyte composition of normal saline, the phenomenon of hyperchloraemic metabolic acidosis, or how to differentiate hyperchloraemic metabolic acidosis from lactic acidosis by calculating the anion gap. A good understanding of fluid therapy is important for all medical staff.

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P315

An individual patient meta-analysis of clinical trials using dopexamine to increase oxygen delivery in high-risk surgical patients

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Critical Care 2007, **11(Suppl 2):**P315 (doi: 10.1186/cc5475)

Introduction Postoperative outcomes may be improved if cardiac output and oxygen delivery are maintained at optimal levels. Trials of the use of dopexamine for this purpose have yielded inconsistent results. This may relate to the use of high doses in some trials. A meta-analysis of data from these trials may therefore identify a benefit of low-dose dopexamine on postoperative mortality and length of stay.
Methods A comprehensive literature review was performed to identify published randomised trials of perioperative dopexamine infusion in patients undergoing major surgery. Individual patient

data were obtained, allowing a meta-regression approach to explore mortality outcomes after correction for age and dose of dopexamine. A Cox proportional hazards model was constructed to examine the length of stay.

Results Five studies fulfilled the inclusion criteria [1-5]. Low-dose dopexamine (≤1 μg/kg/min) was associated with a 49% reduction in 28-day mortality (6.3% vs 12.3%; OR = 0.51 (95% CI 0.29–0.89), $P = 0.008$). The length of postoperative stay was also reduced in the low-dose dopexamine group compared with control (median 13 vs 15 days, HR 0.75 (95% CI 0.65–0.88), $P = 0.004$). High-dose dopexamine (>1 μg/kg/min) was not associated with a difference in mortality (14.5% vs 12.3%; OR = 1.18 (95% CI 0.67–2.08), $P = 0.37$) or length of stay (median 17 vs 15 days, HR 1.10 (95% CI 0.90–1.34), $P = 0.37$) when compared with controls.

Conclusions Perioperative use of low-dose dopexamine decreases mortality and duration of hospital stay in patients undergoing major surgery.

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P316

The onset of ventricular isovolumetric contraction as reflected in the carotid artery distension waveform

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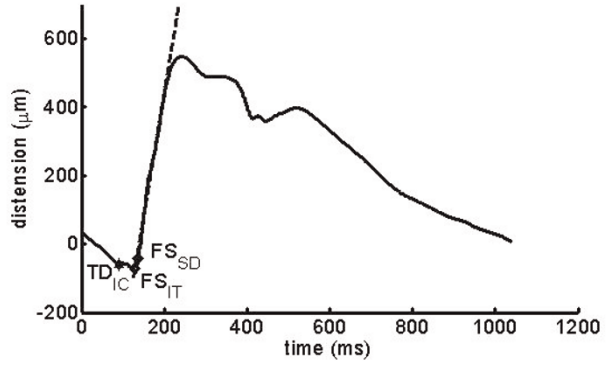
The blood pressure waveform carries information about the cardiac contraction and the impedance characteristics of the vascular bed. Here, we demonstrate that the start of isovolumic ventricular contraction is persistently reflected as an inflection point in the pressure wave as recorded in the aortic root (TPIC) as well as in the carotid artery distension waveform (TDIC) as it travels down the arterial tree. In a group of six patients with normal pressure gradients across the aortic valve after valve replacement, the TPIC had a small delay with respect to the onset of isovolumic ventricular contraction (<10 ms). In a group ($n = 21$) of young, presumably healthy, volunteers, the inflection point occurred persistently in the carotid distension waveform, as recorded by means of ultrasound, before the systolic foot (intersubject delay between inflection point and systolic foot: mean ± SD = 40.0 ± 9.4 ms, intrasubject SD 4.6 ms). Retrograde coronary blood flow during isovolumic ventricular contraction may be the origin of the persistent end-diastolic pressure and distension perturbation. This study shows that the duration of the isovolumic contraction can be reliably extracted from the carotid artery distension waveform.

Figure 1 (abstract P316)



P317

Critical care utilisation following bariatric surgery

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Introduction Following the introduction of a new bariatric surgical service in Sheffield, we aimed to assess the impact upon critical care services and examine how this has changed as the service has evolved.

Method All admissions for bariatric surgery between 1 April 2003 and 30 April 2006 were reviewed retrospectively. These procedures were performed on two sites, the Royal Hallamshire Hospital (RHH) and Thornbury Hospital (TH). The critical care admissions and length of hospital stay (LOS) were reviewed.

Results A total of 497 patients were identified as having had bariatric surgery. After review of hospital and critical care admission data, a total of 473 were identified with complete data. Of these, 94 (19.9%) were open procedures (OP), 260 (55.0%) laparoscopic bandings (LB) and 119 (25.1%) laparoscopic gastric bypasses (LGB). The age range was 16–68 years. The average hospital LOS for OP was 6.8 days, for LGB 4.0 days and for LB 1.9 days. Surgical procedures and HDU admissions increased annually (2003–2006) from 74 to 249, and 21 to 107, respectively. As a proportion, open procedures declined from 60% to 7%, and laparoscopic interventions increased (LB from 40% to 63% and LGB from 0% to 30%). There were a total of 14 admissions to the ITU by 10 patients, of which seven had undergone an initial OP. No admissions were elective and eight patients required further surgical interventions. HDU admissions occurred on both sites, with 148/277 (53.4%) of patients admitted to HDU at TH, and 53/196 (27.6%) at RHH. At TH only three patients required level 2 care, and 95 were discharged within 26 hours. At RHH, 16 patients required level 2 care, and 38 were discharged within 26 hours.

Discussion The requirement for ITU admission in this surgical group is, and has remained, low, despite a significant increase in bariatric surgical procedures. This increase is predominantly laparoscopic surgery. HDU activity has increased as the service has expanded; however, 90.4% of this is level 1 care, particularly at TH, where admission to the HDU is a matter of policy rather than clinical necessity. Availability of a level 1 facility would significantly decrease the requirement for HDU provision – an important consideration when introducing a new bariatric service.

P318

Intrathoracic pressure effects on hepatic flow and inferior vena cava diameter: an ultrasonographic study

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Objective To compare the effect of an increased intrathoracic pressure on the inferior vena cava (ICV) diameter and hepatic flow (HF) in healthy subjects.

Patients and methods Ten healthy subjects (seven females, three males; age 27.3 ± 4.5 years) were investigated in a supine position before and after application of continuous positive airways pressure (CPAP) of 10 cmH_2O by nasal mask. The study was performed using sonographic equipment with a multiprobe (convex 3.5–5 MHz; sector 2.5–3.5 MHz) and color-Doppler capability (Hitachi H 21). IVC was visualized by a two-dimensional echographic sector probe and M-mode was used to measure the inspiratory and expiratory diameters at the origin of the supra-hepatic veins. HF is composed of portal flow (PF) and hepatic artery flow (HAF). Portal velocity, assessed near the liver hilum, was used as a measure of PF, and the left intrahepatic branch resistivity index (RI) was used as a measure of HAF. Measures were repeated twice for each value of intrathoracic pressure by two different examiners and the mean value was given for the statistical analysis. Results are given as the mean ± SD. Data were evaluated by paired *t* test and $P < 0.05$ was taken as statistically significant.

Results CPAP determined a reduction of portal vein velocity: 30.0 ± 9.1 cm/s vs 19.7 ± 5.0 cm/s ($P = 0.01$). IVC diameters are increased by CPAP: inspiratory diameter 9.49 ± 2.5 cm vs 12.05 ± 3.9 cm ($P = 0.002$), expiratory diameter 16.46 ± 2.9 cm vs 18.08 ± 3.65 cm ($P = 0.05$).

Conclusions The results of this study demonstrate that, in healthy subjects, variation of intrathoracic pressure by CPAP influences venous return. HF reduction could be due to an increased IVC pressure, as displayed by the bigger diameters measured during CPAP, other than a diaphragmatic descent. Ultrasonography is able to detect this effect and could be useful in a more complete evaluation of patient haemodynamic status in various clinical settings.

P319

Intra-abdominal hypertension as a risk factor of death in patients with severe sepsis or septic shock

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Introduction Critically ill patients with severe sepsis or septic shock have a very high mortality rate. The aim of our study was to investigate the impact of intra-abdominal hypertension (IAH) on the outcome of patients with or without severe sepsis/septic shock.

Methods Two hundred and fifty-three mechanically ventilated patients admitted to the general ICU of Tartu University Hospital were prospectively studied. Patients who had severe sepsis or septic shock at admission or developed it during their first week of stay were compared with patients not suffering from severe sepsis. IAH was defined as sustained intra-abdominal pressure above or equal to 12 mmHg developing within the first week in the ICU.

Results Severe sepsis or septic shock was observed in 123 patients (48.6%). The ICU mortality among these patients was 33.3% compared with 18.5% in nonseptic patients ($P = 0.005$). IAH developed in 95 patients (37.0%). The incidence of IAH was higher among septic patients (45.5% vs 28.5%, $P = 0.004$). Those septic patients who developed IAH had a mortality rate of 50.0% compared with 19.4% in septic patients without IAH ($P < 0.001$). Mortality among nonseptic patients was not different between the patients with or without IAH (18.9% vs 18.3%). Development of IAH was a significant risk factor for death in septic patients (OR 4.15; 95% CI 1.87–9.26), but not in nonseptic patients (OR 1.04; 95% CI 0.39–2.77).

Conclusion Development of IAH significantly increases the risk of death in patients with severe sepsis or septic shock, but not in nonseptic patients.

P320

Abdominal pressure volume determinants

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The abdominal pressure–volume relation can be described by a linear relation giving an elastance (*E*) and a pressure at zero volume (P_{V0}). The goal of this study was to measure this relation in a large group of patients with different characteristics looking for the factors that influence and explain this relation. It is believed that obese persons have higher abdominal pressures and it is unclear whether muscle relaxation lowers it.

A large group of 70 patients, ASA class I or II, between 21 and 75 years old and scheduled for laparoscopic surgery were included in this study with approval from the hospital ethical committee.

Anaesthesia was induced with propofol 200 mg, sufentanil 20 µg, and sevoflurane 1.5 Mac in 50% O_2/N_2O. Some patients were fully muscle relaxed with nimbex 20 mg while others not. Patients were asked to empty the bladder before surgery. The stomach was emptied by suction through a gastric tube. An Olympus insufflator UHI-3 was initialised and the abdomen was inflated with a stepwise flow to 7, 10, 13 and 16 mmHg. When the pressure was reached, flow was stopped and the actual pressure and volume measured giving four data points. *E* and P_{V0} were calculated by fitting to a linear relation. The following recorded determinants were evaluated by regression analysis for their effect: age, length, weight, BMI, sex, gravidity and muscle relaxation.

P_{V0} increases significantly with body weight and decreases significantly with muscle relaxation.

Table 1 (abstract P320)

	P_{V0}	*E*
Age	0.838	0.003
Length	0.356	0.245
Weight	0.012	0.294
BMI	0.054	0.272
Sex	0.596	0.536
Gravidity	0.305	0.049
Relaxation	0.001	0.376

P321

Bystander CPR for out-of-hospital cardiac arrest in Japan

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Background and aims The aim of this study is to clarify how Japanese citizens are interested in the importance of immediate cardiopulmonary resuscitation (CPR) and defibrillation, and how they understand that importance. In Japan, the out-of-hospital emergency medical service system has been established with the ambulance service and an emergency life saving technician (ELST) belonging to the fire department.

Subjects and methods Patients' records were reviewed for the past 2 years. In Yokohama (3,700,000 people), the cardio-

pulmonary arrest (CPA) patient is transferred to the nearest ED of the selected 11 hospitals with adequate ability of CPR and cerebral resuscitation. We perform ultrasound, chest X-ray, and blood examination including Troponin in all CPA patients, and cerebral plane CT (40%) or chest CT (7%). CT was not performed in patients with a clearly known aetiology.
Results and discussion We treated 624 CPA patients in the past 2 years, 38% were cardiac and 62% were noncardiac aetiology (3% subarachnoid haemorrhage and 5% acute aortic dissection). Restricted in cardiac aetiology patients, 13% showed a ventricular fibrillation (VF) as a first monitored rhythm and 33% showed a VF during resuscitation. In all patients, 50% of VF were witnessed. In witnessed patients, 17% were witnessed by the ELST during transfer and 81% by a layperson, most of whom are patients' families and patients' friends. Fifty-three per cent were witnessed in the patients' home (35% in patients' private room, 1% in bathroom and 7% in lavatory), 4% in an aged people's residence, 1% in a hotel, restaurant, office, and 3% on the road. Only 48% of CPA patients underwent bystander CPR, and 51% of witnessed CPA patients (24% of all CPA patients) underwent bystander CPR by the witness; most patients underwent bystander CPR in the patients' home by the patients' families.
Conclusions In Japan, CPA patients were witnessed mainly in their home by their families or their friends. The aetiology of some CPA patients is noncardiac (subarachnoid haemorrhage or acute aortic dissection, etc.). However, only 24% CPA patients underwent bystander CPR by the witness.

P322

D-Dimer level and outcome in patients after cardiopulmonary resuscitation

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Background Clinical and experimental studies have demonstrated a marked activation of blood coagulation and fibrin formation after prolonged cardiopulmonary resuscitation (CPR). Several experimental studies suggest that thrombolysis therapy acts directly on thrombi or emboli but also enhances microcirculatory reperfusion. In this retrospective study we investigated the extent of blood coagulation and fibrin formation via the plasma D-dimer level, an indicator of endogenous fibrinolytic activity, in patients who underwent inhospital and out-of-hospital cardiac arrest from nontraumatic causes.
Methods and results Forty-five patients were included from 1 January 2004 to 31 March 2005 after CPR in the case of restoration of spontaneous circulation (ROSC). The plasma D-dimer level was measured immediately after admission to the ICU.
Results In 38 patients (84%) cardial reasons for cardiac arrest were found. Marked activation of blood coagulation was found in all patients. After prolonged cardiopulmonary resuscitation (ROSC not within the first 30 min) patients showed significant elevated serum D-dimer level compared with patients after ROSC in the first 30 minutes (663 μg/l vs 3,328 μg/ml, $P < 0.0001$; normal range <0.25 μg/ml). The time period between cardiac arrest and ROSC and plasma D-dimer level correlated significantly ($r = 0.8$, $P < 0.01$) after CPR. Patients who died showed significant elevated serum D-dimer level compared with the surviving patients (1,258 ± 1,587 μg/l vs 3,164 ± 1,974 μg/l, $P = 0.026$ median). The plasma D-dimer level correlated significantly to the negative outcome in these patients ($r = 0.55$, $P < 0.01$).
Conclusions Our data demonstrate a marked time-dependent activation of blood coagulation and fibrin formation after prolonged cardiac arrest and CPR in humans. These changes of the coagulation system may contribute to reperfusion disorders and possibly affect the outcome of these patients. Further studies need to show whether elevation of the D-dimer level in patients after CPR could be a prognostic marker.

P323

Vasopressin alone or with epinephrine may be superior to epinephrine in asystolic out-of-hospital cardiac arrest: an observational study

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Background In patients undergoing cardiopulmonary resuscitation, circulating endogenous vasopressin concentrations were significantly higher in successfully resuscitated patients than in patients who died. Clinical data considering vasopressin to be an equivalent option to epinephrine in cardiopulmonary resuscitation (CPR) are limited. The studies of out-of-hospital cardiac arrest (OHCA) confirm an increasing part of asystole as the initial rhythm. The hypothesis of this study was that vasopressin improves the rate of return of spontaneous circulation (ROSC) and the survival rate in asystolic OHCA, when used early in the resuscitation effort.
Methods This was a prospective cohort study, with a historic group compared trial set in an urban emergency medical services system, serving a population of 200,000. All nonpregnant, normothermic adults (>18 years) suffering nontraumatic OHCA with asystole were eligible. We compared two treatment groups of resuscitated patients with OHCA. In the epinephrine group (EPI) patients received epinephrine 1 mg i.v. every 3 minutes only. In the vasopressin group (VASO) patients received arginine vasopressin 40 IU i.v. only or followed by epinephrine 1 mg every 3 minutes during CPR. *Statistics*. Exact Fisher test, Wilcoxon rank-sum test, and analysis of independent predictors with multivariate logistic regression were used; $P < 0.05$.
Results The investigators enrolled 227 consecutive patients: in the EPI group 183 patients (years 2001–2003) and in the VASO group 44 patients (year 2004). Baseline (demographic and clinical) characteristics were similar for the two groups. Comparing the EPI and VASO groups, any ROSC was achieved in 81/183 (44%) and 34/44 (77%), $P = 0.04$; ROSC with admission in 61/183 (33%) and 27/44 (61%), $P = 0.03$; 24-hour survival in 44/183 (24%) and 23/44 (52%), $P = 0.01$; and discharge from hospital in 17/183 (9%) and 10/44 (23%), $P = 0.04$. Vasopressin was an independent predictor of ROSC with admission with an odds ratio of 2.4 (95% CI = 1.24–4.98).
Conclusions Vasopressin was superior to epinephrine in patients with asystole (better ROSC with admission, 24-hour survival and discharge from hospital). Vasopressin followed by epinephrine was more effective than epinephrine alone in the treatment of refractory cardiac arrest.

P324

Vasopressin, epinephrine, and methylprednisolone in inhospital cardiac arrest

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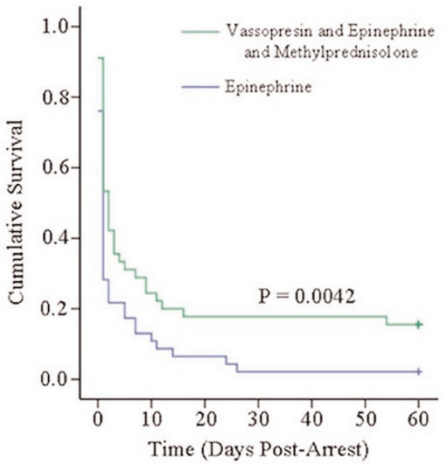
Introduction Combined vasopressin, epinephrine, and methylprednisolone during cardiopulmonary resuscitation (CPR) may improve survival in inhospital cardiac arrest.

Figure 1 (abstract P324)



Methods Ninety-one adults with cardiac arrest were randomized to receive either vasopressin (20 IU/CPR cycle for five cycles) plus epinephrine (1 mg/CPR cycle) plus methylprednisolone (single dose = 40 mg) or placebo plus epinephrine (1 mg/CPR cycle) plus placebo. Primary endpoints were return of spontaneous circulation (ROSC) for ≥15 minutes, and survival to discharge either to home or to a rehabilitation facility.
Results Study group patients had higher rates of ROSC (37/44 vs 24/47; $P < 0.01$) and discharge either to home or to a rehabilitation facility (7/44 vs 1/47; $P < 0.05$). Sixty-day survival was improved in the study group (Figure 1).
Conclusions Combination treatment improves survival in inhospital cardiac arrest.

P325

Procalcitonin is a powerful predictor of outcome after cardiopulmonary resuscitation

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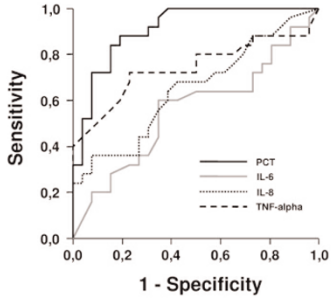
Critical Care 2007, **11(Suppl 2):**P325 (doi: 10.1186/cc5485)

Introduction We evaluated the time course and relationship of proinflammatory cytokines and procalcitonin (PCT) serum levels after cardiopulmonary resuscitation (CPR). We hypothesized that an increase of cytokine levels would precede a marked increase in PCT levels and that PCT would be the best predictor of the final neurologic outcome.
Methods Data were prospectively collected from 71 patients. Blood samples were taken after admission to the hospital and after 6, 12, 24, 72 and 120 hours. PCT, IL-6, IL-8 and TNFα levels were measured using automated assays. On day 14 patients were divided into two neurologic outcome groups according to the Cerebral Performance Categories (CPC 1–3: bad; CPC 4–5: good). Differences between groups were evaluated using a *t* test. ROC curves were computed to analyze the predictive value of the markers for a bad outcome.
Results There was an early and significant increase in TNFα, IL-6 and IL-8 after admission to the hospital (14.4 ± 5.2, 185 ± 248 and 89 ± 81 μg/l) and in the ensuing 6 hours (15.6 ± 8.7, 209 ± 239 and 176 ± 232 μg/l) in patients with bad neurologic outcome. Initially, PCT levels were indistinguishable between the groups; however, a striking increase was observed in patients with bad neurologic outcome peaking after 24 hours (16.7 ± 30.0 vs 6.9 ± 2.1 μg/l; $P < 0.013$). PCT values after 24 hours were the best predictor for a bad neurologic outcome with an area under the curve of 0.91 (cutoff value: 0.44; sensitivity 100%/specificity 62%).
Conclusion TNFα, IL-6 and IL-8 serum levels are significantly elevated in the early phase after successful CPR in patients with bad neurological outcome. PCT increases are subsequently found and have a high prognostic value for the neurologic outcome.

Figure 1 (abstract P325)



P326

Do patient characteristics or factors at resuscitation influence long-term outcome in patients surviving to be discharged following inhospital cardiac arrest?

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Critical Care 2007, **11(Suppl 2):**P326 (doi: 10.1186/cc5486)

Introduction Mortality among patients surviving to be discharged following inhospital cardiac arrest (IHCA) is high. The present study assesses whether this might be explained by differences in patient factor or in factors at resuscitation.
Methods An analysis of IHCA data collected from one Swedish tertiary hospital and from five Finnish secondary hospitals over a 10-year period. The study was limited to patients surviving to be discharged from the hospital. Multiple logistic regression analysis was used to identify factors associated with survival at 1 year from the arrest.
Results Of a total of 1,578 resuscitated patients, 441 (28%) survived to hospital discharge and 359 (80%) were alive at 12 months. Factors associated with survival at 12 months were age (odds ratio (OR) 0.96, 95% confidence interval (CI) 0.935–0.979), no renal disease (OR 0.4, CI 0.2–0.9), good functional status at discharge (OR 2.9, CI 1.4–6.0), and arrest occurring at (compared with arrests at general wards) the emergency ward (OR 5.8, CI 1.8–18), cardiac care unit (OR 2.9, CI 1.3–6.3), ICU (OR 2.6, CI 1.1–6.2), ward for thoracic surgery (OR 12.9, CI 3.4–49.1) and unit for interventional radiology (OR 16.4, CI 4.4–61.2). There was no difference in initial rhythm, delay to defibrillation or delay to return of spontaneous circulation between survivors and nonsurvivors at 12 months.
Conclusion Several patient factors, mainly age, functional status and co-morbid disease, influence long-term survival following IHCA. Location of the arrest also influences survival, but the initial rhythm, the delays to defibrillation and return of spontaneous circulation do not.

P327

Out-of-hospital surface cooling with a cooling-blanket to induce mild hypothermia in humans after cardiac arrest: a feasibility trial

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Introduction Mild hypothermia (32–34°C) is a promising new therapy for patients resuscitated from cardiac arrest. Animal studies suggest that early and fast cooling is crucial for beneficial effect on neurological outcome. Inducing mild hypothermia immediately after successful restoration of spontaneous circulation (ROSC) in the out-of-hospital setting remains a challenge. Therefore, a novel cooling-blanket (EMCOOLSpad®), independent of any energy source during use, was developed. The aim of the study was to evaluate feasibility and safety of out-of-hospital surface cooling with EMCOOLSpad® in patients successfully resuscitated from cardiac arrest.
Methods We included patients successfully resuscitated from out-of-hospital cardiac arrest with an oesophageal temperature (T_{es}) >34°C. The EMCOOLSpad® consists of multiple cooling units (12 mm thick), filled with a mixture of graphite/water, which are stored in a cooling box at −3°C in the ambulance car. Cooling was initiated as soon as feasible by the first treating paramedics and emergency physicians, and was continued in the emergency room. The cooling-blanket was removed when the T_{es} reached 34°C. The target temperature of T_{es} 33°C was maintained for 24 hours. Data are presented as the median and interquartile range (25–75%).
Results From September 2006 to December 2006, 10 patients, weighing 70 (64–93) kg, were included in the study. Cooling was initiated 14 (7–20) minutes after ROSC. The cooling-blanket decreased the T_{es} from 36.5 (36.2–36.7)°C at the start of cooling to 34.0°C within 61 (47–93) minutes, and to target temperature T_{es} 33°C within 83 (61–119) minutes, resulting in a cooling rate of 2.6 (1.6–3.6)°C/hour. Hospital admission was 45 (40–53) minutes after ROSC, and T_{es} 33°C was achieved 78 (32–107) minutes after admission. In eight patients, precooled parts of the cooling-blanket had to be applied repeatedly on the chest and abdomen to maintain the target temperature of T_{es} 33°C for 24 hours. No skin lesions were observed.
Conclusion Noninvasive surface cooling with the EMCOOLSpad® immediately after resuscitation from cardiac arrest, in the out-of-hospital setting, was shown to be feasible and safe. Whether early cooling, as compared with delayed cooling in the hospital, will improve neurological outcome needs to be determined in a prospective randomized trial.

P328

Mild hypothermia induction following cardiac arrest using a water-circulating cooling device

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Introduction The use of mild hypothermia for comatose survivors of cardiac arrest has been endorsed by the American Heart Association and the International Liaison Committee on Resuscitation [1,2]. Unintentional overcooling is common with some techniques such as cool intravascular fluid or the use of ice packs. Nowadays, the maintenance of hypothermia can be facilitated with new technology to avoid unintentional overcooling.
Methods A 77-year-old male with a history of hypertension, previous replacement of aortic valve and a right coronary artery bypass was admitted to our ICU after cardiac arrest. He suffered a collapse while walking. The emergency service arrived within 5 minutes. The initial cardiac rhythm was ventricular fibrillation. The estimated time to return to spontaneous circulation was 20 minutes. The patient arrived in the hospital 50 minutes after collapse and was immediately admitted to the ICU. Thirty minutes after ICU admission, he was unconscious with a Glasgow coma score of 5. Hypothermia was induced by the Artic Sun 2000 cooling system (Medivance, Louisville, CO, USA), and the goal temperature was obtained 105 minutes after induction. The body temperature was monitored continuously with a Foley catheter. Hypothermia was maintained for 24 hours at 33°C and rewarming to the target temperature of 37°C was achieved over 12 hours. No electrolyte imbalances or coagulopathies were observed. No overcooling was observed at any moment. The patient was extubated on day 6 after admission and discharged from the ICU on day 10 without neurological sequelae.
Conclusions Careful monitoring of temperature is important during use of therapeutic hypothermia because unintentional overcooling below 32°C may place the patient at risk for serious complications such as arrhythmias, infection, and coagulopathy. Cooling with a water-circulating cooling device is fast and safe. Clinicians should work to institute protocols for mild hypothermia treatment for such patients as a part of their critical care treatment.
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P329

Induction of mild hypothermia in cardiac arrest survivors with cardiogenic shock syndrome

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Introduction Induction of mild hypothermia (MH) in patients resuscitated from cardiac arrest can improve their outcome. However, benefits and risks of MH induction in patients who remain in cardiogenic shock after the return of spontaneous circulation (ROSC) are unclear. We therefore analysed a group of all cardiac arrest survivors who were indicated for MH induction in our coronary care unit (CCU) and compared the outcome of patients with cardiogenic shock syndrome after ROSC with the outcome of those who were relatively haemodynamically stable.
Methods We performed retrospective analysis of all consecutive cardiac arrest survivors treated by MH in our CCU from November 2002 to August 2006. They were classified into two groups, according to whether they met the criteria for cardiogenic shock or not after ROSC and just before MH initiation. Primary outcome measures were inhospital mortality, and the best inhospital and discharge neurological result. Predicted mortality was evaluated by the APACHE II score, and neurological outcome by Cerebral Performance Category score. MH was initiated as soon as

possible after ROSC and patients were cooled to body temperature 32–34°C for 12 hours.
Results From 50 consecutive patients, 28 fulfilled criteria of cardiogenic shock before MH initiation (group A), and 22 were relatively hemodynamically stable (group B). While predicted mortality was 83.1 ± 13.1% in group A and 63.2 ± 19.0% in group B ($P < 0.001$), real inhospital mortality was 55.6% in group A and only 18.2% in group B patients ($P = 0.009$). The best inhospital neurological outcome was found favourable in 71.4% patients in group A and in 86.3% in group B ($P = 0.306$). Favourable discharge neurological outcome was reached in 100% in group A and in 94% in group B ($P = 1.000$). Patients in both groups did not differ in rate of complications.
Conclusions While inhospital mortality in cardiac arrest survivors treated by MH was expectably higher in those with cardiogenic shock than in stable patients, favourable neurological outcome was frequent and comparable in both groups of patients. Moreover, MH application was safe in both groups. Therefore, induction of MH should be considered also in cardiac arrest survivors with cardiogenic shock syndrome after ROSC.

P330

Changes in urinary 8-hydroxy-2-deoxyguanosine in patients with global brain ischemia undergoing brain hypothermia therapy: comparison of whole body and selective head cooling

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Introduction Oxygen free radicals play an important role in global brain ischemia after cardiac arrest. Brain hypothermia therapy is effective in suppressing free radical expression. The aim of this study was to assess free radical expression under brain hypothermia, and to compare the expression between whole body and selective head cooling.
Methods The subjects were 12 patients treated with mild brain hypothermia (34 ± 1°C) after resuscitation following cardiac arrest in our ICU; five patients received whole body cooling and seven patients received selective head cooling. We examined the hemodynamic changes and the urinary concentration of 8-hydroxy-2-deoxyguanosine (determined by HPLC) during brain hypothermia therapy. Furthermore, we compared the prognosis at 28 days after admission to the ICU.
Results The induction time for whole body cooling was significantly shorter than that for selective head cooling. The rewarming time for head cooling was significantly shorter than that for whole body cooling. The mean arterial pressure and heart rate were both stable in the head cooling group. The urinary 8-hydroxy-2-deoxyguanosine concentrations decreased significantly in both groups, but data were significantly lower in the whole body cooling group compared with the selective head cooling group. Five and seven patients, respectively, exhibited good recovery 28 days after admission, in the whole body and selective head cooling groups.
Conclusions Mild brain hypothermia therapy suppressed the production of free radicals following global brain ischemia. Whole body cooling had a stronger effect of suppression of free radicals compare with selective head cooling. It is considered that selective head cooling exhibits neuroprotection similar to whole body cooling.

P331

Reduction of magnetic resonance spectroscopy brain temperature by convective head cooling in healthy humans

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This pilot study assessed the effect of forced convective head and neck cooling on brain temperature, measured by magnetic resonance spectroscopy (MRS), in five healthy adult humans (three males).
Following a 10-minute baseline, subjects received 30 minutes head cooling followed by 30 minutes head and neck cooling. The cooling device delivered air at 11°C and 15 m/s through a hood and separate neck collar made of a double layer of nylon sheeting, the inner layer pierced with holes. Subjects wore a windproof waistcoat taped round the base of their neck and were wrapped in blankets from the base of the neck down. Bilateral foot warming with chemical hot packs was used to encourage heat loss in the presence of normothermia.
MRS temperature data were collected at the level of the basal ganglia over the baseline and the last 10 minutes of each cooling intervention. MRS detects naturally occurring brain metabolites and interpretation of the relative frequencies of *N*-acetyl aspartate and water allows estimation of tissue temperature in 1 cm^3 voxels. For assessment of regional cooling, voxels lying within the region formed by joining the tips of the lateral ventricles were defined as 'core', voxels within approximately one voxel of the brain surface were defined as 'outer', and all other voxels were defined as 'intermediate'. The oesophageal temperature was measured continuously with a fluoroptic thermometer.
The mean baseline-corrected MRS brain temperature over all voxels reduced by −0.45°C (SD 0.23°C, $P = 0.01$, 5% CI −0.74 to −0.17°C) with head cooling and −0.37°C (SD 0.30°C, $P = 0.049$, 95% CI −0.74 to 0.00°C) with head and neck cooling. Head cooling reduced the mean baseline-corrected MRS brain temperature in core voxels in all subjects. The formal test for gradient was not significant ($P = 0.43$; 95% CI −0.15 to 0.29°C). Head and neck cooling reduced the temperature in core voxels in three subjects; the test for gradient was not significant ($P = 0.07$; 95% CI −0.03 to 0.58°C). The mean baseline-corrected oesophageal temperature reductions for the last 10 minutes of each intervention were −0.16°C (SD 0.04°C) with head cooling and −0.36°C (SD 0.12°C) with head and neck cooling.
Forced convective head cooling reduced the MRS brain temperature at an equivalent of 1.35°C per hour in healthy subjects, and the reduction was apparent across the brain.

P332

Induction of therapeutic mild hypothermia after cardiac arrest: a new combined method to achieve the target temperature

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Background Clinical and experimental investigations have demonstrated that induction of mild hypothermia works after successful cardiopulmonal resuscitation (CPR) neuroprotection. After the presentation of controlled studies, therapeutic hypothermia moved into the topical international guidelines.
Methods and results A total of 50 patients were examined after successful CPR. Twenty-nine patients received 4°C cold infusions after arrival in the heart catheter laboratory. Retrospective data of

21 patients who had received a volume substitute by means of drips from ambient temperature served as a control group. After admission to the ICU, both groups were immediately connected to an external cooling device (CoolGard® or Thermo Wrap®) and were cooled to a target temperature of 33°C (bladder temperature).
Results The average temperature at admission did not differ in both groups (35.5 ± 0.9°C vs 35.89 ± 0.8°C). In the group with initial cooling by means of 4°C cold infusions, a significant temperature decrease could be reached during the invasive coronary diagnostics to admission to the ICU of an average 0.84°C (35.88 ± 0.9°C vs 35.04 ± 0.9°C, $P < 0.0001$). The middle chill duration up to the achievement of the target temperature after admission was significantly shorter with the combined method (341 ± 113 min versus 553 ± 342 min, $P < 0.01$). The period to the achievement of the target temperature after the beginning of the external cooling device with the group of the combined method was significantly shorter (163 ± 91 min versus 342 ± 258 min, $P < 0.01$).
Conclusions The combined method with initial cooling with 4°C cold solutions shows a sure and actual prestationary cooling procedure to the introduction or realisation of mild hypothermia and offers the possibility to reach the purpose temperature significantly faster. Preclinical introduction of mild hypothermia by means of 4°C cold solutions could be a beneficial criteria in the future treatment, and probably affects the outcome of these patients.

P333

A comparison of complications during therapeutic hypothermia between surface cooling and endovascular cooling techniques

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Introduction Therapeutic hypothermia (TH) following cardiac arrest is associated with several complications including symptomatic bradycardia, coagulopathy, and pneumonia [1]. Furthermore, hyperthermia is associated with poor outcome following brain injury. The incidence of these complications may be increased by excessive temperature fluctuations. We sought to compare complications between two techniques used to induce TH; surface cooling (SC) using ice packs, and endovascular cooling (EV), using the Coolgard™ system (Alsius Corp., USA).
Methods A retrospective review was performed of all cardiac arrest patients undergoing TH and surviving ≥48 hours between June 2005 and November 2006.
Results Thirty-five patients underwent our TH protocol (SC group = 21, EV group = 14). The incidence of overcooling (<32°C) in the SC group was significantly higher than the EV group (10 vs 1, $P = 0.01$), whilst a trend towards more episodes of symptomatic bradycardia (SC 9 vs EV 2, $P = 0.07$) and rebound hyperthermia (SC 9 vs EV 2, $P = 0.07$) was also present. The incidence of pneumonia (SC 7 vs EV 4, $P = 0.77$) and coagulopathy/bleeding (SC 2 vs EV 3, $P = 0.32$) were similar between groups.
Conclusions (1) SC is associated with a significantly higher incidence of overcooling than EC and may be associated with an increase in complications such as symptomatic bradycardia. (2) SC may also be associated with an increase in rebound hyperthermia.
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P334

Buspirone and dexmedetomidine synergistically reduce the shivering threshold in humans

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Introduction Hypothermia may be therapeutically beneficial in stroke victims; however, it provokes vigorous shivering. Buspirone, a partial serotonin 1A antagonist, and dexmedetomidine, an α_2 agonist, linearly reduce the shivering threshold (triggering core temperature) with minimal sedation and respiratory depression. We tested the hypothesis that buspirone and dexmedetomidine synergistically reduce the shivering threshold without producing substantial sedation or respiratory depression.
Methods We studied four healthy male volunteers (18–40) on 4 days: (1) control (no drug); (2) buspirone only (60 mg orally); (3) dexmedetomidine only (target plasma concentration 0.6 ng/ml); and (4) combined buspirone and dexmedetomidine in the same doses. Lactated Ringer's solution (3°C) was infused via a central venous catheter to decrease tympanic membrane temperature by ≈2.2°C/hour; the mean skin temperature was maintained at 31°C. An increase in oxygen consumption more than 25% of baseline identified the shivering threshold. Sedation was evaluated using the Observer's Assessment Sedation/Alertness scale. Two-way repeated-measures analysis of variance was used to identify interactions between drugs. Data are presented as means ± SDs; $P < 0.05$ was statistically significant.
Results The shivering thresholds were 36.4 ± 0.5°C on the control day; 34.9 ± 0.6°C ($P < 0.01$ from control) on the buspirone only day; 36.1 ± 0.6°C ($P < 0.01$ from control) on the dexmedetomidine only day; and 34.2 ± 0.5°C ($P < 0.01$ from control) on the combined buspirone and dexmedetomidine day. The calculated mean difference between the thresholds on the combined and the control days was 1.9 ± 0.4°C, while the measured mean difference derived from the difference between the combined and control days was 2.3 ± 0.4°C. There was only trivial sedation with either drug alone or in combination. The respiratory rate and end-tidal PCO_2 were well preserved on all days.
Conclusion Buspirone and dexmedetomidine act synergistically to reduce the shivering threshold with only mild sedation and no respiratory depression. This combination might be a valid treatment to prevent shivering in stroke patients during therapeutic hypothermia.

P335

Bispectral index and suppression ratio are very early predictors of neurological outcome during therapeutic hypothermia after cardiac arrest

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Introduction The bispectral index (BIS) is calculated from frontotemporal electroencephalogram (EEG), and the suppression ratio (SR) estimates the percentage of EEG suppression. We monitored the BIS and SR during therapeutic hypothermia (TH) and compared them with neurological outcomes of encephalopathic survivors of out-of-hospital cardiac arrest (OHCA).
Methods Thirty-two patients with anoxic encephalopathy after OHCA received 18 hours of TH at 32–34°C. BIS monitoring was initiated at the onset of TH, and neuromuscular blockade (NMB) was dosed in response to shivering. Blinded BIS and SR data

were recorded after the first dose of NMB, and compared with the Cerebral Performance Category (CPC) at discharge and 6 months. CPC 1 or CPC 2 was considered a good outcome (GO).

Results Fourteen out of 32 patients (44%) survived, 11 (34%) with GO. Five of the remaining 18 patients died before neurological evaluation at 72 hours, and one patient recovered neurological function but died of cardiogenic shock. No survivor recalled the period of NMB. First NMB was administered a median of 5 hours after cardiac arrest or 87 minutes after initiation of TH, at 35.6 ± 1.7°C. Patients with GO had a higher first post-NMB BIS (39 ± 6 vs 13 ± 14, $P < 0.001$) and a lower SR (10 ± 12 vs 69 ± 29, $P < 0.001$) than those with CPC 3–5. Initial NMB reduced frontotemporal electromyogram (EMG) power from 52 ± 8 to 27 ± 1 db, $P < 0.001$. In 17 of the patients with downloaded EEG data, an increase in EMG power of 17 dB (IQR 10–27) from baseline was associated with clinically detectable shivering. Epileptiform discharges were noted on the monitor during NMB in two patients, and seizure activity was confirmed by formal EEG in both.

Conclusions In cardiac arrest survivors receiving TH, a higher post-NMB BIS score and a lower SR are very early predictors of neurological outcome. The potential benefits of monitoring BIS and SR, as well as EMG power for early recognition of shivering, and continuous frontotemporal EEG to detect seizures, warrant further study.

P336

Role of bedside electroencephalogram in intensive care: a critical review

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Electroencephalogram (EEG) is an appropriate monitoring tool in intensive care because it is linked to cerebral metabolism, is sensitive to ischaemia/hypoxia, can detect neuronal dysfunction at a reversible stage and is the best method to detect seizure activity. Scientific data have proved utility of continuous EEG monitoring in intensive care [1,2]. But there is a paucity of data relating to single recordings of EEG especially in general ICUs.

A retrospective chart review of patients who had bedside EEG in a medical–surgical ICU was done. Data were collected with a focus on: indication for requesting EEG, technical difficulties during the study, the report and its influence on subsequent clinical management.

Forty-two charts were reviewed. The indications were: evaluation of persistent comatose state ($n = 27$), to diagnose/exclude seizure activity and nonconvulsive status epilepsy ($n = 12$), and as an adjunct to support clinical diagnosis of suspected brain death prior to formal testing ($n = 3$). Movement artifacts led to technical difficulty in four studies.

EEG confirmed: moderate to severe nonspecific brain dysfunction as the cause for persistent comatose state by the presence of either diffuse slowing with theta/delta activity, absence of cerebral activity, continuous rhythmic and semi rhythmic lateralized/bilateral epileptiform discharges, burst suppression pattern or continuous bilateral slow U-shaped waves; anoxic brain damage by absence of changes in electrical signals following external application of noxious stimuli; and seizure activity by epileptiform discharges. Twelve reports stated that use of sedation interfered with EEG interpretation.

The following clinical decisions were made based on the EEG report in conjunction with clinical findings: initiating withdrawal of life support or 'do-not-resuscitate orders' in patients diagnosed to have hypoxic ischaemic encephalopathy ($n = 15$); adding/escalating or stopping antiseizure drugs based on the presence/absence of seizure activity ($n = 12$); and continuing supportive care in comatose patients diagnosed to have metabolic encephalopathy/prolonged sedation effect as the cause for coma ($n = 8$).

Based on these results it can be concluded that, despite limitations such as motion artifacts and influence of sedation on electrical signals, EEG impacts on clinical decision-making processes in critical care. Hence it is beneficial, and more widespread use would improve its diagnostic potential.

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P337

Abstract withdrawn

P338

Aneurysmal subarachnoid hemorrhage induces the expression of Pentraxin3 in patients

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Introduction Aneurismal subarachnoid hemorrhage (SAH) is an extremely severe illness associated with a high mortality rate and permanent severe neurological dysfunction in two-thirds of all affected patients. One of the major complications of SAH is vasospasm-associated cerebral ischemia. Clinical and experimental data suggest that vasospasm is linked to the inflammatory response associated with SAH. The goal of this study was to investigate the expression of Pentraxin3 (PTX3), a prototypic long pentraxin protein induced by proinflammatory signals in the brain, in SAH patients to test the hypothesis that SAH is followed by an upregulation of PTX3, and establish a temporal relationship between the expression of PTX3 and the induction of vasospasm. We also attempted to establish that PTX3 is detectable in cerebrospinal fluid (CSF).
Methods We studied eight severe SAH patients admitted to our neuroscience ICU with a median World Federation Neurosurgical Score of 4 and a Fisher score of 4. Arterial, jugular venous blood and CSF samples were routinely obtained every 12 hours for 7 days. PTX3 levels were measured by ELISA in plasma and CSF samples.
Results Compared with plasma levels of PTX3 in normal volunteers (<2 ng/ml [1]), SAH induced a marked increase in plasma PTX3 expression. During the first 48 hours following SAH (acute phase), PTX3 arterial and jugular venous levels increased to 36.93 ± 24.32 ng/ml and 33.64 ± 28.76 ng/ml, respectively, and then subsequently decreased concomitantly with the reduction of the inflammation (48–96 hours: subacute phase). PTX3 is detectable in the CSF: mean CSF levels of PTX3 were 4.07 ± 3.64 ng/ml during the acute phase and 0.69 ± 0.44 ng/ml during the subacute phase (*t* test: $P < 0.05$ compared with the acute phase). In the presence of vasospasm (four patients), we detected a second peak of PTX3 (4.03 ± 2.85 ng/ml) in CSF samples (*t* test: $P < 0.05$ compared with the subacute phase) that was not detectable in plasma.
Conclusions SAH is characterized by the production of PTX3 and the induction of vasospasm is associated with an upregulation of PTX3 in the CSF that is not detectable in plasma.
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P339

Outcome of intensive care unit patients with spontaneous intracerebral hemorrhage

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Introduction We evaluated the factors that may influence the outcome of patients with spontaneous intracerebral hemorrhage (SICH).
Methods Retrospective analysis of prospectively gathered data of 102 patients with SICH treated in our ICU during the past 8 years. On admission the following data were registered: vascular risk factors (high blood pressure, diabetes mellitus), age, gender, APACHE II score, GCS, hemorrhage characteristics (location, side, volume, mass effect), surgical procedure, MODS, blood pressure (systolic, diastolic, mean), pulse pressure, pulse rate, laboratory parameters (hemoglobin, white cell and platelet count, INR, serum values for Na, glucose, lactate, creatinin, bilirubin). Also registered were length of stay (LOS), duration of mechanical ventilation (MV), time of intubation (TT) and patient outcome. Haemodynamic instability was defined as low mean blood pressure and support with vasoactive and inotrop drugs. Statistical evaluation was performed using univariate and multivariate logistic regression, Student's *t* test Pearson's chi-square test and Fisher's exact statistic were used.
Results From the 102 patients (56 men and 48 women) 38 (37.5%) died within the first 30 days, most of them in the first 10 days. Age (OR 13.801, $P < 0.04$), APACHE II score (OR 1.114, $P < 0.008$), GCS (OR 2.158, $P < 0.002$), ICH score (OR 1.183, $P < 0.001$), FiO_2/pO_2 (OR 0.996, $P < 0.009$), haemodynamic instability (OR 2.340, $P < 0.002$), fever (OR 1.245, $P < 0.002$), and INR (OR 13.801, $P < 0.04$) were the strongest associated factors of 30-day mortality. Gender (OR 0.652, $P < 0.301$), prior illness (OR 1.070, $P < 0.870$), MODS (OR 0.978, $P < 0.803$), LOS (OR 0.988, $P < 0.266$), MV (OR 0.994, $P < 0.356$) and TT (OR 0.990 $P < 0.371$) were not associated with mortality. Patients who where operated on had higher mortality but were also more severely ill.
Conclusion Age, severity of illness, ICH score, hypoxemia, haemodynamic instability, and increased temperature are directly related with the outcome of patients with SICH. Gender, LOS, MV, TT, and MODS did not influence mortality.

P340

Maintenance of prehospital medical systems due to clinical advance in acute stroke

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Introduction Recently, the medical treatment in acute stroke has been making rapid progress. Especially, in the ischemic stroke of acute stage, the efficacy of thrombolysis, systemic t-PA or local transarterial urokinase infusion has been proved. However, the effective treatment time is still quite limited. The patients must be brought to the stroke center as soon as possible. We analyzed the reason why most stroke patients delay coming to the stroke center. We extracted the problems and proposed some solutions.
Patients and methods The clinical subjects consisted of 1,112 consecutive patients with ischemic stroke in the acute stage, hospitalized in our hospital between April 2003 and September 2006. We investigated the clinical course, especially the time from the onset to the physical examination, and radiological examinations (CT, MRI, MRA and/or cerebral angiography). The mean age was 72.3 years. Among them, 334 patients were classified as atherothrombosis, 232 were cardiac embolism, 439 were lacunar infarction and 107 were transient ischemic attack. Only 19 patients underwent acute thrombolytic therapy.
Results Two hundred and forty-one patients (21.7%) were hospitalized within 3 hours from the onset, and 365 patients (32.9%) were within 6 hours. Among them, only 438 were admitted by ambulance. We found the following results. The main reason for

the delayed admission is through another hospital, not a stroke center. The patients denied their symptoms are not so rare. The patients or their family often hesitate to request the emergency car.
Conclusions The most significance point for rapid diagnosis and therapy is that people must doubt 'stroke' at first. We should further educate citizens to the warning signs of stroke and also the necessity of emergency admission using an emergency car. In addition, we should justly build a core stroke center in the district and centralize the patients.

P341

Effects of intraaortic balloon counterpulsation on middle cerebral artery blood flow velocities

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Introduction The intraaortic balloon pump has been shown to improve cardiac output and diastolic coronary flow. The aim of our study was to determine the effects of intraaortic counterpulsation (IABP) on cerebral blood flow velocities measured on the middle cerebral artery.
Methods In 11 cardiac surgery patients receiving IABP postoperatively, blood flow velocities in the middle cerebral artery were assessed by transcranial Doppler (TCD). In each patient, measurements of V_{max}, V_{mean} and V_{min} were performed at four different pump settings: without support (WS), and at pump assist pulse with ratio 1:1, 1:2 and 1:3.
Results Repeated-measures analysis of variance: $P = 0.0006$, considered extremely significant variation of TCD measurements among IABP settings. Comparing all pairs of V_{max}, V_{mean} and V_{min} values, we found that V_{max} and especially V_{mean} are significantly greater at the 1:2 and 1:3 pump settings, but not at the 1:1 setting. We also found that the end diastolic velocities (V_{min}) were significant lower during the pump deflation. None of our patients had a significant diastolic flow velocity reversal during the pump deflation.

Table 1 (abstract P341)

	WS vs 1:1	WS vs 1:2	WS vs 1:3
V_{max}	$P > 0.05$	$P < 0.01$	$P < 0.01$
V_{mean}	$P > 0.05$	$P < 0.001$	$P < 0.001$

Conclusions Left ventricular support with IABP significantly changed the flow velocity pattern of our patients. The pump significantly increased the V_{max} and the V_{mean} at the 1:2 and 1:3 settings because of pump inflation during the diastole. We suggest that the velocities did not change at the 1:1 setting because the end-diastolic flow velocities reduce during every pulse, according to pump deflation.

P342

Neuromuscular dysfunction acquired during critical illness: a systematic review

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Background Patients with critical illness can acquire a syndrome of weakness and dependence on mechanical ventilation that has been linked to peripheral nerve and muscle injury. Our aim was to systematically review published data on the diagnosis, risk factors and outcomes of patients with critical illness neuromuscular abnormalities (CINMA).
Methods MEDLINE, EMBASE, CINAHL, and the Cochrane Library were searched, and studies were included if they reported on ICU patients > 16 years old who were evaluated for CINMA clinically and electrophysiologically, and they contained sufficient data to quantitatively measure the association between CINMA and clinically relevant exposures and/or outcomes. Two reviewers independently extracted data on study methodology and quality, methods for diagnosing CINMA, and CINMA prevalence, risk factors, and outcomes.
Results In 1,421 ICU patients who were evaluated in 24 studies, 655 (46%) were diagnosed with CINMA. All enrolled patients were receiving protracted mechanical ventilation, had sepsis, or had multiple organ failure. Diagnostic criteria for CINMA were heterogeneous and few reports explicitly differentiated between the polyneuropathic, myopathic and mixed types of CINMA. CINMA was linked in several studies to hyperglycemia, the systemic inflammatory response syndrome, sepsis, renal replacement therapy, and catecholamine administration. In contrast, across studies there was no consistent relationship between CINMA and patient age, gender, severity of illness, multiple organ failure, and use of glucocorticoids, neuromuscular blockers, aminoglycosides, or midazolam. Mortality was not increased in patients with CINMA, but mechanical ventilation and ICU and hospital stays were prolonged.
Conclusions The risk of CINMA is nearly 50% in a subset of ICU patients with sepsis, multiorgan failure, or protracted mechanical ventilation, but there were no data to support CINMA as an independent predictor of death. The impact of frequently cited risk factors is uncertain, but emerging data indicate glycemic control decreases CINMA risk in vulnerable patients.

P343

Gram-negative bacteremia is an independent predisposing factor for critical illness polyneuromyopathy

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Introduction Critical illness polyneuromyopathy (CIPM) is a major clinical problem in the ICU resulting in prolonged ICU stay and increased morbidity and mortality.
Objective To investigate risk factors of CIPM involved, in a general multidisciplinary ICU.
Patients and participants Four hundred and seventy-four (323 males/151 females, age 55 ± 19) consecutively admitted patients in a 28-bed university multidisciplinary ICU were prospectively evaluated. All patients were assigned admission APACHE II (15 ± 7) and SOFA (6 ± 3) scores and were subsequently evaluated for newly developed neuromuscular weakness. We examined muscle strength according to the Medical Research Council scale, deep tendon reflexes, sensory function and muscle wasting. Laboratory values and medical therapy were recorded daily. Other potential causes of new-onset generalized weakness after ICU admission were excluded before the diagnosis of CIPM was established. Out of the 474 patients, 185 remained in the ICU for ≥10 days.
Results Forty-four (23.8%) out of those 185 patients developed generalized weakness that met the criteria for CIPM. Patients with

CIPM had a higher admission APACHE II score (18.9 ± 6.6 vs 15.6 ± 6.4, $P = 0.004$) and SOFA score (8.4 ± 2.9 vs 7.1 ± 2.9, $P = 0.013$). Multivariate logistic regression analysis showed that risk factors independently associated with the development of CIPM were severity of illness at the time of admission to the ICU, administration of aminoglycoside antibiotics and high blood glucose levels. Analysis according to severity of illness stratification revealed the emergence of Gram-negative bacteremia as the most important independent predisposing factor for CIPM development in less severely ill patients.
Conclusions CIPM has a high incidence in the ICU setting. Our study revealed the important association that Gram-negative bacteremia, aminoglycosides, hyperglycemia and severity of illness have with CIPM development.

P344

Interhospital cooperation after critical and emergency care for patients with cervical–thoracic–abdominal trauma and emergency diseases in the local medical area in a typical urban city of Japan

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Background Capacity of the critical care and emergency center (CCEC) is usually restricted. Transfer of patients from CCEC is one of the most important issues in the CCEC.
Subjects and methods We examined interhospital cooperation after critical and emergency care for life-threatening cervical–thoracic–abdominal trauma ($n = 501$) and thoracoabdominal emergency diseases ($n = 236$) who were treated with intensive care in our CCEC and were able to be discharged or transferred to another acute treatment hospital.
Results Of the trauma patients directly transferred to our center, 48% were transferred to the 'affiliated hospitals', whose medical staffs were dispatched from the 'departments' in our university, 17% were transferred to the nonaffiliated hospitals, and 34% were directly discharged from our center. Of emergency disease patients, 28% were transferred to the affiliated hospitals, 20% were transferred to other hospitals, and 52% were directly discharged. Patients staying in our center for more than 14 days tended to be transferred to the affiliated hospital. Of trauma patients indirectly transferred from other hospital to our center, 30% and 11% were transferred to the affiliated and nonaffiliated hospitals, and 19% were directly discharged. Of emergency disease patients, these values were 21%, 7%, and 13%, respectively. Patients staying in our center for more than 14 days tended to be transferred to the affiliated hospital.
Discussion and conclusion These results are thought to be a common situation in a typical urban city in the world. Now, the interhospital cooperation between city hospital and referral hospital does not function well because of poor understanding of re-transfer to the previous hospital, resulting in dysfunction of the management of critical patients in the local medical area. It is important to construct a new interhospital-cooperation system based on the local medical area.

P345

Early hypothermia in severely injured trauma patients is a significant risk factor for multiple organ dysfunction syndrome but not mortality

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Introduction The objective was to determine the relationship of early hypothermia to multiple organ failure and mortality in severely injured trauma patients.
Methods This prospective observational study was performed at seven Level I trauma centers over 16 months. Severely injured patients with hypoperfusion and a need for blood transfusion during the early hospital course were followed with near-infrared spectroscopy-derived tissue oxygen saturation (StO_2) and clinical variables. Outcomes including multiple organ dysfunction syndrome (MODS) and 28-day mortality were evaluated. Hypothermia was defined as temperature < 35°C within the first 6 hours.
Results Hypothermia was common (43%, 155/359). Hypothermic patients were more likely than normothermic patients to develop MODS (21% vs 9%, $P = 0.003$), but did not have increased mortality rates (16% vs 12%, $P = 0.28$). The maximum base deficit (Max BD) in hypothermic patients did not discriminate between those who did or did not develop MODS (9.8 ± 4.6 mEq/l vs 9.4 ± 4.4 mEq/l, $P = 0.56$) but had good discrimination for mortality in both hypothermic and normothermic patients. Significant predictors of MODS using multivariate analysis included minimum StO_2 ($P = 0.0002$) and hypothermia ($P = 0.01$), but not Max BD ($P = 0.09$). Predictors for mortality with multivariate analysis included minimum StO_2 ($P = 0.0004$) and Max BD ($P = 0.01$), but not hypothermia ($P = 0.74$). Hypothermia remained a significant risk factor for MODS when fluid/blood infusion volumes were included in the multivariate model.
Conclusions Hypothermia is common in severely injured trauma patients and is a risk factor for MODS but not mortality. Minimum StO_2 predicts MODS and mortality in normothermic and hypothermic patients, while the predictive effect of BD for MODS is blunted in the presence of hypothermia.

P346

The nonlactate gap: a novel predictor of organ failure and mortality following major trauma

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Introduction Early identification of patients who are not fully resuscitated following major trauma improves outcome. However, current markers of clinically occult hypoperfusion, such as lactate and base deficit, have serious limitations, and our aim was to establish a new endpoint of resuscitation.
Methods In a prospective study conducted in a Level 1 trauma unit, 49 consecutive patients admitted to the trauma ICU were evaluated. Serum electrolytes, albumin, phosphate and lactate

were measured on admission. We derived the calculated ion gap using a simplified Stewart–Figge equation, and subtracted the measured serum lactate from the calculated ion gap to obtain the nonlactate gap (NLG).
Results See Table 1. The NLG discriminated survivors from non-survivors ($P = 0.008$, analysis of variance). An NLG above 2 mmol/l was associated with an increased risk of mortality ($P = 0.010$, Fisher's exact test). No patient with an NLG less than 2 mmol/l died; 32.4% of the patients with an NLG above 2 mmol/l died. A NLG above 2 mmol/l also correlated strongly with organ failure (Multiple Organ Dysfunction Syndrome score $P = 0.011$, Sequential Organ Failure Assessment score $P = 0.011$, Mann–Whitney U test).

Table 1 (abstract P346)

	Survived	Died	Total
NLG < 2 mmol/l	15 (39.5%)	0 (0%)	15 (30.6%)
NLG > 2 mmol/l	23 (60.5%)	11 (100%)	34 (69.4%)
Total	38 (100%)	11 (100%)	49 (100%)

Conclusions We describe the NLG for the first time, and quantify it using simple bedside calculations derived from routine blood investigations. The NLG is an excellent marker for organ failure and death following major injury, and should be used to guide trauma resuscitation.

P347

Prehospital hypotension that persists on arrival at the emergency department is a powerful predictor of mortality following major trauma

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Objective Outcome following major injury is time dependent. Early identification of high-risk patients allows rapid decision-making and correction of life-threatening disorders. Complex scoring systems are of limited value during major trauma resuscitation. Our aim was to evaluate the utility of a single blood pressure during the prehospital phase in combination with the blood pressure on arrival at the emergency department.
Methods Data were collected prospectively on 1,111 patients admitted to a Level 1 South African trauma unit over a 1-year period. Patients were subdivided into two groups according to the combination of their prehospital (PH) and emergency department (ED) blood pressure. Hypotension was defined as a systolic blood pressure less than 90 mmHg. Mortality was defined as death within 30 days.
Results The mortality in patients ($n = 1,031$) with normal PH and ED blood pressure was 5.4%. The mortality in patients ($n = 80$) with PH and ED hypotension was significantly higher at 45% ($P < 0.0001$, chi-square test) (Table 1).

Table 1 (abstract P347)

	SBP < 90 mmHg	SBP > 90 mmHg
Alive	55.0% ($n = 44$)	94.6% ($n = 975$)
Dead	45.0% ($n = 36$)	5.4% ($n = 56$)

Conclusion The combination of prehospital and emergency department systolic blood pressure is a simple yet extremely powerful predictor of mortality following major trauma and should be used as a triage tool to rapidly identify the highest risk patients.

P348

Traumatic cardiac injury in chest trauma

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Introduction Blunt chest trauma is often accompanied by traumatic cardiac injury (TCI), formerly called cardiac contusion. Severe TCI can affect the prognosis of chest trauma patients due to cardiac arrhythmias, heart failure, or cardiac tamponade. The objective of this study was the detection and evaluation of TCI in chest trauma.
Methods Twenty-seven consecutive patients without cardiac disease history (five females), mean age 37.2 years (63% <35 years) were admitted to the ICU with blunt chest trauma. Five patients had minor head brain injury. The majority needed mechanical ventilation support. The mean Injury Severity Score (ISS) was 21.1 (11–34). The following injuries/lesions of thorax or lung parenchyma were identified on chest and abdominal CT scan: fractures of clavicle, sternum, ribs, scapula or vertebral column, lung contusion, hemo/pneumothorax, hemo/pneumomediastinum, abdominal organ injury. TCI diagnosis was based on auscultation findings (pericardial friction rub, new cardiac murmurs), electrocardiogram (ECG) findings (ST–T disturbances, arrhythmias), cardiac enzymes (CE) (cardiac Tropinin I, CK-MB), transthoracic echocardiography (TTE) (wall motion abnormalities (WMA), reduced left ventricular ejection fraction (LVEF) pericardial effusion (PE)), and thorax CT findings.
Results Twenty-two out of 27 patients (81%) exhibited at least one sign of TCI, 17/27 (63%) had more than two signs: ECG changes (18/22, 81.8%), mostly ST–T disturbances of left precordial or inferior leads, slight CE increase (17/22, 72%), PE in TTE or CT (12/22, 54,5%), WMA, mostly of the interventricular septum wall (6/22, 27%), reduced LVEF (5/22, 23%), or pericardial friction rub (5/22, 23%). Patients with TCI signs had more frequently bilateral or right-sided hemothorax (16/22, 72%), bilateral lung contusion (15/22, 68%), right-sided rib fracture (15/22, 68%), abdominal organ injury (spleen, left kidney/adrenal, liver) (14/22, 63%) or right-sided pneumothorax (13/22, 59%). Two patients (one with flail chest) exhibited PE leading to cardiac tamponade. Pericardiocentesis was performed with success. None of the patients had severe ventricular arrhythmia. Five young patients had mildly reduced LVEF, in almost all cases transient. There was a positive correlation between ISS and TCI severity.
Conclusions TCI is frequent in blunt chest trauma. Additional ECG findings and an increase in CE suggest possible TCI to be confirmed by a bedside TTE study. TCI usually accompanies bilateral hemothorax, lung contusion, or right-sided rib fracture.

P349

Prognosis of blunt abdominal trauma patients with contrast medium extravasation on computed tomography scan

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Introduction Until now there have been few studies concentrating on the diagnostic and prognostic significance of contrast medium

extravasation site computed tomography (CT). In this study we investigated the site and extent of contrast medium extravasation on CT findings and its effect on treatment and predicting clinical outcome in trauma patients.
Methods Fifty patients admitted to our emergency department with blunt abdominal trauma showing contrast medium extravasation on abdominal–pelvic CT scan were included in our study for 33 months. Patients were prospectively collected and medical records were reviewed and analyzed retrospectively. The patients' clinical and laboratory findings, abdominal sonographic (FAST) findings, and CT findings were reviewed. Extravasation sites were classified as intraperitoneal, retroperitoneal, intrapelvic and correlated with post-treatment complications, mortality and morbidity rates.
Results The incidence of extravasation site was intraperitoneal in 33 cases (66%), retroperitoneal in 13 cases (26%), and intrapelvic in four cases (8%). The frequency of injured vessels showing extravasation was 18 (36%) hepatic vessels, nine (18%) splenic vessels and six (12%) iliac vessels. There was no correlation between the extravasation site and ICU or total hospitalization duration ($P > 0.523$). Sixteen patients with intraperitoneal extravasation required surgical intervention, six patients underwent angiography with embolization. In patients with retroperitoneal extravasation, nine were treated conservatively and two with embolization. Over all there were no significant differences between the extravasation site and treatment modality. The intraperitoneal group had the highest mortality with 13 deaths (11/33, 39%) and the highest early mortality rate (10/13, 76%) in the first 24 hours ($P = 0.001$).
Conclusion CT findings in patients with blunt abdominal trauma showed no significant correlation between the contrast medium extravasation site and treatment modality, ICU hospitalization duration, or final results. However, patients with intraperitoneal extravasation required more aggressive transfusion with packed red cells and had a higher mortality rate in the first 24 hours.

P350

Full-body low-dosage X-ray instead of single X-ray series in trauma: a preliminary experience report of a modified advanced trauma life support algorithm

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Introduction Patients presenting with trauma normally require resuscitation according to the advanced trauma life support (ATLS) algorithm. Techniques suggested during primary survey include X-ray of C-spine, chest and pelvis. This can be time consuming and radiation intensive. In comparison with conventional multiple radiographs, Lodox (Statscan), a full-body digital radiology device, performs a.p. and lateral whole-body examinations in 3–5 minutes with about one-third of the irradiation and without the necessity for lifting patients. This is the first device installed in Europe.
Methods This paper describes our experience with the use of a new low-dose X-ray technique as part of our modified ATLS algorithm, where single–total a.p./lateral body radiographs have been implemented as adjuncts to primary survey in favour of several conventional X-rays.
Results There were 94 patients (males = 59; females = 35) between 4 October and 9 December 2006; age range from 1 to 86 years. The ISS ranged from 3 to 75 (ISS > 16 in 54/94 patients). The average time for obtaining LODOX radiographs was 3.5 minutes (range 3–6 min). The mean time in the resuscitation room (during primary and secondary surveys) was 28.7 minutes with the new technique compared with 29 minutes before implementing LODOX (median time 27 min to 24 min). In 54/94 patients an additional full body CT scan was performed as adjunct to secondary survey. In only 14/54 patients were additional conventional X-rays necessary to visualize the skeleton.
Conclusion The implementation of a modified ATLS algorithm using LODOX allows a complete a.p. and lateral whole-body examination without a significant increase in the time taken for resuscitation. Since we are at the very beginning of a learning curve we are confident that in future the time for the ATLS primary survey can be markedly reduced. The LS imaging system seems to be a useful tool for rapid screening and management of trauma patients.

P351

Peripheral oxygen extraction predicts organ failure and mortality following major trauma

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Introduction Current markers of occult hypoperfusion following major trauma have serious limitations. Our aim was to evaluate oxygen extraction as a resuscitation endpoint, and predictor of organ failure and mortality following trauma.
Methods A prospective, noninterventional study of 39 consecutive patients admitted to a Level 1 trauma unit ICU. Blood gas analysis was performed on samples from three locations: central venous line, peripheral venous line, and arterial line. Blood was drawn 6-hourly in the first 24 hours, and oxygen extraction calculated using the Fick equation. Organ failure was assessed using MODS and SOFA scores.
Results See Table 1. Peripheral, but not central, oxygen extraction with a threshold of 150 ml oxygen extracted per litre of blood distinguished survivors from nonsurvivors on admission to the trauma ICU. Low peripheral oxygen extraction (<150 ml) had an odds ratio for risk of death of 5.3 ($P = 0.016$, Fisher's exact test) and was associated with higher organ failure scores ($P = 0.044$, Mann–Whitney U test). A trend of increasing peripheral oxygen extraction was also a strong predictor of mortality ($P = 0.019$, Mann–Whitney U test) and organ failure ($P = 0.003$, Mann–Whitney U test).

Table 1 (abstract P351)

	Survived	Died	Total
Extract < 150 ml	8	6	14
Extract > 150 ml	23	2	25
Total	31	8	39

Conclusions With an arterial and venous blood sample, and a simple equation, we have for the first time demonstrated that absolute and serial peripheral oxygen extraction are powerful predictors of organ failure and mortality following major injury.

P352

Damage control orthopedics can improve outcome in trauma patients

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Introduction Damage control orthopedics (DCO) is a reviewed concept used in major trauma. Advances in critical care

management enable surgical stabilization in the early phase of trauma care. Logistical organization and accessibility to several therapeutic solutions can influence a physician's decisions regarding a trauma patient. The aim of this study is to investigate whether the timing of surgery and method of stabilization in trauma patients with femoral fracture can influence the incidence of pulmonary complication, MOF and the length of stay in the ICU.

Method In a retrospective study performed at a Level I trauma center, we considered all adult patients with major trauma (ISS >15) and femoral shaft fracture admitted between January 2003 and July 2006. Patients were separated into two groups according to the management strategies for the femoral fracture: group 1, no surgery within 72 hours after primary admission; group 2, surgical stabilization within 72 hours (DCO). To compare the two groups we considered age, ISS, RTS, TRISS, SAPS II, GCS, comorbidity, and other associated surgery. Parameters of evaluation were: mortality in the ICU, ICU length of stay, respiratory failure and length of ventilation, and daily SOFA collected for 8 days. Statistics were determined with the Student *t* and chi-squared tests; $P < 0.05$ was considered significant.

Results We identified 48 patients, 24 for each group. The groups were comparable regarding all the considered parameters except for GCS at admission (group 1, 8.63 ± 5.12; group 2, 12.2 ± 3.99; $P = 0.01$) and TRISS (group 1, $62.04 \pm 34.55\%$; group 2, $82.37 \pm 18.60\%$; $P = 0.01$). We observed in group 2 a significant decrease of mortality (5 vs 0; $P = 0.02$), incidence of ALI–ARDS (13 vs 4; $P = 0.01$) and pneumonia (18 vs 6; $P = 0.01$), a decrease of SOFA score (mean SOFA score: 7.58 ± 4.11 vs 3.97 ± 2.39, $P < 0.001$; maximum SOFA score: 9.83 ± 4.36 vs 5.62 ± 2.97, $P < 0.001$; days with SOFA >6: 3.79 ± 3.08 vs 2.16 ± 2.18, $P = 0.04$).

Conclusions We observed an improvement of respiratory parameters and SOFA score in patients treated with DCO. Furthermore, patients with worse neurological conditions at admission do not undergo orthopaedic surgery because it could worsen the cerebral perfusion (risk related to transfer to a far operating room). The physician's decisions (and therefore the patient's prognosis), in our experience, are limited by access to optimal therapeutic solutions that could improve the clinical course of the patient.

P353

Head trauma: risk factors for early brain death – our experience

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Introduction In a group of patients that evolved in brain death after head trauma, we evaluated the risk factors for an early brain death (in the first 3 days) among the parameters collected prehospital, in the emergency room (ER) and during the ICU stay.

Method All the consecutive patients admitted to the ER of Careggi Hospital that evolved to brain death after head trauma during the period January 2004–June 2006 were considered ($n = 54$). The following parameters were considered for the study: prehospital phase: hypoxemia ($SaO_2 < 95\%$), hypotension (SAPS II < 90 mmHg), orotracheal intubation, fluids ($>1{,}000$ or $\leq 1{,}000$ ml), and GCS; ER phase (ATLS approach): hypoxemia, hypotension, orotracheal intubation, fluids, GCS, blood lactate, pharyngeal temperature, and ISS; ICU stay: SAPS II, daily SOFA score, blood lactate, core temperature, glycaemia, and $ScVO_2$ ($>75\%$ or $\leq 75\%$). On the basis of the timing of brain death, the patients were divided into two groups: group 1 ($n = 27$), brain death occurred in the first 3 days; group 2 ($n = 27$), brain death occurred in the days after. Statistics were determined with the Student *t* and chi-squared tests; $P < 0.05$ was considered significant.

Results The significant differences between the two groups are reported in Table 1. A strict relationship exists between early brain death and prehospital treatment. During the ICU stay low levels of $ScVO_2$ and high levels of glycaemia are related to early brain death.

Table 1 (abstract P353)

	Group 1 ($n = 27$)	Group 2 ($n = 27$)	*P*
Prehospital			
Hypotension	22	13	<0.05
ICU stay			
Glycaemia	170.8 ± 49.5	116.6 ± 24.4	<0.05
$ScVO_2 < 75\%$	15	7	<0.05

Conclusion The results of the study confirm that prehospital hypotension is the main risk factor for an early evolution to brain death in head trauma. Also, patients that have prolonged hypoperfusion and neurohormonal imbalance after the postresuscitation phase present an increased risk of brain death.

P354

Sensitivity and specificity of a triage score dedicated to trauma patients in a tertiary-level hospital: preliminary results

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Introduction The aim of the study was to determine the sensitivity and specificity of the triage criteria adopted for multiple trauma patients in order to activate the Trauma Team in our tertiary-level trauma centre.

Methods A cohort study. Between 1 September and 30 November 2006, all trauma patients admitted to the ED triaged red, yellow or green on admission and discharged as a red code from the ED following specific criteria were included. Triage criteria on admission included at least one of the following: GCS <13, systolic BP >220 and <100 mmHg, $SaO_2 < 95\%$ on oxygen 100% or intubated; clinical signs: penetrating wounds, spinal injury, sternal or flail chest, two long-bone fractures, proximal crash or amputation of limbs, post-traumatic seizures at any time, signs of fracture of the skull; major accident mechanics: fatality in the same vehicle, fall from a height >3 m, prolonged extrication time (>20 min), pedestrian hit by a car, ejection, explosion in a close environment. Severely injured patients at discharge from the ED were defined by: invasive resuscitating procedures (that is, tracheal intubation), invasive life-saving procedures (emergency surgery, defibrillation) and need for admission to the ICU. Sensitivity and specificity of the triage criteria assigned on admission were calculated and compared with the patients that were triaged red at discharge from ED.

Results During the time span, 5,142 trauma patients were admitted to the ED: 4,884 were triaged green, 182 yellow and 76 were triaged as red. Of the 76 red on admission, 55 patients fulfilled the abovementioned criteria and were confirmed severely injured at discharge from ED. Out of the 55, 53 patients were

Table 1 (abstract P356)

		Baseline	5 minutes before	15 minutes before	45 minutes before	5 minutes after	15 minutes after	45 minutes after	Mortality
Group A	RoCBF (ml/min.100 ml)	31.92	35.47	19.32	5.25***				100%
	SjO_2 (%)	71.2	32.8	25.7	28.7***				
Group B	RoCBF (ml/min.100 ml)	30.3	14.2*	14.5*	16.4	33.47	38.24	37.67	50%
	SjO_2 (%)	81.1	25.8***	22.7***	24.4***	38.5**	49.5**	57.1*	

*$P < 0.05$, **$P < 0.01$ and ***$P < 0.001$ for comparison with baseline.

correctly identified by triage criteria, while two patients were missed. The sensitivity is 96%. Out of the 76 triaged red on admission, 53 patients were confirmed at discharge from ED. The specificity is 70%.

Conclusions Even if major accident mechanics were included in the admission triage criteria, overtriage was limited to 30%. On the other hand, undertriage was approximate to zero, and the only two yellow codes missed were related to miscommunication by the prehospital team.

P355

Conjunctival and sublingual microcirculation alterations in head trauma patients with increased intracranial pressure

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Introduction Both the conjunctiva and the sublingual tissue have a common blood supply via the common carotid artery trunk. Moreover, the conjunctiva receives blood from the internal carotid artery and the sublingual tissue receives from the external carotid artery. We hypothesized that conjunctival and sublingual microcirculation can be used to evaluate intracranial and extracranial perfusion and to monitor therapy to improve cerebral perfusion pressure in patients after head trauma.

Methods In three groups of patients with increased intracranial pressure (ICP) (high ICP > 30, medium ICP 20–30 and low ICP < 20) following head trauma, both the conjunctival and sublingual microcirculation was measured using sidestream darkfield imaging (MicroScan®; MicroVision Medical, The Netherlands) to evaluate intracranial and extracranial perfusion. Using microvascular analysis software (MAS®; MicroVision Medical), functional density of small (<20 μm), medium (20–50 μm) and large (>50 μm) microvessels were determined in addition to erythrocyte velocities.

Results Conjunctival microcirculatory flow was intermittent in patients with highest ICP, low-continuous in patients with medium ICP, and normal-continuous in patients with lowest ICP. Intracranial perfusion pressure was lowest in patients with highest ICP and vice versa. Functional vessel densities in the conjuctiva were in the same range in all three groups. However, the sublingual functional capillary densities were consistently lower in all groups as compared with controls, suggesting an active intracranial and extracranial regional autoregulation.

Conclusion Conjunctival microcirculatory flow analysis reflects alterations in cranial perfusion pressure and might be a possible noninvasive endpoint to monitor cerebral perfusion and therapy.

P356

The influence of hypotensive resuscitation in hemorrhagic shock with coexisting severe head injury: an experimental protocol

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Introduction We examined the efficacy of hypotensive resuscitation, compared with fluid resuscitation, in patients with closed abdominal trauma and coexisting severe head injury.

Method Female pigs, 25–30 kg body weight, were used. Retrograde catheterization of the internal jugular vein (SjO_2) and laparotomy was performed. A surgical knot 4 mm long was made at the aorta, with a 3.0 diameter stitch. The abdomen was closed. Then a craniotomy and traumatic brain injury (TBI) was made. A regional cerebral blood flow catheter (RoCBF) was placed under the dura. After the TBI the intraabdominal hemorrhage was made by pulling the titch (rupture of the aorta). The animals were assigned into two groups: group A (fluid resuscitation) and group B (hypotensive resuscitation). The animals that survived after 1 hour of hemorrhage were managed by surgical checking and with 1 hour more of fluid resuscitation.

Results See Table 1: RoCBF and SjO_2 before and after the surgical checking of the hemorrhage.

Conclusion In group B there was complete restoration of cerebral blood flow and brain oxygenation, after the surgical checking of hemorrhage. Hypotensive resuscitation causes significant reduction in mortality in patients with closed intraabdominal trauma and coexisting head injury, without putting cerebral function in jeopardy.

P357

Hyperoxemia improves cerebral autoregulation in severe traumatic brain injury

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The intrinsic autoregulation mechanisms of the cerebral vessels that normally maintain a constant cerebral blood flow (CBF) relatively independently from the cerebral perfusion pressure variations are frequently impaired in the severely traumatized. It has been shown that hyperventilation can restore the cerebral autoregulation and controlling intracranial pressure, but much less attention has been given to the effects of the hyperoxic state in the restoration of cerebral autoregulation. The purpose of the study was to compare the autoregulatory response to hyperventilation vs hyperoxia in severe traumatic brain injury.

We prospectively examined 186 (aged 34.4 ± 14.99 years) patients with severe traumatic brain injury (postresuscitation GCS 5.98 ± 3.0957) following admission to the neurosurgical ICU of a level one trauma hospital. Hyperventilation and hyperoxia studies were conducted, recording middle cerebral artery flow velocity and the autoregulation index (ARI) bilaterally and simultaneously at baseline and posthyperventilation (CO_2 reactivity = %ΔCBF/ΔpCO$_2$)/hyperoxia (O_2 reactivity = ΔPbtO$_2$/ΔpO$_2$). Continuous multimodal neuromonitoring, intracranial pressure, mean arterial blood pressure, cerebral perfusion pressure, end-tidal CO_2 (ETCO$_2$), PbtiO$_2$, and SjvO$_2$, was recorded.

The ARI (normal 5 ± 1) in these head-injured patients averaged 2.2 ± 1.5 on day 1 and gradually improved over the 10 days of monitoring. The ARI significantly improved with hyperoxemia, during the first 6 days after injury when compared with the ARI measured at normoxemia. The mean left ARI difference during hyperoxia was 0.4069 ± 1.7948 while the right ARI difference was 0.4708 ± 1.8413. The average change in pCO$_2$ during hyperoxia was 35.6468 ± 5.8778. These changes in the ARI during hyperoxia were smaller than those observed during hyperventilation. Hyperventilation increased the ARI by average 0.8519 ± 0.2310 on the left and 1.0833 ± 0.4654 on the right.

Pressure autoregulation was impaired in these head-injured patients. Hyperoxia significantly improved pressure autoregulation. The very small change in pCO$_2$ induced by hyperoxia does not seem to explain this improvement in pressure autoregulation. Vasoconstriction induced by hyperoxia may partially contribute to the improved pressure autoregulation.

P358

C1-inhibitor attenuates neurobehavioral deficits following controlled cortical impact brain injury in mice

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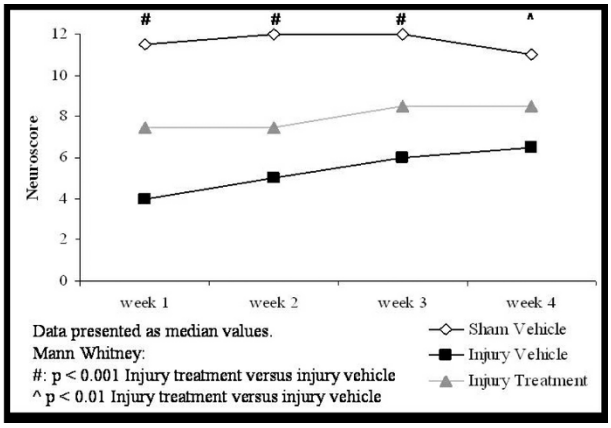
Introduction The goal of the study was to evaluate the neurobehavioral effects of the C1-inhibitor (C1-INH), an endogenous inhibitor of complement and contact-kinin pathways, following controlled cortical impact (CCI) brain injury in mice.

Figure 1 (abstract P358)



Methods Mice were anesthetized and subjected to CCI brain injury. At 10 minutes postinjury, animals randomly received an intravenous infusion of either C1-INH (15 U) or saline (equal volume, 150 μl). A second group of mice received identical anesthesia, surgery, and saline to serve as uninjured controls. The neurobehavioral motor outcome was evaluated weekly (for 4 weeks) by performing a neuroscore, and cognitive function was evaluated at 4 weeks postinjury using the Morris water maze.

Results Consistently, brain-injured mice receiving C1-INH showed attenuated neurological motor deficits during the 4-week period compared with injured mice receiving saline (Figure 1). At 4 weeks postinjury we observed a trend towards a better cognitive performance in mice receiving C1-INH compared with mice receiving saline ($n = 8$ per group, $P = 0.08$).

Conclusion Post-traumatic administration of the endogenous complement inhibitor C1-INH significantly attenuates neurological motor deficits associated with traumatic brain injury.

P359

Haemostatic activation markers in brain injury for mortality prediction: comparison of blood samples from the jugular bulb and central venous line

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Objective Our aim was the identification of coagulopathy disorders and their relation to outcome in severely head-injured patients.

Patients and methods A prospective study was performed June 2003–March 2004. Included were critically ill patients with isolated closed severe head trauma. Collected data were demographics, management prior to and during ICU hospitalization (sedation, catecolamin drug use, blood product transfusion, intracranial pressure monitoring, neurosurgical emergency surgery, etc.), CT-scan results, daily worst Glasgow Coma Scale score, and admission Simplified Acute Physiology Score II. We inserted an arterial catheter for invasive pressure monitoring, a central venous catheter and a unilateral jugular bulb in front of the most damaged brain hemisphere (cf. CT scan). Jugular bulb thrombosis was prevented by continuous infusion of 2 ml/hour isotonic serum without heparin. Blood samples were obtained simultaneously from the central venous line (K) and jugular bulb (B) at admission, 6 hours, 12 hours, and then in case of neurological aggravation or daily until 5 days. We measured the platelet count, prothrombin time (PT), activated partial thromboplastin time (ACT), fibrinogen concentration (Fib), prothrombin fraction 1+2 (F) and thrombin–antithrombin complex (TAT). During the study only central venous blood samples (PT, ACT, Fib and platelet count) could be available if necessary. Otherwise blood samples were centrifuged and preserved refrigerated for post-hoc analysis. Statistical analysis was by Student's *t* test, paired *t* test for paired results and analysis of variance. Significance was set as $P < 0.05$.

Results The total $n = 19$; nine survivors (S) and 10 deaths (NS). No differences between S and NS in demographics, management modalities, admission GCS score (7 ± 3), CT scan, and SAPS II (27 ± 10 vs 30 ± 17, $P = 0.69$). The B vs simultaneous K platelet count was significantly lower in all drawn blood samples, with a trend to decrease over time. S vs NS at day 2 and day 3: 191 ± 60 vs 125 ± 35 ($P = 0.017$). The admission B thrombin fraction was higher in NS (1,000 ± 209 vs 460 ± 294, $P = 0.014$). The B day 1 TAT was higher in NS: 45 ± 20 vs 9.6 ± 12 ($P = 0.02$). No

difference was observed for other tests between B vs K and S vs NS for different paired tests.
Conclusion Procoagulant factors (F and TAT) are valuable prognostic factors at day 1 in closed isolated severe head trauma.

P360

Decreased adrenal reserve after etomidate use in moderate and severe traumatic brain injuries: clinical implications

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Introduction Etomidate is frequently used as an anesthetic induction agent for the intubation of head trauma patients. The clinical impacts of its effects on adrenal function are still debated. Therefore, the primary objective of this study was to determine the length and the importance of relative adrenal insufficiency (RAI) induced by etomidate in moderate and severe head trauma patients. The secondary objective was to determine etomidate's impacts on mortality and morbidity.
Methods This was a prospective cohort study. Eligible participants were intubated moderate to severe head trauma victims aged ≥16 years, admitted to a tertiary neurosurgical reference center between August 2003 and November 2004. The induction agent was chosen by the physician, without any interference by the research team. ACTH stimulation tests (250 µg) were performed on each participant 24, 48 and 168 hours after intubation. Responses to these tests were compared between patients having received etomidate and those having received other induction agents. RAI was defined as an increase in cortisol levels <248.4 nmol/l (9 µg/dl), measured 30 and 60 minutes after the ACTH test. Logistic and linear regression models were used to compare the two groups of patients on outcomes while taking confounding variables into account.
Results Of the 94 patients eligible for this study, 40 (43%) gave consent for the ACTH test. Fifteen patients received etomidate and 25 received other induction agents. At 24 hours, there were no differences in the risk of RAI between groups (OR: 1.8, 95% CI: 0.2–14.3, $P = 0.59$). However, at 24 hours, subjects who had received etomidate presented a significantly lower response to ACTH (adjusted mean: 299.7 nmol/l, 95% CI: 214.7–384.8 versus 503.8 nmol/l, 95% CI: 441.8–565.7, $P = 0.002$). At 48 and 168 hours, this difference disappeared. For all eligible patients ($n = 94$), there was a nonsignificant trend to an increased risk in mortality in the etomidate group (adjusted OR: 4.8, 95% CI: 0.6–35.9, $P = 0.13$). Etomidate was also associated with an increased risk of pneumonia (adjusted OR: 3.0, 95% CI: 1.0–8.7). The adjusted length of stay in the ICU was not different between groups. At discharge, the adjusted motor Functional Independence Measure (FIM) score was significantly lower for subjects in the etomidate group (32 versus 56, $P = 0.002$), but the adjusted cognitive FIM score was not significantly different in the etomidate group (35 versus 46, $P = 0.15$).
Conclusions These results suggest that etomidate decreases the adrenal reserve up to 24 hours after a single dose used for the intubation of traumatic brain injury victims. A larger randomized controlled trial is needed to further assess etomidate's impacts on morbidity and mortality.

P361

Differential effects of *in vitro* norepinephrine on platelets isolated from severely traumatic brain injured patients

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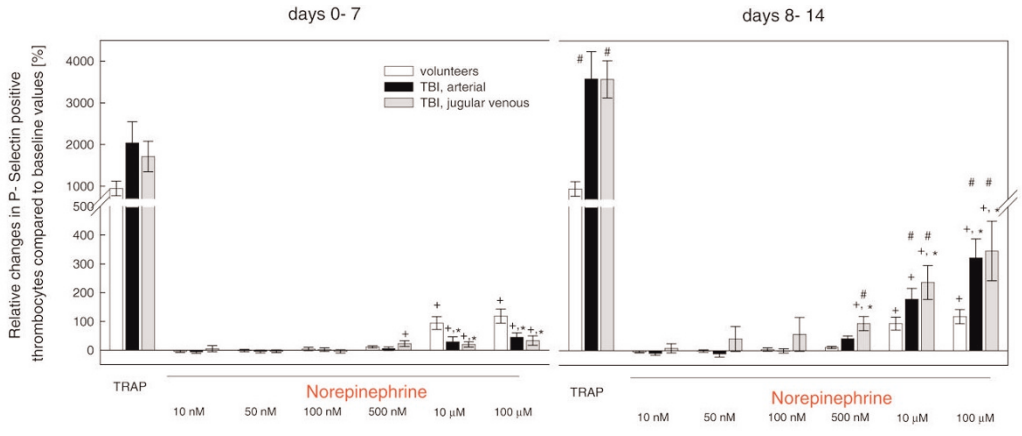
Introduction Norepinephrine used in clinical routine to increase cerebral perfusion following severe traumatic brain injury (TBI) may activate α_2-adrenergic receptors on platelets, thereby possibly promoting formation of microthrombosis and inducing additional brain injury.
Methods Arterial and jugular venous platelets isolated from norepinephrine-receiving TBI patients ($n = 11$) and healthy volunteers ($n = 36$) (cubital vein) were stimulated *in vitro* with increasing

Figure 1 (abstract P361)



Changes in P-selectin expression in isolated platelets stimulated *in vitro* with norepinephrine or TRAP. +$P < 0.001$ vs low-dose norepinephrine; *$P < 0.001$ vs controls; #$P < 0.001$ vs first week.

norepinephrine concentrations (10 nM to 100 μM); thrombin receptor activator peptide (TRAP) served as positive control. P-selectin expression was determined by flow cytometry (FACS).
Results Following TBI, the number of unstimulated P-selectin-positive platelets was significantly decreased in the second week by 60%. During the first week, the *in vitro* stimulatory effect was significantly reduced; in the second week, however, norepinephrine-mediated effects exceeded changes in controls and the first week without a difference between arterial and jugular venous platelets (Figure 1).
Conclusion Clinically relevant norepinephrine concentrations are <25 nM. The present *in vitro* effects occurred at concentrations >500 nM. Thus, a clinically relevant impact appears doubtful.

P362

Ultrasound evaluation and risk factors for deep venous thrombosis in the intensive care unit

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Introduction Critically ill patients have a high risk of deep venous thrombosis (DVT); however, data about prevalence and specific risk factors in the ICU are conflicting and the prophylaxis strategies are still debated. The aim of this study is to evaluate the prevalence and risk factors in an ICU dealing with trauma and major surgery patients.
Methods We analyzed retrospectively data from 142 patients (56 ± 4.8 years) admitted to the ICU from December 2004 to December 2005. We recorded the history, diagnosis, SAPS II, length of stay and major surgery. All patients received standard prophylaxis (LMWH and/or mechanical device). For DVT diagnosis, three compression ultrasound examinations were performed (a) within 48 hours from admission, (b) between the 7th and 10th days, and (c) between the 13th and 16th days. The prevalence of DVT and risk factors were analyzed in the whole population and in the following four groups: ≤40 years, 41–59 years, 60–74 years, and ≥75 years. Statistics were determined using the Wilcoxon and Mann–Whitney tests and one-way analysis of variance on SPSS; $P < 0.5$ was considered significant.
Results One hundred (70%) patients were admitted after trauma, 15 (11%) after surgery, 27 (19%) had medical disease. The mean SAPS II score was 45 ± 15.8 and the mean length of stay was 16 ± 9.84 days. Forty-six patients (32.4%) underwent major surgery following the admission. The overall prevalence of DVT was 17.6% (25/142), with the highest value (24.2%) in the 41–59 year group and the lowest (12.5%) in the >75 year group. DVT was diagnosed in 12/25 (48%) patients within 48 hours from ICU admission and 7/12 (58.3%) had direct venous injury. DVT was diagnosed in the remaining patients after 10 days. We found a strong relationship ($P < 0.06$) between the length of stay and DVT in patients <40 years. No significant differences were found regarding SAPS.
Conclusions In our experience, DVT prevalence showed a bimodal occurrence with a first short-term peak, associated with traumatic or surgical direct venous injury, and a medium-term peak, related to an ICU stay >10 days. We therefore oriented the surveillance to the two periods of higher DVT prevalence and we established a training program for the intensivists to improve DVT detection, relieving the workload of the ultrasound physician.

P363

Venous thromboembolism in critically ill patients: incidence and risk factors

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Objective Despite the high risk of venous thromboembolism (VTE) in ICU patients, only few studies have examined this group of patients systematically. The objective of this study is to examine the incidence and risk factors of VTE among critically ill patients.
Design A prospective cohort study.
Setting A closed university-affiliated ICU in a medical–surgical ICU in the Kingdom of Saudi Arabia.
Patients We enrolled consecutive patients >12 years of age expected to stay in the ICU >48 hours. We excluded patients on systemic anticoagulation and patients with pulmonary embolism (PE) or deep venous thrombosis (DVT) on admission to the ICU or diagnosed within 24 hours of ICU admission. We recorded *a priori* defined VTE risk factors at baseline and daily. Our ICU implements a protocol for thromboprophylaxis, which is based on the evidence-based ACCP guidelines. The primary endpoint was the development of PE or DVT during ICU stay. We used multivariate regression analysis to determine independent predictors of VTE.
Results Among 277 patients with a mean APACHE II score of 25 (+9), the incidence of VTE was 7.2% (95% CI 4.5–11). We identified three independent risk factors for ICU-acquired venous thromboembolism: stroke (OR 13.5, 95% CI 1.9–91.19, $P = 0.008$), femur fracture (OR 4.5, 95% CI 1.18–17.10, $P = 0.03$), and ICU length of stay (OR for each day increment 1.08, 95% CI 1.03–1.13, $P = 0.002$). After adjustment for APACHE II score, VTE was an independent predictor of mortality (OR 3.85, 95% CI 1.11–13.29, $P = 0.03$).
Conclusions VTE is relatively common complication in critically ill patients and is associated with significant mortality. Longer ICU length of stay, stroke and femur fracture are independent predictors for VTE. These findings suggest the need for more effective prophylactic strategies in critically ill patients, especially those at higher risk.
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P364

Cardiopulmonary bypass and recombinant plasminogen activator for treatment of experimental fatal pulmonary embolism

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Introduction Treatment of acute pulmonary embolism (PE), which causes life-threatening cardiovascular collapse, consists of cardiopulmonary bypass (CPB) and surgical embolectomy. In the clinical practice we have treated three such patients successfully with CPB but instead of performing embolectomy, administered recombinant plasminogen activator (rt-PA). We studied the circulatory and respiratory effects of this combined therapy in a swine model of fatal PE.
Methods Seven pigs (90 kg) were i.v. anesthetized, muscle relaxed, tracheally intubated and mechanically ventilated (FiO_2 1.0). A large-bore catheter (8.5 mm ID) was inserted in the right superior vena cava (for injection of preformed blood clots) and large-bore catheters were inserted in the inferior vena cava via the

femoral vein and in the aorta via the femoral artery (for accessing CPB). We measured the mean arterial pressure (MAP), cardiac output (CO), blood gases, pulmonary artery pressure measurement (MPAP), end-tidal CO_2 ($ETCO_2$) and blood gases. Then 100–300 ml preformed blood clot was injected until systemic circulation ceased (systolic AP < 25 mmHg) and a 5 minute interval was allowed before start of CPB (flow rate of 4–7 l/min). Heparin 10,000 IE was given i.v., and rt-PA 10 mg as an i.v. bolus followed by an i.v. infusion of 90 mg during 2 hours. If ventricular fibrillation occurred, cardioversion was performed. After 145 minutes CPB was weaned off, and after a further 40 minutes the experiment was ended.

Results Five animals developed ventricular fibrillation, while one animal maintained sinus rhythm. After 2 hours all animals had an atrial rhythm. All animals were weaned off CPB and survived until the experiment ended. Values before and after CPB (median and range): MAP (mmHg) 101 (86, 109) and 75 (46, 106); CO (l/min) 6.7 (4.3, 11) and 6.2 (3.6, 7.8); MPAP (mmHg) 22 (19, 36) and 44 (31, 82) ($P < 0.05$); $ETCO_2$ (kPa) 5.6 (4.3, 6.5) and 2.7 (2.4, 3.4) ($P < 0.05$); $PaCO_2$ (kPa) 6.2 (5.2, 7.2) and 6.1 (4.8, 7.3); PaO_2 (kPa) 60 (50, 68) and 55 (30, 64).

Conclusion Although there were signs – that is, lower $ETCO_2$ and higher MPAP – that the massive clots were not fully dissolved after 185 minutes, this study shows that fatal PE might be treated effectively with CPB combined with simultaneous thrombolytic therapy.

P365

Early coagulation alterations in intensive care unit burn patients

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Critical Care 2007, **11(Suppl 2):**P365 (doi: 10.1186/cc5525)

Introduction The aim of the present study was to examine the coagulation status of patients in the early postburn period.

Method Coagulation and fibrinolysis parameters – antithrombin III (ATIII), protein C (PrC), free protein S (PrS), plasminogen activator inhibitor 1 (PAI-1), tissue plasminogen activator (t-PA), thrombin/antithrombin complexes (TAT), plasmin/α_2-antiplasmin complexes (PAP), fibrin degradation products (F1.2) – were measured at ICU admission and daily thereafter for 7 postburn days.

Results Forty-five patients were screened (nine nonsurvivors and 36 survivors). All patients had a severe deficiency of the coagulation inhibitors on admission. Normalization of these levels in survivors was observed at day 5 for ATIII and PrC, and at day 7 for PrS. All patients had elevated levels of TAT during the investigation period, but survivors had significantly lower levels at day 7 postburn (6.2 ± 4.9 vs 11.4 ± 4.5 μg/l, $P < 0.001$). PAP levels were within the physiological range in both groups at day 1, remained low in survivors, but raised significantly in nonsurvivors at day 7 (19.3 ± 14 vs 80.9 ± 10.4 μg/l, $P = 0.003$). The t-PA levels were elevated permanently only in nonsurvivors. PAI-1 levels were increased at day 1 in both groups, but returned to normal values at day 5 in survivors. The degree of PAI-1 activation was significantly higher than this of t-PA. The F1.2 levels were permanently elevated and there was no statistically significant difference in both groups. A logistic regression analysis revealed that ATIII and PrS at days 3, 5 and 7, Pr C at days 5 and 7 and TAT at day 7 were independent predictors of ICU death.

Conclusion Our findings indicate the early postburn dysregulation of the hemostatic balance characterized by the activation of procoagulant pathways. Although fibrinolysis was activated, the inhibition of fibrinolysis was more pronounced at the same time. The coagulation inhibitors and TAT levels seem to be early predictors of ICU mortality.

P366

Fibrinolysis during cardiopulmonary bypass detected with thromboelastography

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Background Fibrinolysis is a common haemostatic abnormality during cardiopulmonary bypass (CPB). Thromboelastography (TEG) is a good method to detect both types of fibrinolysis.

Methods Four hundred and ninety-nine patients during mild hypothermic CPB and elective surgery were monitored with TEG (first – after the induction, second – after rewarming, third and fourth – at the end of surgery native and heparinase). No prophylactic antifibrinolytics were used. The data of the study group were compared with a control group of 475 patients monitored only with laboratory tests (fibrin degradation products (FDP) and D-dimers). Peroperative and 24 hour postoperative bleeding, number of transfusions, aprotinin therapy and reexploration were recorded. Correlations between the presence of fibrinolysis and blood loss and transfusion therapy and between aprotinin administration and blood loss and number of transfusions were evaluated.

Results The frequency of fibrinolysis measured with TEG: before surgery – primary 3.2%/secondary 3.4%; during CPB – 18.8%/0.6%; after surgery – 7%/1.4% (native), 5.6%/0.6% (heparinase). Positivity of fibrinolysis detected with laboratory tests was 100%. The TEG parameter of fibrinolysis (LY30) was significantly increased during CPB. The frequency of aprotinin administration was 12% TEG, 10.7% control. No correlation between positivity of fibrinolysis and peroperative/postoperative blood loss and red blood cells (RBC) and fresh frozen plasma (FFP) transfusions were recorded. No correlation between aprotinin administration and peroperative/postoperative blood loss and RBC transfusion were recorded. Positive correlation between aprotinin administration and FFP transfusion were recorded

Conclusion Fibrinolysis was usually not associated with serious bleeding. There was no positive effect of aprotinin to reduce bleeding or transfusion therapy. FDP and D-dimers are not useful to detect fibrinolysis in cardiac surgery.

P367

ROTEM® thrombelastometry in on-pump cardiac surgery patients

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Objective On-pump cardiac surgery is frequently associated with intraoperative and postoperative bleeding. ROTEM® is a point-of-care method that reflects more closely than classical coagulation tests the *in vivo* haemostatic activity and the contribution of fibrinogen and platelets to clot formation.

Methods Two hundred and thirty-two patients (age 67 ± 10 years) with elective cardiac surgery and an on-pump time >45 minutes (mean 112 ± 52 min) were enrolled. Preoperative, intraoperative and postoperative blood samples were taken from an arterial catheter. The ROTEM® system and test kits (INTEM/EXTEM =

intrinsic/extrinsic activation, FIBTEM = EXTEM with inhibition of platelets) were from Pentapharm (Munich, Germany).
Results The clot formation time (CFT) and maximum clot firmness (MCF), but not clotting time (CT), were strongly correlated with the fibrinogen level and platelet count. Surgery significantly decreased the ROTEM haemostatic activity, but normalised in most patients within 14–18 h postoperation. Lowest haemostatic activity (dramatic increase in CT and CFT, decrease in MCF) was seen when patients were conditioned for cardiopulmonary bypass (CPB). When connected to CPB, the CT and CFT turned to recover, but MCF in EXTEM remained unchanged and MCF in FIBTEM declined further indicating continuous fibrinogen consumption. In 12.5% of our patients, postoperative MCF in FIBTEM was reduced to <9 mm indicating a need for fibrinogen substitution. Low postoperative activity in ROTEM® was associated with high postoperative blood loss. The positive predictive value and specificity of FIBTEM were clearly superior to those of the APTT or prothrombin time. Up to 50% of patients had an increased haemostatic activity in preoperative ROTEM®, and this was associated with high CRP levels and intraoperative blood loss.
Conclusions ROTEM® is a valuable tool to monitor perioperative haemostasis. The decreases in haemostatic activity and postoperative bleeding are probably due to anticoagulant therapy as well as fibrinogen and platelet consumption. An increased preoperative haemostatic activity is probably due to an acute phase reaction associated with advanced atherosclerosis, and the high intraoperative bleeding in these patients might be due to the atherosclerotic vessels rather than due to an insufficient haemostasis.

P368

Low-frequency hemoviscoelastography: a new method of diagnostics for coagulation disorders after abdominal surgery for cancer

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Critical Care 2007, **11(Suppl 2):**P368 (doi: 10.1186/cc5528)

Background Venous thromboembolism is one of the most common complications seen in cancer patients and may be due to the hypercoagulable state of the malignancy and to its surgical treatment. Despite clinical and laboratory evidence of perioperative hypercoagulability, there are no consistent data evaluating the extent, duration, and specific contribution of platelets and procoagulatory proteins by *in vitro* testing.
Materials and methods Patients undergoing planned curative open surgery for abdominal cancer received MEDNORD (Ukraine Co analyser) analysis (HVG), a viscoelastic test that measures clot formation and includes information on the cellular, as well as the plasmatic coagulation, system. We examined the efficacy of a variety of coagulation tests. A complete coagulation screen, activated clotting time, thromboelastography (TEG) and hemoviscoelastography (HVG) were performed before surgery, at the end of surgery, and on postoperative days 1, 2, 3, and 7; they were analyzed for the reaction time and the maximal amplitude (MA). We tested the hypothesis that the parallel use of standard TEG and HVG can assess postoperative hypercoagulability and can estimate the independent contribution of procoagulatory proteins and platelets.
Results and discussion We calculated the elastic shear modulus of standard MA (Gt) and HVG MA (GH), which reflect the total clot strength and procoagulatory protein component, respectively. The difference was an estimate of the platelet component (Gp). There was a 14% perioperative increase of standard MA, corresponding to a 48% increase of Gt ($P < 0.05$) and an 80–86% contribution of the calculated Gp to Gt. We conclude that serial standard TEG and the HVG viscoelastic test may reveal the independent contribution of platelets and procoagulatory proteins to clot strength. Using multiple linear regression, all coagulation, TEG and HVG variabilities were used to model postoperative hypercoagulation. Results showed that some components of the TEG failed to identify hypercoagulation ($r < 0.2$, $P > 0.75$). However, three components of the routine coagulation assay, including bleeding time, prothrombin time, and platelet count, could be modeled to show prolonged postoperative hypercoagulability ($P < 0.01$). We conclude that all components of the HVG test reflect postoperative coagulopathies; these results suggest that it may be useful in determining the coagulation status of cancer patients perioperatively.
Conclusion Postoperative hypercoagulability, occurring for at least 1 week after major cancer abdominal surgery, may be demonstrated by the HVG viscoelastic test. This hypercoagulability is not reflected completely by standard coagulation monitoring and TEG, and seems to be predominantly caused by increased platelet reactivity. The HVG viscoelastic test provides a fast and easy to perform bedside test to quantify *in vitro* hemocoagulation.

P369

Thrombin generation in on-pump cardiac surgery patients

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Critical Care 2007, **11(Suppl 2):**P369 (doi: 10.1186/cc5529)

Objective Cardiac surgery, in particular when done with cardiopulmonary bypass (CPB), is frequently associated with excessive intraoperative and postoperative bleeding. Here we employed the Technothrombin® thrombin generation assay (TGA; Technoclone) to monitor changes in perioperative haemostasis.
Methods One hundred and forty-eight patients (age 66.0 ± 9.8 years; 103 males, 45 females) with elective cardiac surgery and a CPB time >45 minutes (mean 114 ± 56 min) were enrolled. Arterial blood samples were obtained preoperative, postoperative and 14–18 hours postoperative and centrifuged within 30 minutes after withdrawal, for 5 minutes at 5,000 x *g*. Plasma samples were stored until analysis at –80°C. Thrombin generation (TG) induced by the TGA RC low reagent (71.6 pM tissue factor) was measured in 96-well multiplates using a FLUOstar OPTIMA fluorescence reader (MWG Labtech).
Results Due to cardiac surgery, the lag-phase and time-to-peak of TG increased by 45% and 35%, respectively. In parallel, the peak thrombin concentration and maximum slope decreased by 42% and 51%, respectively ($P < 0.000001$). Both the lag-phase and time-to-peak returned to basal values within 14–18 hours postoperative, but the peak thrombin and maximum slope of TG rose above the preoperative values (+39% and +68%, $P < 0.0005$). The on-pump time was positively correlated with lag phase and time to peak and negatively correlated with peak thrombin and maximum slope of TG when measured at 14–18 hours postoperative, but there was no correlation at early postoperative. With respect to classical coagulation parameters, significant correlations were observed between TG and activated partial thromboplastin time at preoperative and 14–18 hours postoperative, and between TG and prothrombin time at postoperative ($P < 0.025$–0.001). At 14–18 hours postoperative there was a significant correlation of TG with platelet as well as leukocyte counts ($P < 0.025$).

Conclusions The data provide clear evidence for a marked decrease of TG during cardiac surgery followed by an excess restoration in the postoperative phase. Factors released from platelets and leukocytes (procoagulant microvesicles?) might contribute to the enhanced TG observed at 14–18 hours postoperative.

P370

Activated clotting time (ACT) measuring devices used simultaneously do not produce correlating ACT values

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Introduction The lack of a 'gold standard' activated clotting time (ACT) measuring device gives rise to the broad range of ACT measuring devices currently on the market. The present study focused on the inter-device and intra-device differences (for example, reproducibility of ACT measurement) in four different ACT measuring systems.
Methods (1) Hemochron celite tubes, (2) Aktalyke celite tubes, (3) Actalyke ACT-Max tubes and (4) Hemochron Junior low-range (LR) or high-range (HR) cartridges were simultaneously filled with blood drawn (n = 3,997) at baseline, at 3 minutes following administration of heparin (300 IU/ kg), 5 minutes after starting cardiopulmonary bypass (CPB), every 30 minutes during CPB and thereafter at 15 minutes following protamine administration.
Results The ACT values measured simultaneously using four different ACT measuring devices did not correlate with each other at any measurement time. Reproducibility of ACT measurement (for example, intra-device difference) was, in descending order, best for Hemochron Junior, Actalyke ACT-Max, Hemochron celite and Aktalyke celite.
Conclusion The Hemochron Junior ACT measuring device showed the smallest intra-device measuring error. No correlation, however, could be established between ACT values measured with the four devices tested.

P371

Orgaran® use in intensive care unit patients with heparin-induced thrombocytopenia and acute renal failure

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Introduction Orgaran® (danaparoid sodium) is a low-molecular-weight, nonheparin glycosaminoglycan antithrombotic that is currently a first-line treatment for heparin-induced thrombocytopenia (HIT). This study reports on the safety of Orgaran® in ICU patients suffering from HIT and acute renal failure requiring continuous renal replacement therapy (haemofiltration).
Methods Data on 96 case reports from personal experience and publications have been collated.
Results Nineteen females and 59 males (18 unknown gender) with a median age of 60 years (range 22–95 years) presented with a variety of clinical problems that either preceded or complicated their HIT; for example, postoperative/accidental trauma or overt bleeding in 61, sepsis/septicaemia/septic shock in 37, thromboembolism in 23, multiple organ dysfunction syndrome in 14, disseminated intravascular coagulation in eight and other miscellaneous serious problems in 38.
A variety of continuous extracorporeal haemofiltration circuits was used for from 1 to 39 days (median 7 days). The Orgaran® dosing schedule was usually initiated with a 2,000–2,500 U intravenous bolus injection. After two step-down dose periods the subsequent maintenance infusion was usually titrated according to each patient's thromboembolic and bleeding risk status. Hence most patients received 100–400 U/hour, but 11 patients required up to 600 U/hour temporarily to control extracorporeal circuit clotting.
There were 12 minor bleeding events, occurring mostly during the maintenance infusion rate adjustment period and which responded to transient interruption and/or lowering of the infusion rate. Eleven nonfatal major bleeding events occurred (four due to procedural errors) and eight fatal major bleeds, two of which occurred 3 days and 8 days after Orgaran® discontinuation.
Plasma anti-FXa levels were reported for 38 patients. During seven of the eight fatal bleeding episodes the plasma anti-FXa levels were ≥0.8 U/ml in three patients and 0.31–0.66 U/ml (that is, within the target range) in the other four patients. The highest anti-FXa response of 2.00 U/ml was associated with minor bleeding from an angiomatous malformation and stopped when the Orgaran® dose was reduced. However, of the 11 patients receiving >400 U/hour, four suffered major bleeding (three fatal) and two developed minor bleeding. Most of these patients received continuous arterio-venous haemodiafiltration treatment, which may have been a contributory factor.
Conclusions We recommend that maintenance Orgaran® infusion rates ≥400 U/hour should be avoided unless serious circuit clotting is grossly affecting the haemofilter life. The infusion rate should be monitored clinically; that is, on the basis of bleeding and circuit clotting rather than the patients' plasma anti-FXa responses.

P372

High incidence of positive heparin antibodies in a multidisciplinary intensive care unit

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Introduction Heparin-induced thrombocytopenia (HIT) presents with thrombocytopenia and high risk for venous and/or arterial thrombosis, as an adverse effect of heparin (especially unfractioned).
Objective To evaluate the incidence of positive heparin antibody test in a multidisciplinary ICU for the time period from 1 January 2006 to 30 November 2006.
Methods We retrospectively reviewed all laboratory tests for heparin antibodies requested from the ICU for the period of January–November 2006. The blood sample analysis was performed with ELISA (Asserachrom® HPIA; Diagnostica Stago, Asnieres, France). All patients were receiving fractioned heparin subcutaneously for prophylaxis when indicated. Flushes of unfractioned heparin for catheter clotting prevention were given to all patients. Only 'positive' results were considered positive, whilst 'mildly positive' and 'uncertain' results were considered negative.
Results During that period 300 patients were admitted (mean duration of stay 15 ± 16 days, 25th–75th 4–22 days) to the ICU; 212 (70%) were survivors and 88 (30%) were nonsurvivors. All patients presenting with thrombocytopenia (platelets < 150,000/dl) or showing a decrease >50% of their admission day's platelet count were checked for heparin antibodies. Fifty-two samples retrieved from 48 patients suspicious for HIT were sent for heparin antibody analysis. Of the 48 patients checked, 15 (31%) were positive and 33 (68%) negative. Three of the suspected patients

suffered from pulmonary embolism and were treated with therapeutic doses of i.v. unfractioned heparin; one of them was positive for heparin antibodies.
Conclusions Our findings of high incidence of positive heparin antibodies may be mainly due to unfractioned heparin flushes. The use of heparin flushes with the new high-quality catheters and monitoring kit is questionable. Since low doses of unfractioned heparin could lead to the production of antibodies and subsequently to HIT, further studies should examine the risk-to-benefit ratio of the use of unfractioned heparin flushes in the ICU setting.

P373

The beneficial effects of the combined methods in investigating heparin-induced thrombocytopenia

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Introduction Heparin-induced thrombocytopenia (HIT) type II is a serious side effect of unfractionated heparin, and to a lesser extent of low molecular weight heparins. It is mediated through an immunological mechanism and leads to platelet aggregation. The occurrence of HIT varies between 1% and 5% of patients receiving heparin while a substantial fraction of them develops thrombosis (HITT). Therefore, the rapid and accurate confirmation of HIT is a necessity. The laboratory assays available for the diagnosis of HIT are based on the detection of HIT antibodies or on the consequences of platelet activation (functional methods).
The purpose of the present study was to improve HIT recognition by the combination of functional and antibody determination assays.
Patients and methods Fifty-three patients who presented thrombocytopenia while receiving UFH or LMWH participated in the study. A positive control group consisting of 15 patients known to suffer from HIT/HITT was used. Moreover, 19 healthy donors never exposed to heparin also participated as negative controls.
The antibody determination was performed using commercially available ELISA kits. In the functional assays, heparin-induced platelet activation/aggregation (HIPA) and a flow cytometric technique for the detection of platelet microparticles released (platelet microparticle assay) were included.
Results None of the negative control individuals were positive in any applied method. In contrast, all the participants of the positive control group were found positive in all the applied methods. No HIT was detected in 10 patients, seven of whom were pregnant at different gestational ages. The remaining 43 thrombocytopenic patients were positive in HIPA and 39 of them were also positive in the platelet microparticle assay. Out of these 39 patients, only 16 were positive in the ELISA assay.
Conclusions In comparison with the HIT-positive control group it was found that: a 92% agreement existed between the HIPA and the platelet microparticle assays; and the positive results in the ELISA were significantly lower than in the functional methods, indicating perhaps a lower sensitivity (41% agreement with the flow cytometric method and 32% with the HIPA). Therefore, the combination of functional and antibody detection assays is a necessity for the HIT recognition since both could give pseudo-positive or pseudo-negative results.

P374

The effect of male-donor-only fresh frozen plasma on the incidence of acute lung injury following ruptured abdominal aortic aneurysm repair

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Introduction Transfusion-related acute lung injury, due to plasma from female donors containing antileucocyte antibodies, may be a common contributor to the development of acute lung injury (ALI) in the critically ill. In July 2003 the English Blood Service stopped using female donor plasma for the manufacture of fresh frozen plasma (FFP). Patients undergoing repair of ruptured abdominal aortic aneurysm (AAA) receive large amounts of FFP and often develop ALI. We investigated whether the change to male-only FFP was associated with a change in incidence of ALI in patients undergoing emergency AAA repair.
Methods A before-and-after, observational, single-centre study. Subjects were 211 consecutive patients undergoing open repair of a ruptured AAA between 1998 and 2006. Primary outcome was development of ALI ($PaO_2/FiO_2 < 300$ and bilateral pulmonary infiltrates on chest X-ray) in the first 6 hours after surgery. Secondary outcomes were time to extubation, and survival at 30 days. Chest X-rays were examined independently by two radiologists who were blinded to the study hypothesis.
Results One hundred and twenty-nine patients were operated on before and 82 after the change in FFP procurement. Groups were well matched, with respect to age, sex, co-morbidities and severity of illness, and received similar volumes of i.v. fluids and blood products from admission to 6 hours postoperatively (mean units of FFP, 8.6 before and 8.39 after, $P = 0.833$). The maximum tidal volume, PEEP, and CVP were similar in both groups. Norepinephrine was given to 8.5% of patients in the before group compared with 24.4% after ($P = 0.001$), otherwise inotrope use was similar. Primary outcome: there was significantly less ALI following the change to male-only FFP (36% before vs 21% after, $P = 0.042$). Secondary outcomes were not statistically different between groups; however, patients with ALI in either group had a poorer 30-day survival (59% vs 80%, $P = 0.005$).
Conclusion Exclusion of female-donor FFP was associated with a statistically significant reduction in the incidence of ALI in patients undergoing repair of a ruptured AAA.

P375

A biochemical comparison of Octaplas with a universally applicable development product (Uniplas) and single-donor fresh-frozen plasmas subjected to methylene-blue dye and white-light treatment

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Introduction The aim of this study was to perform an extensive biochemical comparison of the pharmaceutically licensed coagulation active plasma Octaplas with an identical, but universally applicable, development product (Uniplas) and single-donor fresh-frozen plasma (FFP) units subjected to a medical device treatment using a combination of methylene-blue dye and subsequent white-light exposure (MB plasma).

Methods Twenty-four batches of Octaplas of different blood groups and different plasma sources, three batches of Uniplas (both products manufactured by Octapharma PPGmbH, Vienna, Austria) and 20 random commercially available bags of MB plasma of different blood groups were analysed. Beyond the global coagulation parameters, the activities of coagulation factors and protease inhibitors, as well as plasminogen, activated factor VII, plasma turbidity and lipid components, were quantified.
Results Similar to Octaplas, Uniplas showed standardised levels of coagulation factors, plasminogen and protease inhibitors (decreased protein S and antiplasmin activities) according to the product specifications. MB plasma revealed fibrinogen levels close to or below the physiological range (<1.5 mg/ml). Coagulation factor activities in single MB plasma units both below and above the normal ranges for FFP were found in this study, reflecting the considerable variability of clinically important plasma proteins. Moreover, MB plasma revealed a higher turbidity after thawing, probably due to the elevated lipid parameters.
Conclusion This study showed that there are significant differences in the biochemical characteristics between Octaplas and MB plasma, while Uniplas revealed the same high quality as Octaplas. The variability of several plasma proteins in the 20 individual MB plasma units tested was high compared with Octaplas/Uniplas. For plasma prescribers and physicians it is also important to consider the significant loss of functional fibrinogen in MB plasma when planning and monitoring the treatment of severely ill patients.

P376

Octaplex in routine clinical use for prophylaxis and therapy of bleeding in patients with prothrombin complex factor deficiency

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Introduction Octaplex is a new prothrombin complex concentrate that is indicated for treatment or perioperative prophylaxis of bleeding in patients with deficiency of the prothrombin complex coagulation factors, such as deficiency caused by treatment with vitamin K antagonists or by liver failure, when rapid correction of bleeding is required. The study was conducted to demonstrate both prevention of bleeding and achievement of haemostasis in acute bleeding and to obtain further information about the safety of administration of Octaplex.
Methods One hundred and one patients were included in this observational study with determination of the INR as part of routine clinical management. The endpoint of this study was perioperative prophylaxis of bleeding or successful treatment of acute bleeding according to clinical signs.
Results The total dose administered per patient varied from 5.6 to 63.5 IU/kg bodyweight with a median dose of 20.4 IU/kg bodyweight. The median infusion rate was 3 ml/minute; in some cases up to 10 ml/minute were administered without any adverse reactions. The administration of Octaplex reduced the INR on average from 2.3 to 1.5. Infusion of 25 IU Octaplex per kg body weight resulted in an average decrease of about 1.2 in INR. A subgroup analysis of those patients with a postinfusion measurement within 1 hour after application of Octaplex showed a fast onset of action. The investigators evaluated the overall efficacy of Octaplex in 84.2% of cases as 'very good' and in 14.9% of cases as 'moderate'. No adverse drug reactions or interactions were reported.
Conclusions Octaplex is effective in perioperative prophylaxis of bleeding in patients with a coagulation deficit caused by treatment with vitamin K antagonists. Octaplex is also effective in treatment of acute bleeding. Octaplex was well tolerated, with no adverse reactions being reported during the study.

P377

Reversal of oral anticoagulation with prothrombin complex concentrate (Octaplex)

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Introduction Oral anticoagulant therapy with vitamin K antagonists may need to be rapidly reversed if acute bleeding occurs or surgical intervention is required. This can most effectively be achieved by administering prothrombin complex concentrates (PCCs), which correct the INR more quickly than fresh frozen plasma without the problem of volume overload. Octaplex, a virus-inactivated PCC containing balanced potencies of coagulation factors and the regulating proteins C and S, was developed with the intention of making a rapid contribution to coagulation whilst limiting the risk of thrombosis.
Methods The objective of this prospective, open-label study was to demonstrate that Octaplex, when individually dosed, efficiently corrects the INR within 1 hour post infusion. Sixty patients were included, 56 of them evaluable in terms of efficacy.
Results The median total dose was 41.1 IU/kg body weight (range 15.3–83.3 IU/kg body weight). In total the mean infusion rate was 6.42 ml/minute for the first infusion. In about one-third of the patients an average infusion rate of ≥8 ml/minute was used. The median INR decreased from 2.8 (1.5–9.5) to 1.1 (1.0–1.9) after 10 minutes and remained at that level at measurements 30 and 60 minutes after infusion. There was a rapid increase in coagulation factor activity within the first 10 minutes as well. This activity remained stably elevated for at least 4–6 hours, confirming the INR results. Of 56 patients evaluable for efficacy, for 51 (91%) the geometric mean of postinfusion values was equal to or less than the predetermined target INR. Overall haemostatic efficacy was assessed as 'excellent' by investigators in all 56 patients. Three of the 60 patients had minor adverse drug reactions possibly related to Octaplex. No evidence of thrombotic side effects was observed.
Conclusions Octaplex corrects quickly, effectively and safely the INR to a predetermined level in patients with vitamin K antagonist-related deficiency of prothrombin complex coagulation factors.

P378

Experience of NovoSeven administration in the management of severe haemorrhage following cardiac surgery of nonhaemophilic patients

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Introduction Severe bleeding in cardiac surgery is often difficult to manage. The aim of this study is clinical evaluation of efficacy of

rFVIIa in the treatment of bleeding during and after cardiac surgery.

Patients and methods rFVIIa (NovoSeven; NovoNordisk, Bagsvaerd Denmark) was used in 20 adult patients aged between 41 and 74 years, average BMI 25.48 ± 4.03, who underwent open heart surgery (five coronary artery bypass surgery, two valvular surgery, four double valve operations, five combining operations (coronary artery bypass with valve repair) and four surgery for aortic aneurisms) in 2004–2006. All patients had normal coagulation parameters before surgery. We used questionnaires for indications and effectiveness of treatment. We compared the amount of blood lost within 12 hours before and within 12 hours after giving rFVIIa, the dynamics of bleeding (assessed in ml/hour) before and after treatment. We also compared the haemoglobin level, haematocrit, number of platelets and laboratory coagulation profile parameters before treatment, 2 hours and 12 hours after treatment. NovoSeven was administered 5–49 minutes after neutralization of heparin with protamin sulfate. The dosage of rFVIIa was 39.23 ± 20.70 μg/kg (range 14.45–81.35). We used Student's *t* test for statistical analysis the laboratory data prior to and after rFVIIa.

Results Indications for administration of the rFVIIa were considered when there was a postsurgical bleeding (exceeding 400 ml/hour) in the absence of surgical sources of the bleeding and lack of efficacy of the conventional hemostatic procedures. After administration of the first median dose (14.45–81.35 μg/kg) rFVIIa bleeding stopped in 11 patients. A marked decrease occurred in seven patients during 2 hours. The average blood lost within 12 hours before treatment was 2,510 ml and the average blood lost within 12 hours after treatment was 1,057 ml. The average dynamic of bleeding before treatment was 1,057 ml/hour and 87.90 ml/hour after treatment. The reduction in transfusion requirements was statistically significant.

Conclusions NovoSeven produces a potent haemostatic effect in bleeding events refractory to the conventional therapy complicating the cardiosurgical interventions, and substantially decreases the demand for blood transfusion.

P379

Evaluation of the role of recombinant activated factor VII (NovoSeven) as a rescue haemostatic therapy in postcardiopulmonary bypass surgical patients

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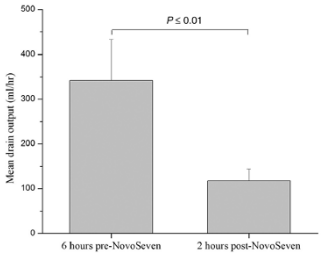
Objective Evaluation of the safety and efficacy of recombinant activated factor VII (NovoSeven) when used as a rescue haemostatic agent in refractory bleeding post bypass surgery.

Methods A retrospective cohort study of all postcardiopulmonary bypass patients with uncontrolled bleeding despite conventional treatment (platelets, fresh frozen plasma, cryoprecipitate, and Aprotonin) who received recombinant factor VII as a rescue therapy over 12 months in a cardiothoracic centre.

Results Eight patients received NovoSeven (90 μg/kg). Seven achieved significant reduction in blood loss. The mean blood loss via thoracic drains 6 hours before and 2 hours after NovoSeven administration were 341 ml/hour vs 117 ml/hour ($P = 0.01$) (Figure 1). On average, 5.3 units/patient packed red blood cells, 2 pools/patient platelets, 19 ml/kg/patient fresh frozen plasma and 148 ml/patient cryoprecipitate were used prior to NovoSeven administration. Five patients required further blood transfusion with a mean of 2.2 units/patient over the next 12 hours. Two of the eight patients developed thromboembolic complications including portal vein thrombosis and spinal cord infarction. Of these two, one died secondary to coagulopathic complications post initiation of warfarin therapy 2 weeks post surgery.

Figure 1 (abstract P379)



Mean hourly drain output 6 hours pre and 2 hours post NovoSeven administration.

Conclusion Our results support the evidence that recombinant factor VII is an effective haemostatic agent that can be used in patients with uncontrolled bleeding in postcardiopulmonary bypass surgery. Despite its high cost, there is an advantage in terms of effectiveness to support its use. However, its potential thrombo-embolic risk remains a concern and current evidence may restrict its use only as a rescue therapy following failed conventional treatment.

P380

Factor VII for intractable bleeding after cardiac surgery

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Introduction Recombinant activated factor VII (rFVIIa) (NovoSeven®; Novo Nordisk, Denmark) was developed primarily for the treatment of bleeding episodes in hemophilic patients. Little information is available on the use of rFVIIa in other situations, such as intractable postsurgical or post-traumatic bleeding. In the field of cardiac surgery, only a very few cases of treatment with rFVIIa are described. Because of the difficulty in performing randomized trials in this setting, information based on case studies is very valuable

Methods We studied 22 consecutive patients treated with rFVIIa due to refractory postoperative bleeding. rFVIIa was given only after all other options, including revision, to stop bleeding was failed. The amount of bleeding, the number of transfused units of red cells, platelets and other blood products were recorded both before and after administration of rFVIIa.

Table 1 (abstract P380)

Treatment	Before	After
Bleeding (ml/hour)	350	135
RBC	7.8 ± 2.3	1.5 ± 1.4
FFP	8.5 ± 2.4	2.5 ± 2.4
Platelets	14.5 ± 6.2	2.4 ± 2.1
Cryo	5.1 ± 1.4	0

Results See Table 1. In all patients, bleeding was decreased significantly. Seven of 22 patients survived and were discharged from the hospital

Conclusion rFVIIa is effective in promoting hemostasis after cardiac surgery. rFVIIa should be considered as a possible treatment option in intractable bleeding treatment.

P381

Recombinant activated factor VII treatment of severe bleeding in cardiac surgery patients: a retrospective analysis of dosing, and efficacy and safety outcomes

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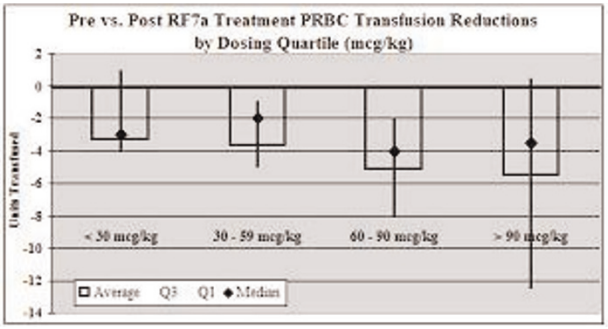
This study describes patient characteristics, recombinant activated factor VII (RF7a) dosing and clinical outcomes of cardiovascular surgery patients treated with RF7a for intractable bleeding. Use of RF7a for postsurgical bleeding, trauma or other uses in non-hemophiliac patients is considered off-label in the USA. Comprehensive studies evaluating RF7a in cardiac surgery patients are limited. Published reports cite success with RF7a administration in massive intractable bleeding. However, patient selection, dosing, efficacy, safety and pharmacoeconomic benefit remain undefined. Patients receiving RF7a between January 2004 and September 2005 were identified via pharmacy records. Clinical databases and electronic medical records were reviewed, collecting data elements needed to assess study objectives. One hundred and twenty patients were identified. Twenty-seven patients were excluded because they lacked documentation of RF7a administration, were treated for neurologic indications or had incomplete medical record data. Ninety-three patients were analyzed. RF7a effectively achieves hemostasis in patients with intractable bleeding, reducing blood product transfusions within 6 hours of treatment (Figure 1). Our findings suggest differences in PRBC transfusion reduction between RF7a doses. We observed no additional reduction PRBC transfusions in patients administered doses greater than 60–90 μg/kg (Figure 2). Effects of RF7a on surgical re-exploration and other potential related adverse events (stroke, AMI, VTE, etc.) are forthcoming. Our study, like others evaluating RF7a for this indication, are limited by the retrospective scope. Randomized trials comparing RF7a doses are under way. Although RF7a therapy is costly, minimal reductions in surgical re-exploration may offset the cost of RF7a therapy provided that adverse events are not increased.

Figure 1 (abstract P381)

Transfusion Reductions from Periods 6hrs Before vs. 6hrs After RF7a Dosing				
	Average	Stdev	Median	Pvalue
PRBCs	-4.28	6.74	-3	<0.0001
Cryoprecipitate	-8.38	30.31	-7.5	0.012
Platelet	-5.15	12.09	-3	0.001
Fresh Frozen Plasma	-5.21	7.068	-4	<0.001

Figure 2 (abstract P381)



P382

The influence of severe preeclampsia on maternal cerebral perfusion

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Introduction The method of transcranial color scan can be used to improve and to simplify cerebral blood flow investigations. Combination of digital wide-range neurosonography and transcranial energetic Doppler scan provides a possibility of effective monitoring of cerebral blood flow. The goal of this study was to analyze cerebral flow disturbances in pregnant patients with preeclampsia.

Methods Eighty-eight patients with severe preeclampsia, age 17–32 years (mean age 26 ± 4.6 years), and 90 patients with normal pregnancy, third trimester, without significant co-morbid states, age 19–34 years (mean age 25.9 ± 4.2 years), were included in the study. Patients with the following features were excluded from both groups: potentially haemodynamically significant stenosis or occlusion of magistral arteries of the head and basilar region; clinical features of congestive heart failure; arrhythmia. All patients underwent duplex scan of extracranial portions of brachiocephalic arteries with a linear probe and transcranial duplex scan (TCDS) in the area of the middle cerebral artery (MCA). By the transtemporal approach in the MCA M1 segment we determined the peak systolic flow velocity (V_{ps}), maximal end-diastolic velocity (V_{ed}), time-adjusted maximal velocity (TAMX), resistance index (RI), pulsative index (PI), and systolic/diastolic ratio (S/D). Significance of mean values differences in groups was estimated using Student *t* criteria.

Results All haemodynamic values in preeclamptic patients were decreased in comparison with the same values in healthy pregnant women: PI (mean 0.71 vs 0.84, $P < 0.0001$); RI (mean 0.49 vs 0.54, $P < 0.0001$); V_{ps} (mean 72.8 vs 104.8 cm/s, $P < 0.0001$); V_{ed} (mean 34.7 vs 48.7 cm/s, $P < 0.0001$); TAMX (mean 48.5 vs 67.5 cm/s, $P < 0.0001$); S/D (mean 1.94 vs 2.05, $P < 0.001$). These pathophysiological changes of cerebral haemodynamics were consistent with the Dopplerographic pattern of diminished perfusion and are typical for vascular segments, which are located proximally to the zone of abnormally high haemodynamic resistance.

Conclusion The results of the performed study showed that patients with severe preeclampsia had decreased cerebral perfusion and TCDS is an effective method for estimation of preeclampsia severity.

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HELLP syndrome: utility of specific classifications as prognostic tools

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Introduction HELLP syndrome is a specific complication of pregnancy characterized by hemolysis, elevated liver enzymes and

low platelet count. Maternal mortality was reported to be as high as 24%. Two classifications of the HELLP syndrome are widely used (Tennessee [1] and Mississippi [2]). The aim of this study is to determine mortality of HELLP syndrome as defined by each classification and try assessing the most relevant.

Patients and methods Prospective data collection as part of the APRiMO study (Assessment of Prognosis and Risk of Mortality in Obstetrics). Included were all obstetric patients transferred from a referral center for high-risk pregnancies in our independent multidisciplinary ICU. The study period was January 1996–September 2004. Demographic data, obstetric history, morbid events, length of stay (LOS), severity of illness scoring systems and organ dysfunction scores at day 1 of admission were collected. Exclusion criteria were LOS < 4 hours. The main outcome of interest was survival status at ICU discharge. Two groups were compared: patients with HELLP syndrome as defined alternatively by the two classifications (Group I), and patients without hepatic dysfunction (Group II). Results are expressed as the mean ± standard deviation. $P < 0.05$ was considered significant. Discrimination of the classifications was assessed by the area under the receiver operator characteristic curve (AuROC). Calibration was assessed by the Hosmer–Lemeshow (HL) goodness-of-fit test. Data were computed on SPSS 11.5, Win-XP compatible.

Results and discussion Differences between Group I and Group II were statistically significant concerning obstetric hemorrhagic complication ($P < 0.001$), incidence of acute renal failure ($P = 0.01$), mortality ($P = 0.001$), LOS (6.5 ± 7 days vs 4.4 ± 4 days, $P = 0.001$), SAPS-Obst score (24.5 ± 8 vs 16.8 ± 7, $P < 0.001$). The Mississippi classification discriminated well, but calibrated badly. In contrary, the Tennessee classification was a poor discriminator but calibrated very well. See Table 1.

Table 1 (abstract P383)

Number of patients, discrimination and calibration statistic tests for each classification

Classification	Dead	Alive
Tennessee	$n = 45$ (20.3%)	$n = 177$
Mississippi	$n = 20$ (26.7%)	$n = 55$
	ROC	HL
Tennessee	0.75	0.001
Mississippi	0.64	0.533

Conclusion Both models classified patients according to different criteria but were correlated with mortality. None of the classifications discriminated and calibrated well at the same time. The two models seem to be complimentary. Development of an aggregate classification could refine the models.

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Stroke and pregnancy: etiology, timing and outcome

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Background and goal Most previous studies on stroke during pregnancy have mainly focused on incidence and risk factors. These studies have not reported details of etiology and stroke outcome. The present study focuses on the evaluation of the etiology, timing and outcome of stroke occurring during pregnancy.

Materials and methods We conducted a retrospective analysis on all obstetric patients who have been diagnosed with stroke during pregnancy or within 8 weeks postpartum. These patients were transferred to our multidisciplinary ICU between January 1996 and December 2004. All patients were investigated with a CT scan of the brain, and MRI and/or cerebral angiography.

Results Eighty-eight patients were included, 34 of them were excluded (incomplete investigations or nonstroke diagnosis: reversible leucoencephalopathy, cerebral abscess, etc.). Fifty-four patients with a diagnosis of stroke were identified: 30 patients with ischemic stroke (IS) and 24 patients with hemorrhagic stroke (HS). The majority of events (45 patients, 83%) occurred in the third trimester and postpartum period ($P = 0.02$). A specific cause was identified in 24 patients (80%) of IS and in 21 patients (87%) of HS. Causes of IS include preeclampsia/eclampsia in 11 patients, venous thrombosis and coagulopathies (deficiencies of protein C, protein S, and activated protein C resistance) in nine patients, valvular heart disease with history of prior stroke in four patients and six patients had no definable cause. The major causes of HS were preeclampsia/eclampsia in eight patients, four patients presented with hemorrhage secondary to aneurysmal rupture, three patients presented with bleeding from arterio-venous malformations (AVM), bleeding as a consequence of disseminated intravascular coagulation (DIC) occurred in two patients and seven patients had hemorrhagic events of unknown origin. Hypertensive disorders of pregnancy were the most common comorbid conditions (32%).

Nineteen deaths (35%) occurred in our study, eight patients with infarction and 11 patients with hemorrhage. Thirty-one patients left the hospital with neurologic deficits, requiring chronic care or rehabilitation.

Discussion and conclusion The results of the present study complement the findings of previous studies on timing of stroke in pregnancy [1,2]. We found that preeclampsia/eclampsia and intracranial vascular malformations were the major causes of stroke in pregnancy, which agrees with other findings [2,3]. Our study shows a high mortality rate of 35%, which indicates that careful management of at-risk patients during the first postpartum weeks is warranted.

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Acute renal failure in obstetrics: risk factors and outcome

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Introduction Acute renal failure (ARF) was newly recognized as a specific mortality risk factor [1] and is in general associated with a high mortality rate.
Hypothesis Identifying risk factors for ARF could help reduce mortality. We shall try to describe them in critically ill obstetric patients, and explain ARF association with multiple organ failure (MOF) and outcome using the Sequential Organ Failure Assessment (SOFA) score and Logistic Organ Dysfunction (LOD) score.
Methods An open prospective observational cohort study in a multidisciplinary ICU. All critically ill obstetric patients were analysed unless diagnosed with chronic renal failure or kidney transplant. ARF was defined as serum creatinine ≥ 100 µmol/l and/or urine output ≤ 500 ml/day and/or doubling of baseline serum creatinine levels.
Results Six hundred and forty patients were reviewed (mortality rate 13.3%). ARF was diagnosed in 223 patients. Main risk factors present at admission were: acute circulatory failure, transfusion and association with haemolysis elevated liver enzyme and low platelet count (HELLP) syndrome. ARF patients with HELLP syndrome on admission were most likely to develop and alter multiple organ dysfunctions/failures. ARF is associated with an elevated relative risk of mortality (x1.5). Anuria and a serum creatinine level > 300 µmol/l were independent risk factors for mortality (OR 2 and 7, respectively). The ICU mortality of ARF patients increased with the number of failing organs on admission, especially persistent circulatory failure over time. The LOD score is at least as good as the SOFA score in evaluating the association MOF–ARF with mortality. In fact, LOD cutoff values defining cardiovascular, respiratory hepatic and hematologic organ failures fit particularly our obstetric population.
Conclusions Most important risk factors for ARF or mortality are often present on admission. During the ICU stay, other organ failures (especially cardiovascular) are important risk factors to develop or alter renal function, especially persistence of circulatory shock; thus, aggressive fluid challenge and volume infusion policy could help ARF prevention. HELLP syndrome and ARF is a particularly morbid association because of accumulating organ failures.

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The majority of patients in a Swedish university hospital intensive care unit have reduced glomerular filtration rate measured by Cystatin C

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Introduction Renal dysfunction is associated with increased morbidity and mortality in intensive care patients. The aim of this study was to investigate the use of laboratory markers in an ICU, especially glomerular filtration rate (GFR) markers, and to compare two GFR markers, creatinine and Cystatin C. A secondary aim was to assess the frequency of reduced GFR in this patient group using the creatinine and Cystatin C estimated GFRs as several pharmaceuticals are prescribed according to renal function.
Methods A retrospective observational study was performed in a general ICU at a Swedish university hospital. All adult patients treated at the ICU during 2004–2006 were included. Reduced kidney function was defined as ≤80 ml/min/1.73 m^2.
Results GFR markers are frequently ordered in the ICU. The majority of the patients had a reduced kidney function as evaluated by Cystatin C and/or p-creatinine. A total 92.1% of the patient test results had Cystatin C estimated GFR (eGFR) ≤ 80 ml/min/1.73 m^2, 75.3% had eGFR ≤ 50 ml/min/1.73 m^2 and 30.4% had eGFR ≤ 20 ml/min/1.73 m^2. In contrast, only 46% of the patients had reduced renal function assessed by plasma creatinine.
Conclusions The GFR is commonly assessed in the ICU. Cystatin C is a more sensitive GFR marker than creatinine. A majority of the ICU patients had a reduced GFR. Many of the pharmaceuticals used in the ICU are cleared by the glomeruli. It is thus important to monitor kidney function regularly, using an adequate assay. When possible, drugs with a plasma concentration that is less influenced by the GFR should be used.

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Fractional excretion of urea in the follow-up of acute renal failure due to prerenal azotemia

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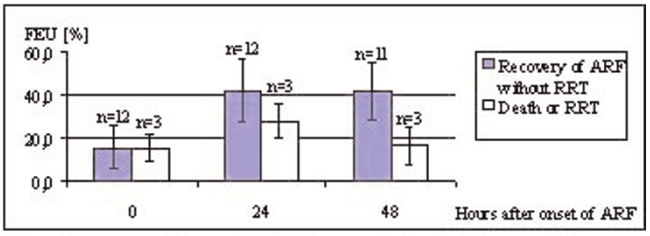
Fractional excretion of urea (FEU) is a major issue to discriminate between prerenal azotemia and acute tubular necrosis in acute renal failure (ARF). Its role in the course of ARF remains unclear. The aim of this study was to evaluate FEU in the follow-up of ARF due to prerenal azotemia in order to predict the necessity of renal replacement therapy (RRT).
The prospective study took place at the ICU of Stadtspital Waid, Zürich. All patients admitted starting from 19 February 2006 were evaluated for ARF according to the RIFLE classification. ARF due to prerenal azotemia was defined as ARF combined with FEU of less than or equal to 35%. FEU was calculated as [(urine urea/blood urea)/(urine creatinine/plasma creatinine)] x 100. Urine specimens were taken and FEU was calculated daily until complete or partial renal recovery was reached or the criteria for RRT were met. The goal of therapy was reconstitution of renal function by treatment of the underlying condition. RRT was initiated according to the usual criteria. Statistics were determined using Fisher's exact test.

Figure 1 (abstract P387)



Fractional excretion of urea (FEU) in the follow-up of acute renal failure (ARF) due to prerenal azotemia. Data presented as mean ± SD. n = number of patients.

By 7 December 2006, 15 patients met the inclusion criteria for ARF due to prerenal azotemia (nine males, six females). The mean age was 71 ± 11 (SD) years for male patients and 58 ± 31 years for female patients. Twelve out of the 15 patients responded to conservative management and had complete or partial renal recovery. Three patients needed RRT. Two of them refused RRT and died during the course of the disease. During the first 48 hours after initiation of conservative therapy, FEU remains less than or equal to 35% in all three patients who needed RRT. By contrast, nine out of 12 patients in whom renal function recovered without RRT showed a FEU of more than 35% within the first 48 hours ($P < 0.05$) (Figure 1).

In patients presenting with ARF due to prerenal azotemia, an increase of FEU above 35% within the first 48 hours after initiation of conservative therapy for ARF is a valuable parameter to predict renal recovery. After initiation of conservative therapy, measurement of FEU is of no value concerning discrimination of prerenal azotemia and acute tubular necrosis in ARF.

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Hemodynamic goal-directed intermittent hemodialysis

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Introduction Intermittent hemodialysis (IH) is the commonest form of renal replacement therapy (RRT) in the majority of Indian ICUs as each continuous veno-venous hemofiltration session for 24 hours costs around €250, against IH that costs around €25/4 hour session. The major concern of IH in septic shock patients is hemodynamic instability. Whether stringent hemodynamic monitoring and maintaining preset goals would reduce these instabilities and deliver optimal RRT is not clear. We undertook a prospective study to evaluate this concept.

Methods Preset goals of keeping the mean arterial pressure (MAP) > 75 mm, cardiac output (CO) > 5 l/min and cardiac index (CI) > 2.5 l/min/m^2 throughout the session were attempted to achieve by a stepwise protocol as follows: (1) fluid boluses, (2) increase in vasopressor/inotrope dose, (3) adjustment in the ultrafiltration rate between 250 and 700 ml/hour, and (4) adjustment in the blood flow rate between 150 and 300 ml/minute on a hemodialysis machine. Dopamine, norepinephrine, vasopressin and dobutamine were used alone or in combination to achieve these goals. Hemodynamic monitoring and data collection were done with Datex S-5 and Flo-Trac Vigileo monitors.

Results Nineteen IH sessions of seven patients with septic shock were monitored and managed in the ICU. The baseline APACHE II score was 24.10 ± 4.98 and all patients had at least three organ failures. The average duration was 4.42 ± 1.30 hours and fluid removal was 2,000 ± 527 ml per IH session. The preIH MAP, CO and CI were 81.10 ± 10.80 mmHg, 6.23 ± 2.24 l/min and 3.45 ± 1.07 l/min/m^2, respectively. The MAP, CO, CI were 81.42 ± 8.44 mmHg, 6.27 ± 2.24 l/min and 3.49 ± 1.07 l/min/m^2 at 60 minutes; 79.36 ± 15.33 mmHg, 6.24 ± 2.65 l/min and 3.46 ± 1.31 l/min/m^2 at 120 minutes; 82.83 ± 14.00 mmHg, 6.48 ± 2.36 l/min and 3.60 ± 1.06 l/min/m^2 at 180 minutes; and 84.44 ± 13.98 mmHg, 6.46 ± 2.17 l/min and 3.6 ± 0.95 l/min/m^2 at 240 minutes, respectively. Preset goals were maintained with fluids alone in four patients, fluids and escalation of vasopressor was required in seven patients, and fluids, vasopressor escalation with ultrafiltration and blood flow adjustments in six patients. Only 2/19 sessions were terminated at 120 and 90 minutes, due to development of new myocardial infarction in one and persistent hypotension in other.

Conclusion Goal-directed hemodynamic management during IH can reduce hemodynamic instability and deliver reasonably optimum RRT in the absence of continuous veno-venous hemofiltration facilities.

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Predictive factors of dialytic acute kidney injury in patients admitted to the intensive care unit after nontraumatic emergency abdominal surgery

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Introduction Although postoperative risk factors for dialytic acute kidney injury (DAKI) are well described in a wide range of clinical settings, we have few data regarding nontraumatic emergency abdominal surgery. The aim of this study was to describe these factors in this subgroup of patients.

Methods We have conducted a retrospective cohort study in order to identify independent risk factors. We reviewed data from patients admitted to the ICU after nontraumatic emergency abdominal surgery from April 2003 to October 2006. Epidemiological data, outcome and ICU resource utilization were recorded. Statistical analysis was performed by univariate analysis (Fisher's exact test, chi-square test) followed by multivariate stepwise logistic regression.

Results There were 168 consecutive patients (86 males). The mean age was 55 ± 19 years. The mean APACHE II score was 11 ± 8. Main reasons for ICU admission according to APACHE II classification were gastrointestinal perforation/obstruction $n = 100$, gastrointestinal surgery due to neoplasia $n = 21$, vascular surgery $n = 18$, gastrointestinal bleeding $n = 6$, hemorrhagic shock $n = 5$, sepsis $n = 5$, chronic cardiovascular disease $n = 4$, respiratory failure $n = 3$, cardiovascular $n = 3$, metabolic disturbance $n = 2$ and renal surgery due to neoplasia $n = 1$. The mean LOS was 5 ± 13 days. The DAKI frequency was 6.5% ($n = 11$). By means of univariable analysis, risk factors for DAKI were male sex, creatinine level ≥ 1.5 mg/dl at admission, APACHE II score ≥ 25, use of a pulmonary artery catheter, need for mechanical ventilation ≥ 48 hours, hemoglobin level ≤ 7 g/dl, and enteral and parenteral nutritional support. In the multivariate analysis, only APACHE II score ≥ 25 (OR 14.9; 95% CI 1.9–111.6, $P = 0.008$), use of enteral support (OR 20.3; 95% CI 3.5–117.7, $P < 0.001$) and use of pulmonary artery catheter (OR 10.7; 95% CI 1.3–88.5, $P = 0.028$) were independent predictors of DAKI. The overall postoperative mortality rate was 10.7%; it was 54% in patients with DAKI compared with 7.6% in patients without DAKI.

Conclusions DAKI following nontraumatic emergency abdominal surgery has a high mortality rate, and APACHE II score ≥ 25, use of enteral nutritional support and use of pulmonary artery catheter are its postoperative predictive factors.

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Long-term outcome of patients with contrast-induced nephropathy

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Introduction Despite the use of several prophylactic approaches, contrast-induced nephropathy (CIN) remains a clinical problem.

CIN is the third leading cause of hospital-acquired renal failure. CIN is associated with several risk factors such as diabetes and hypertension as well as with prolonged hospitalization and increased mortality. Little is known about long-term renal outcome. Within the last 10 years we have performed nine controlled studies on prophylaxis of CIN with a total number of about 1,200 patients. It was the aim of this study to investigate the long-term outcome of patients with CIN within these studies.

Methods This study presents the data of the first 25 patients with CIN (planned: 80 patients) including serum creatinine 1 week, 1 month, 6 months and 1 year after the contrast medium. The outcome was investigated by chart review and telephone call.

Results All patients were Caucasian and had a mean age of 69.6 ± 10.6 years. Eight were female, 17 were male. Twenty-four patients had risk factors for CIN such as diabetes (8%), hypertension (44%) or both (28%) and preexisting renal impairment (15%) prior to contrast medium application. Their mean serum creatinine before contrast medium application was 1.81 ± 1.21 mg/dl. The contrast procedure was coronary angiography in 18 patients and CT in seven patients. For prophylaxis of CIN, six patients received *N*-acetylcysteine and three patients received both *N*-acetylcysteine and theophylline prior to contrast medium exposition. Mean serum creatinine 48 hours after contrast medium was 2.36 ± 1.36 mg/dl ($P < 0.01$ vs 0 hours). The mean maximum creatinine increase was 0.64 ± 0.26 mg/dl ($P < 0.01$ vs 0 hours). Four patients (16%) died during the first week after contrast medium, one of them despite initiation of dialysis 2 days after contrast application.

One year after CIN, the mean serum creatinine in the survivors was 1.85 ± 1.39 mg/dl ($P = 0.48$ vs 0 hours). A clinical relevant increase of >0.3 mg/dl compared with baseline creatinine was found in six (24%) patients.

Conclusion CIN is a serious complication of contrast medium administration and is associated with an increased mortality and long-time morbidity.

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Survey of acute renal failure in patients after cardiovascular surgery

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Introduction Acute renal failure (ARF) is one of the major complications after cardiovascular surgery. To investigate the incidence and prognosis of ARF after cardiac surgery, we performed a retrospective study. Our hypothesis is that ARF is more common in patients who underwent surgery for great vessel diseases than in those who underwent coronary or valve surgery.

Methods We enrolled patients over 18 years old who underwent cardiovascular surgery and entered our ICU between 2004 and 2005. The background diseases were classified into two groups: great vessel disease, and coronary/valve disease. We determined ARF when serum creatinine increased by more than 50% of the preoperative values, or when renal replacement therapy was newly started. By reviewing ICU charts, we collected data before, on admission to the ICU and during the ICU stay.

Results ARF occurred more frequently in patients with great vessel disease than in those with coronary/valve disease (33.5% vs 11.2%, $P < 0.05$). The prognosis of patients with ARF was poorer than those without ARF in both groups (Figure 1). Patients with ARF showed a longer operation time, larger intraoperative bleeding and a higher level of blood lactate on admission to the ICU than those without ARF. Patients with ARF showed higher incidence of liver dysfunction, and needed a longer mechanical ventilation and ICU stay.

Figure 1 (abstract P391)

	Great vessel disease		Coronary/valve disease	
	ARF(-)	ARF(+)	ARF(-)	ARF(+)
Number	244	123	714	90
Age (y.o.)	64	68	65	66
Preoperative creatinine (mg/dl)	0.95	1.14*†	0.96	0.94
Operation time (min)	412	527*	317	455*
Intraoperative bleeding (ml)	1907	3085*	1006	2102*
Lactate on admission to ICU (mmol/l)	2.8	4.5*	1.6	3.2*
Maximum ALT (U/l)	43	118*	28	336*
CNS disorder (%)	5.4%	23.6%*	2.1%	4.4%
Mechanical ventilation (hr)	28	175*	14	106*
Renal replacement therapy (%)	0%	14.6%	0%	15.6%
Length of ICU stay (day)	4.6	12.6*	2.9	8.6*
Mortality (%)	0.4%	8.1%*	0.1%	5.6%*

Average values are shown. *, p<0.05 vs. ARF(-) †, p<0.05 vs. Coronary/valve disease ARF(+)

Conclusion ARF is common after cardiovascular surgery, especially after surgery for great vessel disease. ARF was associated with more postoperative organ disorders.

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Antifibrinolytic agents and angiotensin-converting enzyme inhibitors: the effect on postoperative renal dysfunction in cardiac surgery

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Objective To investigate the effect of the antifibrinolytic agents aprotinin and tranexamic acid on the occurrence of acute postoperative renal dysfunction in cardiac surgery on patients treated preoperatively with angiotensin-converting enzyme (ACE) inhibitors.

Methods A total of 7,420 patients who had undergone nonemergency coronary artery bypass graft or valve surgery in the Bristol Royal Infirmary from January 2000 until end of March 2006 were included in a retrospective observational study. The incidence of postoperative renal dysfunction was compared in patients given aprotin, tranexamic acid or no antifibrinolytic agent, using propensity-adjusted multivariable logistic regression. Further analysis was performed comparing patients taking ACE inhibitors preoperatively with those not taking ACE inhibitors. Renal dysfunction was defined as creatinine higher than 200 μmol/l and/or renal dialysis. Patients with a previous history of renal dysfunction were excluded from the study.

Results Using propensity-adjusted multivariable logistic regression (C-index, 0.82), the use of aprotinin in patients taking ACE inhibitors was associated with more than doubling the risk of acute postoperative renal failure in patients undergoing nonemergency cardiac surgery (odds ratio 2.64; confidence interval 1.32–5.27). Tranexamic acid was also associated with a significant increase in the risk of renal failure (odds ratio 1.59; confidence interval 1.09–2.31) in patients taking ACE inhibitors. However, in this study, there was no association between either aprotinin (odds ratio 1.01) or tranexamic acid (odds ratio 1.19) and postoperative renal failure in patients not taking ACE inhibitors.

Conclusion In cardiac surgery, there is a significant association between use of the antifibrinolytic drugs aprotinin and tranexamic

acid and the occurrence of acute postoperative renal dysfunction, in patients taking ACE inhibitors. The potential blood-saving benefits of antifibrinolytic drugs should be weighed up against this serious postoperative complication.

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Preoperative assessment of patients undergoing abdominal aortic surgery: chronic kidney disease is almost always present

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Introduction A number of preoperative patient-specific risk factors contribute to increased perioperative cardiovascular risk (myocardial infarction, heart failure, death) in patients undergoing major noncardiac surgery [1]. Renal impairment is one predictor. Creatinine values are a poor reflection of true renal function. Measures of the glomerular filtration rate provide a more accurate measure of renal function; as such, the true prevalence of renal impairment in this population may be significantly higher than previously appreciated. Our aim was to identify that proportion of elective vascular patients undergoing abdominal aortic surgery that have CKD, assessed by the estimated glomerular filtration rate (eGFR, ml/min/1.73 m^2 body surface area; creatinine, μmol/l) [2].

Methods A retrospective analysis of our 'ABC study' database was undertaken. The ABC study is an ongoing study looking at preoperative risk assessment using cardiopulmonary exercise testing in patients undergoing elective aortic surgery.

Results Sixty-six patients were included in the analysis. All patients were Caucasians, 62 males (94%). No patient had a pre-existing diagnosis of chronic renal impairment. No patients had stage 4/5 CKD (severely reduced kidney function, eGFR < 30). Moderately reduced kidney function (eGFR 30–59, CKD stage 3) was seen in 20 (30%) patients, and mildly reduced kidney function (eGFR 60–89, CKD stage 2) in 44 (67%). Only two patients had normal kidney function. The mean total cholesterol for the cohort was 4.6 mmol/l (±1 mmol/l). See Table 1.

Table 1 (abstract P393)

CKD stage	Stage 1	Stage 2	Stage 3	Total
n	2	44	20	66
Age (years)	64.7 (3.4)	69.9 (8.3)	75.5 (7.7)	71.5 (8.4)
eGFR	92.5 (0.7)	69.4 (7.2)	52.35 (7.4)	64.9 (11.6)
Creatinine	78 (1.4)	97.8 (9)	125.2 (19.9)	105.5 (18.8)
Cholesterol	4.5 (0.5)	4.8 (1.1)	4.3 (0.9)	4.6 (1)
BP	1 (50%)	21 (48%)	9 (45%)	31 (47%)
Smoking	2 (100%)	31 (70%)	14 (70%)	49 (74%)
Diabetes	0	1 (3%)	2 (10%)	3 (5%)

Conclusion The majority of vascular patients undergoing elective aortic surgery in our unit have impaired renal function that is not accurately reflected by creatinine values. Management of patients with stage 2 and 3 CKD is primarily cardiovascular risk assessment with aggressive treatment of modifiable vascular risk factors [3]. The full impact of risk factor modification on perioperative outcome in vascular patients requires further detailed investigation.

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P394

A comparison of Gc globulin and neutrophil gelatinase-associated lipocalin in patients with liver disease

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Introduction Gc globulin, a hepatically synthesized actin binding protein, is known to decrease in both acute and chronic liver disease, and low levels are associated with poor prognosis. Neutrophil gelatinase-associated lipocalin (NGAL), a member of the lipocalin family of proteins, has been shown to be an early biomarker of ischaemic renal damage. We prospectively investigated the use of these proteins as markers of severity of illness and prognostication in acute and acute-on-chronic liver failure requiring intensive care.

Methods NGAL and Gc globulin were measured on admission to our unit using a sandwich ELISA technique (AntibodyShop®) in 17 patients with acute liver failure (ALF) and 11 patients with acute-on-chronic liver disease (ACLD). Biochemical and physiological variables were collected prospectively and entered into a physiological database (ICARE). All measurements were taken on day 1 of admission. Results are expressed as the median and interquartile range.

Results Admission parameters: serum creatinine 185 μmol/l (89–266), urine output/24 hours: 340 ml (0–1,111), APACHE II score 20 (15–25), lactate 2.6 (1.8–4.68), INR 2.6 (1.6–3.8) and AST 1,404 (124–6,349). There were significant differences between median Gc globulin in ALF patients compared with ACLD: 25 mg/l (10–50) vs 50 mg/l (25–129), $P = 0.036$. No significant differences were seen for NGAL. Gc globulin correlated with admission creatinine ($r = 0.44$, $P < 0.01$), INR ($r = 0.68$, $P < 0.01$), and SOFA score ($r = 0.419$, $P < 0.01$) in both patient groups. These relationships persisted when admission Gc globulin was examined in regard to day 5 parameters. Admission Gc globulin correlated with D3 urine output ($r = 0.619$, $P < 0.001$). NGAL correlated with urine output throughout the first 5 days of admission ($r = -0.593$ on day 1, $r = -0.674$ on day 3, $P < 0.001$) and also with SOFA score. High admission NGAL was associated with requirement for renal replacement therapy on day 3 (ROC AUC 0.91 (0.895–1.022, $P < 0.001$)), outperforming both admission Gc globulin and admission creatinine. A low admission Gc globulin more accurately predicted the need for haemofiltration on day 5 (AUC 0.889, 0.734–1.044, $P < 0.007$) than either NGAL or creatinine on admission.

There were significant differences observed for Gc globulin examining 30-day survival (transplantation from ITU being analysed as 'death'): 50 mg/l (29–94) vs 18 (4–40), respectively, AUC

0.813, $P = 0.006$. There were no significant differences in NGAL values between survivors and nonsurvivors for the whole group. NGAL was significantly lower in survivors than nonsurvivors in the ACLD group (AUC 0.875, $P = 0.47$).
Conclusion Gc globulin and NGAL are potentially useful methods of identifying patients with a particularly poor prognosis and those needing renal replacement therapy. Further larger prospective studies are needed to elucidate their exact role not only in liver disease but also in the general ITU population.

P395

Fibrinogen as a prognostic indicator in hepatic failure

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Introduction Fibrinogen as a prognostic test of mortality in acute hepatic failure has not been reported. Two hundred and sixty patients admitted to the liver intensive therapy unit (LITU) with hepatic failure (that is, subacute, acute and fulminant) between 1 January 2004 and 30 September 2006 were identified from the LITU database (I-Care, UK). Twelve patients without fibrinogen testing on admission were excluded from the analysis.
Methods The mean (±SD) age was 38.1 (14) years. Ninety-seven patients were male and 151 female; 116 had taken a paracetamol overdose (POD). The mean (±SD) fibrinogen on admission was 1.88 (1.24) g/l. Overall ICU mortality was 30.2% (POD 43.4%; non-POD 26.1%). Forty-nine patients received a transplant (14 POD and 35 non-POD).
Results Fibrinogen levels (all in g/l) in survivors were higher than in nonsurvivors (1.98 ± 1.26 vs 1.63 ± 1.15; $P = 0.033$). Fibrinogen was higher in survivors of POD (1.81 ± 1.0 vs 1.41 ± 0.94; $P = 0.039$) and not significantly different between groups in non-POD hepatic failure (2.13 ± 1.43 vs 1.85 ± 1.31; $P = 0.28$). Fibrinogen was higher in those who survived after transplant (1.49 ± 0.83 vs 1.23 ± 0.23; $P = 0.27$). A cutoff value of fibrinogen of ≤1 g/l has sensitivity 0.47 and specificity 0.74 (positive predictive value (PPV) 0.44) for prediction of death in acute hepatic failure. In POD the sensitivity is 0.51, specificity 0.81 and PPV 0.59; in non-POD hepatic failure the values are 0.29, 0.73 and 0.31 respectively. In those POD who did not receive a transplant, fibrinogen ≤1 g/l has sensitivity 0.61, specificity 0.78 and PPV of 0.57 for death. Fibrinogen is higher in survivors of hepatic failure after POD.
Conclusion Fibrinogen ≤1 g/l performs better than INR > 6.5 in predicting mortality after POD (sensitivity 0.69, specificity 0.61), but not as well as the combined King's College Criteria (sensitivity 0.69, specificity 0.96). Fibrinogen of ≤1 g/l in POD not meeting King's College Criteria for transplantation may identify a group with poor prognosis. A low fibrinogen level on admission may predict death after transplant (more data required).

P396

Telephone triage for a liver intensive care unit – advise or admit?

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Objective To determine the referral pattern and organ dysfunction severity of interhospital consultations, and triage practice at a specialised liver intensive therapy unit (LITU).
Methods A prospective audit was conducted from 1 March to 30 November 2006, for all interhospital telephone referrals to our 15-bed LITU as recorded on a standardised proforma. Data evaluated were: referral diagnoses; reasons for refusal to LITU ('too well to benefit', 'too sick to benefit' or 'no beds'); triaged destination of care ('ward' at referral hospital or our hospital liver ward, 'IC' at referral hospital high-dependency unit/ICU or 'LITU'); and parameters for Sequential Organ Failure Assessment (SOFA) score.
Result A total of 620 calls were received for 439 referrals (37% during the 17:00–24:00 hours period, 11% during 00:00–08:00 hours), with 38% from the London region. Drug-induced acute liver dysfunction/failure (ALDF) was the most common reason for consultation (39%), with paracetamol being most common (163/172), most of whom were triaged to a referral hospital ward (63% vs 14% to LITU). Patients with diagnosis of 'ischaemic hepatitis' tended to be triaged to IC (82%), and pancreatobiliary disease and trauma to the LITU (69% and 80%).
Of the patients not admitted to our LITU (162 to ward and 176 to IC), 79% were deemed too well to benefit and 2% due to no beds. the mean ± SD SOFA score for the too sick to benefit group (19%) was 11.5 ± 4.3 (63% had decompensated chronic liver disease (d-CLD), 36% with malignancy, major sepsis or morbid cardiocerebral event). The mean ± SD SOFA scores for the ward, IC and LITU groups were 2.5 ± 2.4, 7.9 ± 4.6 and 7.8 ± 4.5, respectively. The SOFA liver score was highest in all three triage groups, overall mean of 2.3 (ward, 1.9 ± 1.4; IC, 2.6 ± 1.2; LITU, 2.4 ± 1.2), compared with other components (respiratory 0.9, cardiovascular 0.7, coagulation 0.9, renal 1.1, central nervous system 0.8). Patients with INR > 6 were more likely to be triaged to LITU (OR 4.2).
A total of 97 patients were admitted to our LITU (five of 17 patients triaged at referral to our hospital liver ward); six patients died before arrival and three patients were diverted to another liver intensive care facility for family convenience. Fifteen patients underwent liver transplantation (10/49 with ALDF, 5/37 with d-CLD). Mortality in the LITU group was 36%, and highest with d-CLD (57% vs 25% with ALDF). Mean referral, post-transfer and 48-hour SOFA scores of LITU nonsurvivors were 10.7, 12.7 and 13.9, respectively (6.5, 7.7 and 7.5 for survivors).
Conclusions The refusal rate to our LITU due to no beds was low. Paracetamol remains a common cause for drug-induced liver injury, although few are severe cases. The triage decision appeared to be influenced by the INR, d-CLD with or without a reversible cause and the presence/absence of morbid extrahepatic diagnoses.

P397

What is the role of carboxyhaemoglobin in patients with liver failure?

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Background Patients with liver failure have haemodynamic and respiratory instability, the aetiology of which is unclear. Unregulated vasoactive mediators may have an important role in this physiological phenomenon. Carbon monoxide, a vasodilator, has been extensively studied and is easily measured using circulating carboxyhaemoglobin (COHb). The levels of circulating COHb have been reported as being elevated in patients with stable cirrhosis and hepatopulmonary syndrome. It is unknown whether the levels of COHb are elevated in patients with liver failure.
Methods Patients admitted with acute liver dysfunction to the ITU between January 2003 and December 2005 were considered. Sixty-eight patients with acute liver failure (ALF) and 132 patients with decompensated chronic liver failure (DCLF) had a full dataset available on day 1 of admission. Patient demographics, physiological

parameters, blood results and organ dysfunction were recorded prospectively and entered into a patient management system database (ICARE).

Results There was no statistical difference in patient demographics, organ failure scores or physiological parameters between the groups. The median COHb percentage for ALF was 0.9% (0.7–1.2) and for DCLF 1.5% (1.2–1.8). In patients with DCLF, COHb negatively correlated with PaO_2 ($r = -0.4$, $P = 0.05$) and child Pugh ($r = -0.4$, $P = 0.07$). There was significant difference between grouped COHb and MAP in patients with ALF; there was a trend towards statistical significance with higher COHb. The arterial pH correlated with COHb in ALF ($r = 0.4$, $P = 0.01$).

Conclusions These results suggest that COHb maybe an important mediator in haemodynamic and metabolic instability in ALF. In DCLF, COHb is an important factor in hypoxia and possible pulmonary shunting.

P398

Predictive value of indocyanine green clearance in acute liver failure in children: comparison with King's College and Clichy scores

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Introduction Indocyanine green clearance (ICG), measured by the percentage disappearance rate (PDR), detects alterations in liver function and may be used as a noninvasive determinant of hepatic reserve in liver failure as well as a marker of graft function following liver transplantation. The administration of blood products does not interfere with the ICG-PDR as occurs with other prognostic scores (King's College and Clichy scores). The aims of this study were to compare in acute liver failure the ICG-PDR with King's College and Clichy scores and to determinate its predictive value.

Methodology Between 2003 and 2006, 114 ICG-PDRs were performed in 38 children (mean age 2.6 years (range 1 month–16 years)) with acute liver damage. ICG was administrated intravenously and its blood concentration was detected over time by transcutaneous pulse densitometry using a commercially available bedside monitor. The PDR was performed under hemodynamic stability (systolic mean pressure >60 mmHg; saturation of central venous blood saturation >70% and CO_2 arterio-venous difference <8 mmHg).

Results The mean number of PDRs/patient was three. The mean PDR was 17% (range: 3.3–51%). In two out of 38 patients, the PDR could not be detected due to hemodynamic instability. PDR < 5% was a predictor value for irreversible liver failure ($P = 0.000$). In nine (25%) out of 36 patients, the PDR was <5%. Of those nine, two patients recovered its synthetic function and seven (78%) patients developed irreversible liver failure (four died of liver failure and three underwent liver transplantation) (see Table 1).

Conclusions ICG-PDR <5% is a significant predictor of irreversible liver failure. It is a good complement of such scores for decision-making.

Table 1 (abstract P398)

	King's score	Clichy score	ICG-PDR
Sensitivity (%)	100	71.4	100
Specificity (%)	87	90	93
PPV (%)	64	63	78
NPV (%)	100	93	100

P399

Pulmonary effects of desferrioxamine in the treatment of an experimental model of fulminant hepatic failure

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Introduction Desferrioxamine (DFX) is a clinically approved iron chelator used to treat iron overload. It has also shown beneficial effects in experimental acute liver failure (ALF) by inhibiting oxidative damage [1]. Lung dysfunction commonly complicates ALF. Iron-mediated processes have been shown to contribute to it [2]. We hypothesized that inhibition of oxidative reactions by means of iron chelation could attenuate lung injury after ischemic ALF.

Methods In 14 domestic pigs fulminant hepatic failure was induced by surgical devascularization of the liver, and animals were monitored postoperatively for 24 hours under general anaesthesia. Seven randomly assigned pigs (DFX group) were treated with intravenous desferrioxamine (14.5 mg/kg/hour for 6 hours and 2.4 mg/kg/hour for the next 18 hours), whereas the remaining (control group) received standard care. Bronchoalveolar lavage fluid (BALF) was obtained after central line placement, after surgery, at 7 hours, and 24 hours postoperatively and was analysed for cell counts, biochemical and oxidative markers of lung injury.

Results DFX resulted in maintenance of blood pressure (mmHg) (84 ± 27 in DFX vs 51 ± 16 in control, $P < 0.05$) and attenuated the increase of intracranial pressure (mmHg) (19 ± 10 in DFX vs 36 ± 9 in control, $P < 0.01$) at 24 hours. Protein levels in BALF were increased in controls whereas in the DFX group protein (μg/ml) was significantly lower (at 7 hours 398 ± 219 vs 187 ± 67, respectively, $P < 0.01$; and at 24 hours 261 ± 112 vs 162 ± 52, respectively, $P < 0.05$). Nitrites in BALF were elevated at 7 hours in controls whereas a reduction was observed in the DFX group (3.924 ± 3.67 μM vs 0.590 ± 0.69 μM, respectively, $P < 0.05$). Phospholipase A_2, platelet-activating factor acetylhydrolase, nitrates, total cell counts, neutrophils and macrophages in BALF all increased in the control and DFX groups but did not differ significantly between them.

Conclusion Treatment of ALF with DFX attenuates the increase of protein and nitrites in BALF, but does not seem to significantly affect phospholipase A_2, platelet-activating factor acetylhydrolase, nitrates, macrophages or neutrophils. The observed effects may suggest a protective role of DFX on lung inflammation during the first 24 hours of ALF.

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P400

Comparison of terlipressin and norepinephrine on cerebral perfusion, intracranial pressure and cerebral concentrations of lactate and pyruvate in patients with acute liver failure: a microdialysis study

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Introduction Volume expansion and inotropic support with catecholamines are often insufficient to ensure adequate blood pressure and cerebral blood flow in acute liver failure (ALF). The

aim of this study was to determine whether terlipressin increases cerebral perfusion and to compare the effect with that of norepinephrine (NE). Furthermore, the effect on intracranial pressure (ICP) and cerebral concentrations of lactate and pyruvate were recorded.
Methods A retrospective study in a national four-bed liver ICU that treated 127 patients with ALF between 2001 and 2006. Thirty-eight of these patients were treated with terlipressin, and 10 patients (median age 42.5 years; range 15–66 years; five females) who also had an ICP and a microdialysis catheter placed in the cerebral cortex were included in this study. Concomitant measurements of mean arterial pressure (MAP), ICP, cerebral perfusion using transcranial Doppler sonography (V_{mean}) and cerebral concentrations of lactate and pyruvate were made before and after an increase in the NE infusion rate and i.v. injection of 1 mg terlipressin.
Results NE infusion and terlipressin injection increased the MAP and V_{mean} ($P < 0.01$). Also, the ICP increased during NE infusion ($P < 0.01$) but not after terlipressin. The cerebral lactate concentration was unchanged during NE infusion, while it decreased after terlipressin ($P < 0.05$).
Conclusion This study shows that terlipressin increases the MAP and cerebral perfusion in patients with ALF with no influence upon ICP and the cerebral concentrations of lactate and pyruvate. These findings indicate that terlipressin may be valuable, as an additive, or alternative, treatment of arterial hypotension in patients with ALF to secure brain viability.

P401

Relative adrenal insufficiency in patients with severe acute pancreatitis

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Background Inadequate cortisol levels and adrenal dysfunction may play a role in the pathophysiology of severe acute pancreatitis. This study aimed to analyse the incidence of relative adrenal insufficiency (RAI) in these patients, to identify factors associated with relative adrenal insufficiency and to describe how adrenal responsiveness affects outcome.
Methods In a prospective observational multicenter study, a short Synacthen test (SST) was performed within 5 days after admission to the hospital in 25 patients with severe acute pancreatitis, after signed informed consent was obtained. The incidence of RAI, defined as an increment after SST of less than 9 μg/dl, was the primary endpoint of the study. Serum cortisol was measured at baseline and 30 and 60 minutes after 250 μg adrenocorticotropic hormone administration.
Results The median baseline cortisol level was 26.6 μg/dl, and increased to 43.2 μg/dl and 48.8 μg/dl after 30 and 60 minutes, respectively. RAI was found in 16% of all patients, and in 27% of patients with organ dysfunction. Patients with RAI were more severely ill and had higher SOFA scores from day 4 through day 7 after admission. All patients with RAI developed pancreatic necrosis, and all of them needed surgical intervention. Mortality was significantly higher in patients with RAI (75% vs 10%, $P = 0.016$). Patients who died had a lower increment in cortisol levels after the SST than patients who survived.
Conclusion RAI is frequent in patients with severe acute pancreatitis and organ dysfunction. It occurs in patients with more severe pancreatitis and is associated with an increased mortality rate.

P402

The relative sensitivity of serum lipase versus amylase for radiological image-positive pancreatitis

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Background Due to the absence of a 'gold standard' test for the diagnosis of pancreatitis, the sensitivities of pancreatic enzyme tests for pancreatitis are still debated. We compared the relative sensitivities of lipase and amylase at their upper limit of normal values for image-positive pancreatitis in a large consecutive series of patients who had simultaneous tests of amylase and lipase.
Methods Consecutive patients with a clinical diagnosis of pancreatitis defined by constant epigastric pain and elevation of the amylase or lipase to greater than 106 U/l or 59 U/l, respectively, were imaged by abdominal sonography or computerized axial tomography (CAT) scan. All included patients had positive radiological evidence of acute pancreatitis.
Results The pancreas was visualized in 399/473 (84%) patients with suspected pancreatitis and 127/399 (38%) had radiological evidence of pancreatitis. Elevation of the lipase to >59 U/l detected 127/127 cases of image-positive pancreatitis, while elevation of the amylase to >106 U/l detected 113/127 cases (88% sensitive (0.82–0.94)). All cases of acute biliary pancreatitis were detected by both the lipase and amylase. The amylase missed 14 of 65 patients with nonbiliary etiologies of pancreatitis. Four of these were alcoholics.
Conclusion Our study shows a high degree of relative sensitivity of the lipase compared with amylase for pancreatic injury that is demonstrable on CAT or sonographic imaging. Our findings demonstrate a relative lack of sensitivity of amylase for nonbiliary etiologies of pancreatitis. We recognize that the absolute sensitivity of lipase for image-positive pancreatitis cannot be determined by this retrospective methodology that required elevation of one marker for inclusion.

P403

The significance of gallbladder sludge in the patient with acute pancreatitis

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Background The significance of gallbladder sludge as a potential cause of acute biliary pancreatitis is debated. We report the incidence and outcome of patients with gallbladder sludge in a large population of patients with pancreatitis.
Methods Pancreatitis was defined as constant epigastric pain with lipase greater than three times the upper reference value for our laboratory (177 U/l). Consecutive patients with first episodes of acute pancreatitis were identified over a 2-year period and data were evaluated retrospectively. Patients were followed prospectively for 2 years more.
Results All patients had gallbladder ultrasound examinations. First episodes of acute pancreatitis were identified in 356 patients. Initially 236 patients had stones directly visualized in the gallbladder. Of the remaining 120 patients, 13 had sludge, 11 had a dilated common bile duct, one had a positive sonographic Murphy sign, and 95 had no abnormalities. During the time course of the study, 23 of these 120 patients were demonstrated to have stones; by the surgical pathology report (12), endoscopic retrograde cholangio-pancreatography (10), and cholecystostomy

(one). Seven of 13 patients with sludge underwent cholestectomy and all had evidence of stones. Four of six nonoperated patients with sludge (67%) returned with recurrent pancreatitis over the course of the study. Ten of 97 patients (10%) with suspected nonbiliary etiology of the pancreatitis returned with recurrent pancreatitis over the same period. The nonoperated patients with sludge were more likely to have other risk factors for nonbiliary pancreatitis than were the operated patients.
Conclusions The presence of sludge on the gallbladder ultrasound suggests the presence of stones and is associated with a high rate of recurrence of pancreatitis in nonoperated patients.

P404

Recurrence rates in patients with first episodes of acute pancreatitis

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Introduction The timing of operative intervention in patients with suspected biliary pancreatitis is debated. Recurrence rates of pancreatitis in patients with biliary lithiasis are compared in operated and nonoperated patients. Recurrences in patients with suspected nonbiliary pancreatitis are also reported.
Methods First episodes of acute pancreatitis were identified in consecutive emergency department patients over a 2-year period. Data were evaluated retrospectively and then the identified patients were then followed prospectively for 2 years more.
Results Pancreatitis was defined clinically as constant epigastric pain associated with elevation of the serum lipase to greater than three times the upper reference value (177 U/l) and no other identified cause of abdominal pain. Of 356 patients with first episodes of acute pancreatitis, 259 had pancreatitis that was ultimately associated with biliary lithiasis based on abdominal ultrasound ($n = 236$), positive endoscopic retrograde pancreotography ($n = 11$), surgical pathology report ($n = 11$), or cholecystostomy ($n = 1$). Ninety-seven patients had no identified stones during the study period. Cholecystectomy was performed in 235/259 at the time of admission for pancreatitis. Reasons for nonoperative management were death (three cases), medical contraindications (15 cases), pregnancy (two cases) and delayed diagnosis due to negative abdominal sonogram (four cases). During the study period 10% (10/97) of patients without demonstrated stones returned with recurrent episodes of pancreatitis. There were two recurrences in 235 operated patients with stones (0.85%). Twelve of 19 nonoperated survivors with biliary lithiasis returned with complications of biliary lithiasis, including 10 recurrences of biliary pancreatitis (53%) and two episodes of common bile duct obstruction, one of which resulted in death from cholangitis. The median time to recurrence of pancreatitis in nonoperated patients with stones was 50 days, range 26–581 days.
Conclusion Cholecystectomy reduced the incidence of recurrence of pancreatitis in patients with biliary lithiasis.

P405

Replacement of albumin after abdominal surgery

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Introduction Replacement of albumin in hypoalbuminemic patients is not proven to reduce postoperative morbidity and mortality but no broad consensus is reached yet on abandoning the use of albumin in intensive care and perioperative settings for the bad prognostic value of hypoalbuminemia. As the albumin decrease in major surgery is mostly due to extravascular leakage of albumin (systemic inflammatory response), we regard hypoalbuminemia just as a marker of inflammatory response to surgery that albumin replacement cannot change. So the postoperative morbidity, mortality and length of stay would not differ in patients without albumin replacement.
Materials and methods We retrospectively studied 76 successive patients operated on in the abdomen at the Oncologic Institute in Ljubljana in 1997/98 (group 1 – postoperative hypoalbuminemia treated with 20% albumin solution) and in 2000/01 (group 2 – no albumin treatment), because of abandoning albumin use in our surgical department. We compared serum albumin concentrations in the first week after surgery (three values) as well as the postoperative complication rate and the length of hospital stay. We looked for correlation between the postoperative albumin concentration and the duration of surgery, amount of transfusion and amount of infusion during surgery.
Results The two groups of 38 patients were comparable in age (52.4 and 56.5 years), ASA physical status (1.9 and 2.0), preoperative albumin concentration (39.0 and 38.1 g/l), duration of operation (5.9 and 6.1 hours), transfused red blood cells (3.3 and 2.0 l) and crystalloid infusion during surgery (5.3 and 4.5 l). In both groups there was very significant drop of albumin concentration in the first week after surgery ($P < 0.001$). In group 2 albumin concentrations were very significantly lower than in group 1 until the fifth postoperative day ($P < 0.001$). The difference diminished after the sixth postoperative day ($P < 0.03$). There was negative correlation between the postoperative albumin concentration and the duration of surgery ($r = -0.44$, $P < 0.008$). We found no difference in the postoperative complication rate (surgical or medical), length of stay and mortality between the groups.
Conclusion Postoperative serum albumin concentrations were reduced in both groups, but more in group 2 with no albumin treatment, and in longer operations. Morbidity, mortality and length of stay were not influenced by albumin replacement.

P406

Extravascular lung water following resuscitation of hemorrhagic shock in swine: comparison between Ringers' lactate and normal saline

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Introduction Pulmonary edema is a common consequence of hemorrhagic shock resuscitation. The type and amount of fluid used in resuscitation may be important determinants of the amount of edema formed. Ringers' lactate (RL) and normal saline (NS) remain common resuscitative fluids. These experiments were designed to measure the extravascular lung water (EVLW) after resuscitation from hemorrhagic shock with RL vs NS, to determine whether the fluid type results in differences in the amount of EVLW, and to determine whether there exists a threshold amount of fluid that results in the development of edema.
Methods This was a randomized controlled trial using 20 female Yorkshire crossbred pigs. Animals were mechanically ventilated. Anesthesia was maintained using 2% isofluorane in 100% oxygen. Continuous hemodynamic monitoring, blood sampling, and determination of EVLW by single indicator transpulmonary dilution was done using a PiCCO plus monitor (Pulsion Medical System, Munich, Germany). The animals underwent a midline celiotomy,

suprapubic Foley catheter placement, and splenectomy. The spleen was weighed and, based on randomization, either LR or NS solution was infused to replace three times the spleen weight in grams. Following a 15-minute stabilization period, a standardized Grade V liver injury (injury to a central hepatic vein) was then created using a specialized clamp. Following 30 minutes of uncontrolled hemorrhage, we blindly randomized the swine to receive either NS or RL resuscitation at 165 ml/min. Resuscitation fluid was administered to achieve and maintain the baseline mean arterial pressure (MAP) for 90 minutes post injury.

Results All animals spontaneously stopped bleeding within 12 minutes of injury after losing approximately 25% of their blood volume. There were no differences in initial blood loss between the two groups – estimated blood loss (mean ± standard error) RL group 22 ± 1.7 ml/kg vs NS group 19.0 ± 1.7 ml/kg, $P = 0.15$. During the resuscitative phase the NS group required more fluid to maintain the goal MAP than the RL group: 330.8 ± 38.1 ml/kg vs 148.4 ± 20.2 ml/kg, $P = 0.001$. There was nearly a fourfold increase in mean EVLW between the groups: 5.24 ± 1.26 ml/kg NS vs 1.46 ± 0.57 ml/kg RL, $P = 0.013$. The difference in EVLW was accounted for entirely by the difference in the volume infused ($P = 0.008$), with no difference seen with fluid type ($P = 0.7$). The EVLW began to increase immediately with fluid administration without exhibiting a threshold effect. An increase of 1 ml/kg EVLW occurred at a resuscitative volume of 63 ± 25 ml/kg.

Conclusion In this swine model of traumatic hemorrhagic shock, resuscitation with RL as compared with NS required less fluid to maintain goal MAP and resulted in less EVLW formation. The near fourfold difference in EVLW increase was accounted for entirely by the differences in volumes needed to maintain goal MAP with no differences seen with fluid type. This study suggests that, in order to limit increases in EVLW during early resuscitation of hemorrhagic shock prior to the arrival of blood products, RL should be used preferentially instead of NS and the volume infused limited to approximately 60 ml/kg.

P407

Neutrophil elastase suppression by medium-molecular-weight hydroxyethylstarch in orthopaedic surgery

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The aim of this study was to compare the effect of hydroxyethylstarch (HES) and human albumin solution (HAS) on human neutrophil elastase (HNE) release in patients undergoing elective knee replacement surgery.

Forty-three patients (ASA 1 or 2) were randomly allocated into two groups. Group A ($n = 21$) received 5 ml/kg of 4.5% HAS preoperatively and a further 5 ml/kg HAS as an intraoperative replacement. Postoperatively the patients received Ringers' lactate at the discretion of the anaesthetic team. Group B was given 5 ml/kg HES (Fresenius-Kabi) preoperatively and a further 5 ml/kg HES intraoperatively. Thereafter fluid management was as in group A. Arterial blood samples were taken preoperatively and at 5 minutes, 30 minutes, 60 minutes, 120 minutes, 240 minutes and 24 hours post-tourniquet release for HNE and arterial blood gas analysis.

Repeated measures of analysis of variance established a significant difference in the pattern of change of HNE levels (log transformed) and the PaO_2/FiO_2 ratios with time between the two groups. Follow-up *t* tests revealed significantly lower levels of HNE (Table 1) and also significantly higher PaO_2/FiO_2 ratios in Group B post-tourniquet release.

In conclusion, the results suggest that infusion of HES lowers HNE release from activated neutrophils in postoperative knee replacement patients and may lead to less lung injury.

P408

Toxicity of two lipid emulsions on human lymphocytes and neutrophils

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Introduction The incorporation of lipid emulsions in parenteral diets is a requirement for energy and essential fatty acid supply, and may prevent many metabolic disturbances associated with intravenous feeding amino acids and glucose alone in critically ill patients. For different parenteral fat emulsions, a significant impact on the immune system has been shown. In this study, the toxicity of soybean oil-based emulsion and olive oil-based emulsion on leukocytes from healthy volunteers was investigated.

Methods Twenty-four volunteers were recruited and blood samples were collected before infusion of a soybean oil-based emulsion or olive oil-based emulsion, immediately afterwards and 18 hours later. The cells were studied immediately after isolation, and after 24 hours or 48 hours in culture. The following determinations were made: composition and concentration of fatty acids in plasma, lymphocytes and neutrophils, and lymphocyte proliferation. The toxicity was determined by plasma membrane integrity, DNA fragmentation, phosphatidylserine externalization, mitochondrial depolarization, production of reactive oxygen species and neutral lipid accumulation.

Results Both lipid emulsions decreased lymphocyte proliferation and induced cell death, but the effects of soybean oil-based emulsion were more pronounced. Soybean oil-based emulsion provoked apoptosis and necrosis, whereas olive oil-based emulsion caused neutrophil and lymphocyte necrosis only. Evidence is presented that lipid emulsion is less toxic to neutrophils than to lymphocytes. The mechanism of cell death induced by this lipid emulsion involved mitochondrial membrane depolarization and neutral lipid accumulation, but did not alter production of reactive oxygen species.

Conclusions Olive oil-based emulsion can be an alternative to soybean oil-based emulsion, avoiding leukocyte death and the susceptibility of patients to infections.

Table 1 (abstract P407)

Group	Preoperative, mean (SD)	5 minutes	30 minutes*	60 minutes*	120 minutes*	240 minutes*	24 hours
A	2.31 (0.21)	2.59 (0.35)	2.74 (0.34)	2.83 (0.26)	2.74 (0.24)	2.78 (0.29)	2.68 (0.19)
B	2.39 (0.25)	2.4 (0.32)	2.41 (0.15)	2.43 (0.13)	2.54 (0.2)	2.53 (0.15)	2.65 (0.31)

*$P < 0.01$.

P409

Haemoglobin concentration influences the chloride–bicarbonate but not the strong ion difference–bicarbonate relationship

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Introduction Chloride and bicarbonate concentrations share an inverse reciprocal relationship during either acidosis or alkalosis. This relationship is, in part, due to the red cell chloride shift. However, according to the Stewart quantitative approach to acid–base balance, it seems conceivable to expect a greater relationship between the strong ion difference (SID) and bicarbonate, rather then between chloride and bicarbonate. We propose that, with decreasing haemoglobin (Hb) levels, the SID preserves its independent role with respect to bicarbonate, while chloride gradually loses its relationship.
Methods We retrospectively collected blood gas analysis and electrolytes, from 206 patients, measured on a single blood sample taken on admission. We calculated the apparent SID through the following formula: $[Na^+] + [K^+] + [Ca^{2+}] + [Mg^{2+}] - [Cl^-] - [Lact^-]$ (mEq/l). We divided patients into three groups based on Hb levels: group A ($n = 54$) with Hb levels between 12 and 15 g/dl, group B ($n = 104$) with Hb levels between 9 and 12 g/dl, and group C ($n = 48$) with Hb levels below 9 g/dl. We calculated Pearson's coefficients between the SID and bicarbonate and between chloride and bicarbonate in these three groups of patients.
Results Correlation strength between the SID and HCO_3^- was high and significant even at a Hb concentration below 9 g/dl (see Table 1). Pearson's coefficients for chloride and bicarbonate showed a moderate but significant inverse correlation in group A and group B; eventually this correlation was completely lost in group C.

Table 1 (abstract P409)

Group	Hb (g/dl)	SID–HCO_3^-, r/r^2	*P*	Cl^-–HCO_3^-, r/r^2	*P*
A	12–15	0.76/0.58	0.001	–0.6/0.36	0.001
B	9–12	0.83/0.70	0.001	–0.56/0.32	0.001
C	<9	0.80/0.65	0.001	–0.31/0.09	ns

Conclusion These results give further validation to Stewart's theories: the SID appears to maintain the role of an independent variable with respect to bicarbonate even at low haemoglobin levels, while chloride loses this relationship at haemoglobin levels below 9 g/dl.

P410

Transfusion from male-only vs female donors in critically ill recipients of high plasma volume components

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Objective To reduce the incidence of transfusion-related acute lung injury (ALI), the American Association of Blood Banks (AABB) has recently recommended rapid implementation of strategies to minimize transfusion of high plasma volume components, fresh frozen plasma and apheresis platelets, from potentially alloimunized donors, especially females. The objective of this study was to evaluate the effect of transfusing components from male-only vs female donors on development of ALI, gas exchange, and outcome in critically ill patients.
Methods In this retrospective case–control study we identified patients who received more than two units of high plasma volume components from male-only donors and compared them with patients matched by severity of illness, postoperative state and number of transfusions but who received high plasma volume components from female donors.
Results From a database of 3,567 patients who received a total of 46,101 units fresh frozen plasma and 6,251 units apheresis platelets, we identified 112 patients who received three or more male-only donor components and 112 matched controls. Baseline characteristics, ALI risk factors and development of ALI were similar between the two groups. Arterial oxygenation (PaO_2/FiO_2) worsened after the female donor components (mean difference –52, 95% CI –14 to –91, $P = 0.008$) but not after male-only donor product transfusion (mean difference +22, 95% CI –23 to + 67, $P = 0.325$). Male-only component recipients had more ventilator-free days (median 28 vs 27, $P = 0.006$) and a trend towards lower hospital mortality (14% vs 24%, $P = 0.054$).
Conclusion In critically ill recipients of high plasma volume components, gas exchange worsened significantly after transfusion of female but not male donor components. Prospective studies are needed to evaluate the effect of AABB recommendations on outcome of transfused critically ill patients.

P411

Evaluation of red blood cell transfusion effects in lactate and central venous oxygen saturation in patients with severe sepsis and septic shock

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Introduction Red blood cell (RBC) transfusion is very often performed in critically ill patients despite its potential complications. Its effects on oxygen delivery and microcirculation are not well known. This study aimed at evaluating RBC effects in blood lactate levels (LAC) and central venous oxygen saturation ($SvcO_2$) in patients with severe sepsis and septic shock.
Methods A prospective study enrolling patients admitted to an ICU at a university hospital with severe sepsis and septic shock presenting hemoglobin (Hb) levels below 9.0 g/dl. These patients were randomized for maintaining Hb >9 g/dl (Group 1) or >7 g/dl (Group 2). Before (preT) and at least 1 hour after each transfusion (postT) LAC, $SvcO_2$ and Hb data were collected. Data were analysed by analysis of variance, paired *t* test and paired Wilcoxon test. Results were considered significant if $P \leq 0.05$.
Results Thirty-six transfusions were evaluated in 21 patients (mean age 59.0 ± 15.8 years, 11 females/10 males) with APACHE II score of 13.8 ± 4.1. Each group included 18 patients. The levels of Hb preT and postT were 7.51 ± 1.03 and 8.48 ± 1.15 ($P < 0.05$). There was a significant difference between preT and postT $SvcO_2$ (70.9 ± 8.66 and 73.6 ± 7.2, $P = 0.01$) but not in LAC levels (24.1 ± 8.9 and 22.9 ± 7.6, $P = 0.45$). When groups were analyzed separately, only in Group 2 was a significant difference found ($P = 0.0005$ and 0.05, respectively for $SvcO_2$ and LAC). In 10 transfusions a worsening of $SvcO_2$ postT was

observed and all these patients had preT $SvcO_2 > 70\%$. Although there was no significant correlation between a worsening in $SvcO_2$ and preT Hb, eight of these patients were allocated to Group 1. Another 13 transfusions were done with a $SvcO_2$ preT < 70, and 10 of them improved ($> 5\%$) after transfusion (mean percentage of improvement = 18.9%). Only four of these patients were allocated to Group 1. Patients with high levels of preT LAC ($n = 21$) only improved (reduction $> 10\%$) in 42.9% of cases. A total 53.3% of patients with normal preT LAC levels worsened (rising $> 10\%$) postT. The mean preT Hb from these patients was 8.18 ± 0.9.

Conclusion In patients with $SvcO_2 < 70$ and/or Hb < 7.0 g/dl, transfusion seems to result in an improvement of perfusion parameters. However, in patients with $SvcO_2 > 70$ or normal lactate levels, transfusion seems to impair tissue perfusion.

P412

Transfusion profiles in intensive care units from a university hospital

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Introduction Red blood cell (RBC) transfusion is very often performed in critically ill patients despite its potential complications. New guidelines recommend that doctors should have conservative behavior regarding its use. The objective of this study was to evaluate the transfusion profile among patients in ICUs at a university hospital in Brazil.

Methods A prospective evaluation of all patients admitted to six ICUs (surgical–medical, private, neurosurgery, medical, pneumology and coronary units) that have received a RBC transfusion as indicated by assistant physicians during October/November 2005. Clinical data as well as the characteristics of the transfusion were collected and submitted to univariate statistical analysis (chi-squared and Student's *t* test). Results were considered significant if $P \leq 0.05$.

Results Four hundred and eight transfusions were made in 71 patients (38 females, 33 males), 35 medical/36 surgical, with a mean age 57.2 ± 8.4 years, mean APACHE II score 17.7 ± 5.3, and mean SOFA score on the day of transfusion 6.09 ± 3.99. At admission, 60 patients (84.5%) had comorbidities, 10 (14.1%) had chronic coronary disease. At transfusion, 54.9% had sepsis, severe sepsis or septic shock, and 9.9% had acute coronary syndrome. The mean hemoglobin (Hb) level at ICU admission was 9.69 ± 2.3 g/dl and the mean level that triggered transfusion was 6.88 ± 1.1 g/dl. The most important transfusion indication was Hb levels (49.8%), followed by active bleeding (31.8%). The mean number of RBC transfused per time was 1.68 ± 0.96 and the mean age of RBC was 14.3 ± 7.83 days (46.6% had more than 14 days). Adverse events occurred in 3.4%. The 28-day mortality rate was 47.1%. Only the SOFA score at the day of transfusion correlated with mortality ($P = 0.004$). There was no correlation with age, type of ICU, APACHE II score, total number or age of RBC, Hb at admission or Hb pretransfusion. There was a significant difference between the pretransfusion Hb ($P < 0.00001$) and the number of RBC transfused at the same time considering all ICU enrolled in the study ($P < 0.00001$).

Conclusions The Hb level that triggered transfusion was in agreement with recent guidelines regarding critically ill patients, although there was a difference between all ICUs. Despite the fact that there is a scarceness of RBC, the RBC were higher in age. The missing correlation with mortality can be due to the small sample size.

P413

National survey of transfusion practices

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Introduction The awakening of the residual risks of blood transfusion leads, everywhere in the world, to efforts to reduce them. The aim of the study was to assess the transfusion practices in Tunisia.

Patients and methods A multicentric prospective observational study of about 1,000 transfusions practiced during 2004 in Tunisia. Data were determined by the prescriptor of the transfusion. The data were analyzed with SPSS 12.0.

Results The mean age of the transfused patients was 35.78 years. The sex ratio was 1.2. A total of 48.3% of the patients had transfusion history. Allogeneic immunization and viral serology conversion were reported in 2.1% of these patients. The indications were generally carried in front of chronic medical pathologies (36.9%), acute medical pathologies (28.2%) and surgical pathologies (elective 11.7%, urgent 11.2%). The haemoglobin threshold for transfusion was 7.29 g/dl and depended on the indication of the red cell transfusion: 6.16 g/dl for urgent medical pathologies, 6.22 g/dl for chronic medical pathologies, 7.74 g/dl for urgent surgical pathologies, 10.38 g/dl for elective surgery, 6.15 g/dl for urgent obstetrical pathologies. The mean platelet count was 24,000 (patients transfused by platelet units). The ABO and rhesus determination were made in 99% of the cases. A phenotypic determination was required in only 34.5% of the cases. The search for irregular agglutinins was made in 20.7% of the cases. The test of compatibility at the laboratory was practiced in 95.4% of the cases. The amount of blood transfused was 2 units. Immediate incidents were reported in 2.5% of the cases. The post-transfusion haemoglobin average was of 9.15 g/dl.

Discussion and conclusion The evolution of the blood transfusion was remarkable, since the use of total blood in the 1980s, with the acquisition of the first techniques of separation of the blood components. The transfusion practice in Tunisia is far from being to the standards. The results obtained make it possible to transmit to the clinician the failures of the system, to better include how to prescribe a blood product, to follow its effectiveness and its possible side effects, and to apprehend the impact of the innovated biotechnologies to improve quality of transfusion medicine in coherence with the security requirements.

P414

Could the combination of bleeding time and platelet function predict the perioperative transfusion requirements in cardiac surgery patients?

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Introduction The reduction in platelet count and function is the most important, unsolved, nonsurgical cause of postoperative bleeding after open heart surgery. On the other hand, the bleeding time (BT), the only comprehensive test to explore primary haemostasis, detects otherwise unknown defects in platelet–vessel wall interactions. The present study was undertaken in order to clarify whether the BT and platelet function tested preoperatively could predict the perioperative transfusion requirements in cardiac surgery patients.

Patients and methods Sixty-eight patients (54 males/14 females) participated in the study. Thirty-two patients underwent valve(s) replacement (group A) and the remaining underwent coronary artery bypass grafting(s) (group B). The BT determination was performed according to the Mielke technique using Surgicutt devices (ITC, USA). Platelet function was evaluated by the aggregation procedure using four agonists: ADP, arachidonic acid, collagen and ristocetin at a final concentration of 4 x 10^{-6} M, 0.5 mg/ml, 0.19 mg/ml and 1.2 mg/ml, respectively.
Results (1) In the immediate postoperative time, a significant reduction in haemoglobulin levels was observed in both groups compared with that of the preoperative time (13.3%, $P < 0.05$ for group A and 28.4%, $P < 0.01$ for group B). No difference existed in haemoglobulin levels between groups postoperatively. (2) Platelet values were slightly different between the groups. A significant decrease in platelet count was observed in both groups postoperatively (28.7%, $P < 0.03$ for group A and 22.4%, $P < 0.05$ for group B). (3) The results of BT and platelet activation (performed preoperatively) were similar for patients who underwent valve replacement and patients who underwent coronary artery bypass grafting – although in this group platelet activation with arachidonic acid and ADP was ~11% lower with both agonists. (4) The transfusion requirements were slightly higher for patients in group A, and more patients in group B received no transfusion (one vs four patients).
Conclusion In patients undergoing cardiac surgery with a negative history of bleeding and early interruption of antiplatelet treatment, the BT and platelet function do not offer much in the setting to predict perioperative bleeding.

P415

Emergency staff is in danger

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Objective To investigate the ratio and characteristics of aggression, threat and physical violence directed towards staff in emergency departments as a model of state hospitals.
Methods A questionnaire were filled in by the staff working in the emergency department of three high-volume inner-city state hospitals. The individualized data collected were relevant to the pattern of violence, age, sex, number of years in the profession, nature of the job, and the behavioral characteristics of assailants, and outcome of incidents. The data were abstracted between 1 May and 31 May 2006.
Results A total of 109 staff reports were reviewed. The relationship of aggression with sex, age and years of experience were insignificant (P values were 0.464, 0.692, and 0.298, respectively), while profession was very significantly related ($P = 0.000$). The relation between threat and sex is $P = 0.311$, experience 0.994, profession 0.326, age 0.278. The relationship of threat with sex, years of experience, profession and age were insignificant (P values were 0.311, 0.994, 0.326, and 0.278, respectively). On the other hand, physical assault was found significantly related to sex, years of experience, profession and age (P values were 0.042, 0.011, 0.000, and 0.000, respectively).
Conclusion Violence to the staff is common. There is not a significant relationship between aggression, threat and personal characters. However, male sex, >5 years experience, emergency doctor, ≥31 years of age are the risk factors for physical violence.

P416

Shaken baby syndrome: the classical clinical triad is still valid in recent court rulings

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Introduction Subdural haemorrhage, retinal bleeding and hypoxaemic encephalopathy have long been considered a diagnostic clinical triad for the so-called shaken baby syndrome (SBS). The classical triad, however, has been challenged in the recent past by the so-called 'unified hypothesis' by Geddes and colleagues [1] with subsequent implications in court rulings in suspected cases of SBS.
Judicial and scientific dilemma The unified hypothesis by Geddes suggested an alternative cause for SBS injuries that did not involve significant shaking. The Geddes theory led to the speculation that subdural and retinal haemorrhage was not caused by traumatic shearing of subdural and retinal veins but by a combination of cerebral hypoxia, raised intracranial pressure and raised arterial and central venous pressure. The publication of this theory was met with scepticism by many forensic and paediatric pathologists but was enthusiastically embraced by defence attorneys. This dilemma resulted in the UK with several appeals against prior convictions of murder/manslaughter because of alleged traumatic shaking of young children. The forensic community awaited with great interest the ruling of the Court of Appeal in London on 21 July 2005.
Court ruling of 21 July 2005 Four cases of alleged SBS were brought to the Court of Appeal in London. Two convictions were upheld, one conviction was dismissed and one conviction was reduced from murder to manslaughter. In their written judgement their Lordships clearly stated: 'In our judgment, it follows that the unified hypothesis can no longer be regarded as a credible or alternative cause of the triad of injuries'. The Crown Prosecution Service made a press release that 'Today's judgement sends a clear signal validating the CPS in prosecuting Shaken Baby Syndrome cases. The Geddes theory will no longer be used by the defence.'
Conclusions Diagnosing SBS is a very complex and delicate matter. The mere presence of the classic triad does not automatically or necessarily lead to a diagnosis of nonaccidental head injury or a conclusion of unlawful killing. Diagnosis of (intentional) SBS must be based on the combination of: medical elements, elements from police inquiry, and forensic and crime scene elements. Physicians, particularly those working at the medico-legal interface (such as emergency physicians), should realise that medical observations may play a pivotal role in the diagnosis of SBS. As important is the realisation that, despite alternative hypothesis in medical literature, the classical triad of symptoms (subdural haemorrhage, retinal bleeding, hypoxaemic encephalopathy) is still valid as diagnostic for SBS according to recent (UK) court ruling.
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P417

Organophosphate poisoning and related mortality with oxime perfusion

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Introduction A retrospective study performed between 1 January 2001 and 31 October 2006 in patients admitted to the ICU with

organophosphate poisoning (OPP). The aim of the study was to determine the relation between mortality and: (a) toxicity of organophosphate, (b) time between ingestion and management of the patient, (c) coligernic manifestations, (d) time and doses of oximes and atropine.
Methods Were admitted to the ICU 29 patients with OPP. The data were treated by SPSS 14 for Windows and the analysis consisted of a descriptive study, analytic study (chi-square analysis, Spearman association analysis) and comparison between groups (Student *t* analysis, Wilcoxon Mann–Whitney and Kolmogorov–Smirnov tests). The receiver operating characteristic (ROC) was applied for the Sequential Organ Failure Assessment (SOFA) score.
Results Twenty-nine patients were included in the study, 21 males and eight females. The mean age of the males was 47.71 years (SD = 13.58) and of females was 41.0 years (SD = 11.66), and 62.7% were from a rural area and 37.3% from an urban area. Mortality does not have a significant statistic relation ($P > 0.05$) with toxicity of organophosphate, time and doses of atropine. However, statistical significance was found between mortality and: (a) time between ingestion of the poison and treatment (Spearman test, $r_s = -0.596$, $P < 0.05$), (b) muscarinic manifestations (chi-square test, $\chi^2 = 4.152$, $P < 0.05$), (c) time of oximes (Kolmogorov–Smirnov test with $Z = 1.439$, $P < 0.05$) and doses of oximes (Kolmogorov–Smirnov test with $Z = 1.412$, $P < 0.05$). The ROC analysis reveals that for the respiratory SOFA at 9 days, the area under the ROC curve was 0.917; this means that this SOFA score can predict correctly in 91.7% of the cases.
Conclusion In our study we concluded that the mortality rate was increased with prolonged perfusion of oximes and with muscarinic manifestations of OPP but not with the time and dose of atropine. The respiratory SOFA score at 9 days matches with prediction in above 90% of the cases.

P418

Approaches of Turkish anesthesiologists to delirium observed in intensive care unit patients

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Objective To determine attitudes and practices of the Turkish anesthesiologists and residents about delirium in the ICU.
Methods An anonymous questionnaire consisting of 22 questions [1] was mailed to 258 anesthesiologists and residents.
Results One hundred and fifty-four questionnaires were returned (60% response). Of the respondents, 57% were male and 61% were residents. One-half of respondents work in hospitals with more than 800 beds; 65% of respondents had an ICU facility of 7–12 beds. Seventy-two percent of the respondents had seen delirium in the ICU and also 70.2% of these respondents observed delirium in <25% of patients who were on mechanical ventilation. Although delirium was accepted a significant or very serious problem by 92.5% of the respondents, underdiagnosis was acknowledged by 74%. Routine screening for delirium was performed by 41.6% of the anesthesiologists and 88.1% of them were repeating daily. Clinical assessment was used in 76.7% of the screenings. Delirium was treated with haloperidol and benzodiazepine by 61.5% and 24% of the respondents. Of the respondents, 93.4% were not able to attend a meeting related to delirium and 67.6% did not read even an article about delirium.
Conclusions Turkish anesthesiologists and residents consider delirium a relatively common and serious problem. However, they seldom perform screening tests and try to update their knowledge regarding delirium.

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P419

A comparison of the confusion assessment method for the intensive care unit and the NEECHAM confusion scale in intensive care delirium assessment

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Introduction Reports indicate an incidence of intensive care delirium of 11–87%. The confusion assessment method for the intensive care unit (CAM-ICU) is widely used in delirium assessment in ICUs. However, its binomial results constrain the evaluation of severity. The NEECHAM confusion scale has recently been validated for use in the ICU and uses a numeric assessment. This scale allows the patients to be classified in four categories of delirium severity (normal, at-risk, mild to early, moderate to severe). In this study we investigated the diagnostic value of the NEECHAM referring to the CAM-ICU.
Methods A consecutive sample of 106 patients in a mixed ICU (cardiac surgery (CS) 35%, noncardiac surgery (NCS) 26%, internal medicine (IM) 39%, age 62 ± 14 years, male 63%) was assessed after a stay in the ICU ≥24 hours. All patients with a Glasgow Coma Scale ≥ 10 and age ≥ 18 years were included. A nurse researcher simultaneously assessed both scales once daily in the morning. A total of 272 paired observations were made. Data were analyzed using the NEECHAM cut-off values of ≤26 (at-risk), ≤24 (mild delirium), and ≤19 (severe delirium).
Results Using the CAM-ICU the overall prevalence was 15%. Prevalences in CS, NCS and IM were 9%, 14% and 21%, respectively. Using the NEECHAM scale, the overall prevalence was 33% (16.5% mild, 16.5% severe) and 36%, 21% and 38% for the three patient categories, respectively. Sensitivity was 100%, specificity was 79%, positive predictive value was 46% and negative predictive value was 100%. Using the cut-off value ≤19, sensitivity was 83% and specificity was 96%. All positive CAM-ICU patients were detected by the NEECHAM (85% severe, 15% mild). However, 21% of the CAM-ICU negative patients had a NEECHAM value that diagnoses delirium (4% severe, 17% mild). Consequently, 27% of the CS group (19% severe, 8% mild), 7% of the NCS group (7% mild) and 17% of the IM group (2% severe, 15% mild) were diagnosed to be delirious using the NEECHAM and not delirious using the CAM-ICU.
Conclusion The NEECHAM delirium scale identified all cases of delirium that were detected by the CAM-ICU. Moreover, additional delirious patients were identified, especially in the CS group. In this pilot experience, the NEECHAM scale was a valuable screening tool for intensive care.

P420

The occurrence of delirium is severely underestimated by intensivists and intensive care unit nurses during daily ICU care

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Introduction Patients improve faster in the ICU if sedatives are stopped as soon as possible with inherent occurrence of sleeping disorders, and delirium, which could compromise the recovery

process and prolong the ICU stay. We investigated whether intensivists and ICU nurses could clinically identify the presence of delirium in ICU patients during daily care.

Methods All patients in a 3-month period who stayed >48 hours in the ICU were evaluated daily for the presence or absence of delirium by treating intensivists and ICU nurses responsible for daily care. Patients were evaluated independently for the occurrence of delirium by a trained group of ICU nurses who were not involved in the daily care of the patients under study. Since communication with ventilated patients is compromised due to the inability to speak, a specific scoring system was used (confusion assessment method for the intensive care unit (CAM-ICU)), which has been developed for the evaluation of the presence of delirium. Delirium as judged present by this CAM-ICU correlates well with a DSM-IV delirium diagnosis by a trained psychiatrist. Values are expressed as the median and interquartile range (IQR).

Results During the study period, 46 patients (30 males, 16 females), age 73 (IQR = 64–80) years with an ICU stay of 6 (4–11) days were evaluated. CAM-ICU scores were obtained during 481 patient-days. Considering the CAM-ICU as the gold standard, delirium occurred in 50% of the patients with a duration of 3 (1–9) days. Days with delirium were poorly recognized by doctors (sensitivity = 29.8%; specificity = 99.7%; PPV = 99.6%) and ICU nurses (sensitivity = 35.6%; specificity = 97.8%; PPV = 84%). Patients with a delirium were longer on the ventilator (6 (4–25) days), and had a longer ICU (9 (6–26) days) and hospital stay (29 (21–41) days) than those without delirium during their ICU stay (4 (1–6), $P = 0.01$; 5 (3–8), $P = 0.002$; and 19 (7–30), $P = 0.01$), respectively. APACHE II and SAPS II scores were comparable in both groups.

Conclusion Delirium is badly recognized in the ICU by intensivists and ICU nurses. In view of the impact of delirium on ICU and hospital stay, more attention should be paid to the implementation of a delirium screening instrument during daily ICU care.

P421

Sedation practices in Denmark

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Introduction The interest of sedation in ICU patients has been increasing the last 10 years. The benefits of protocol-driven care have become evident.

Objective The aim of the study was to describe current practice of sedation in Danish ICUs addressing the use of protocols and the wake-up call test.

Methods Two doctors and two nurses from all the Danish adult ICUs were identified to participate in an Internet-based survey. These persons answered questions about sedation practices, use of sedation scorings systems, and withdrawal symptoms.

Results Twenty-nine (82.9%) out of a total of 35 possible hospitals answered, including 113 (57.7%) answers out of a total of 196 possible answers. Ninety-seven per cent of the physicians were specialists in anaesthesiology. Eighty-seven per cent of the nurses were certified intensive care nurses. Forty-seven per cent were from university hospitals. Twenty-six per cent had a sedation protocol, 37% of the physicians and 14% of the nurses. Only one-third of the ICUs had a protocol for sedation. Sixty-eight per cent having a protocol used it always or often, whereas 32% never use it. Sixty-seven per cent had a sedation scoring system in their departments. The scoring systems used was: Ramsay 49%, Sedation Agitation Score 10% and own (locally made) scoring system 41%. Twenty-two per cent answered that the scoring systems was always used, 58% often and in 20% the scoring systems was seldom used. Forty per sent use the 'wake-up call' test, 63% physicians and 37% nurses. Sixty per cent answered 'no we do not use' the wake-up call test, 47% physicians and 53% nurses. Withdrawal symptoms were experienced more than three times as frequently by nurses compared with physicians (31% vs 9%). Five times as many experienced withdrawal symptoms in the group not having a sedation and analgesia protocol (84% vs 16%).

Conclusions There is still a great educational potential for improving the use of sedation protocols and implementing sedation scoring systems and the wake up test in Danish ICUs. This potential could perhaps reduce the incidence of withdrawal symptoms. Effort should also be placed in implementing the sedation protocol in the ICU, illustrated by the differences in numbers of doctors and nurses having a sedation protocol.

P422

Evaluation of two sedation techniques in a casualty department

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We compare the efficacy, adverse events, and recovery duration of etomidate and propofol for use in procedural sedation in the emergency department (ED). A randomized nonblinded prospective trial of adult patients undergoing procedural sedation for painful procedures in the ED was made. Patients received either propofol or etomidate. Doses, vital signs, nasal end-tidal CO_2 ($etco_2$), pulse oximetry, and bispectral electroencephalogram analysis scores were recorded. Subclinical respiratory depression was defined as a change in $etco_2$ greater than 10 mmHg, an oxygen saturation of less than 92% at any time, or an absent $etco_2$ waveform at any time. Clinical events related to respiratory depression, including an increase in supplemental oxygen, the use of a bag-valve-mask apparatus, airway repositioning, or stimulation to induce breathing, were noted. Etomidate and propofol appear equally safe for ED procedural sedation. Etomidate had a lower rate of procedural success and induced myoclonus in 20% of patients (see Table 1).

Table 1 (abstract P422)

Agent	Etomidate ($n = 53$)		Propofol ($n = 55$)	
Subclinical respiratory depression	Yes ($n = 18$)	No ($n = 35$)	Yes ($n = 23$)	No ($n = 32$)
Increased supplemental oxygen	1/9 (2.1, 0.9–11.2)	2/34 (2.9, 0.8–7.2)	2/23 (4.4, 1.2–14.4)	1/32 (1.6, 0.2–5.5)
Bag-valve mask (%)	2/18 (6.9, 1.9–13.9)	0/34 (0, 0–2.3)	2/23 (4.4, 1.4–11.9)	0/32 (0, 0–2.7)
Airway repositioning	3/18 (9.7, 2.9–16.0)	3/34 (5.1, 1.4–8.7)	3/23 (6.5, 1.5–11.6)	3/31 (4.7, 1.1–8.0)
Stimulation to induce breathing	4/18 (11.1, 5.1–19.6)	2/34 (2.9, 0.8–7.1)	3/23 (7.6, 3.2–14.5)	3/31 (4.7, 1.8–9.6)

P423

Comparison of dexmedetomidine with propofol/midazolam in sedation of long-stay intensive care patients: a prospective randomized, controlled, multicenter trial

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Introduction Sedation is a major problem in long-stay intensive care patients despite use of sedation stops and scores. We hypothesized that the α_2-adrenoceptor agonist dexmedetomidine (DEX) is at least equivalent to standard-of-care sedation (SOC), and may reduce the length of ICU stay and improve other clinically relevant outcomes.
Methods We performed a pilot ($n = 85$), phase III, multicenter, prospective, randomized, double-blind, double-dummy, active comparator (SOC: either propofol or midazolam) study to define the feasibility and size of a pivotal trial. Patients with expected ICU stays ≥48 hours and a need for sedation for at least 24 hours after randomization were included within the first 72 hours of ICU stay. The maximum duration of study sedation was 14 days, with a 45-day follow-up from randomization. Sedation was Richmond Agitation Sedation Scale (RASS)-score targeted, with daily sedation stops.
Results Forty-one patients received DEX and 44 SOC (28 propofol). The goal was moderate (RASS 0 to −3) sedation in most patients (78% in DEX and 80% in SOC). Patients were at the target RASS 55% (DEX) and 57% (SOC) of the sedation time (not significant): for RASS target 0 to −3, 68% (DEX) and 64% (SOC) of the time (not significant) and for RASS target −4, 31% (DEX) and 63% (SOC), respectively ($P = 0.006$). Median time from admission/randomization to ICU discharge was similar (DEX 6.6/5.7 days, SOC 6.7/5.5 days, not significant). Mechanical ventilation was shorter for DEX with RASS target 0 to −3 (DEX 70.2 hours, SOC 92.5 hours, $P = 0.027$), and patients' ability to communicate (multidimensional visual analog scale) was better with DEX ($P < 0.001$). Occurrence rates and number of patients with overall and serious adverse events were similar.
Conclusion DEX is well tolerated and comparable with SOC in long-term sedation, but not suitable as the sole agent for deep sedation. DEX enhances the patient's ability to communicate. Its effects on relevant outcomes (for example, duration of mechanical ventilation) should be tested in a large randomized controlled trial.

P424

Multimodal short acting sedation using NMDA antagonist and remifentanil in brain trauma patients: a prospective randomised study

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Critical Care 2007, **11(Suppl 2):**P424 (doi: 10.1186/cc5584)

Introduction We hypothesize that using a multimodal short-acting sedation regimen based on remifentanil and NMDA-antagonist receptors such as ketamine, clonidine and magnesium will improve cerebral protection and make clinical patient examination easier without hemodynamic impairments.
Methods Sixty-eight ventilated brain trauma patients (mean Glasgow Coma Scale: 5 ± 3) with controlled invasive ventilation during 6.4 (± 4) days were prospectively randomized into two groups (G1 $n = 32$; G2 $n = 36$) using different sedation protocols to reach a mean hourly Ramsay Score of 4. Sedation in G1 was based on morphine (0.1 ± 0.1 mg/kg/hour) and midazolam (0.4 ± 0.4 mg/kg/hour); in G2 on remifentanil (0.25 ± 0.25 μg/kg/min), magnesium (0.08 g/kg/day), ketamine (0.15 ± 0.15 μg/kg/min), clonidine (0.001 ± 0.001 μg/kg/min) and propofol (2 ± 1.5 mg/kg/hour). The cerebral parameters (mean intracranial continuous pressure (mICP); mean cerebral perfusion pressure (mCPP)) and the needs of norepinephrine (Ne) were evaluated hourly. Preloading was adapted by a continuous central venous pressure measurement before Ne adaptation requirements to keep the mCPP over 60 mmHg. For statistical analysis a Shapiro–Wilk test, a Wilcox test and a Student *t* test were used.
Results Demographic data (age, gender, trauma severity score) were comparable in both groups. The waking time was significantly shorter in G2 (5 ± 8 min) compared with G1 (35 ± 20 min) ($P < 0.05$). The mICP was more stable in G2 (9 ± 4 mmHg) compared with G1 (10 ± 9 mmHg) ($P = 0.02$). The mCPP were comparable in G1 (62 ± 10 mmHg) and in G2 (63 ± 0.2 mmHg) but with a 24% swing in dose requirement adaptation of Ne in G1 compared with a 6% daily swing in G2 ($P < 0.02$).
Conclusion By using a multimodal short-acting sedation protocol based on remifentanil and NMDA-antagonist receptors we were able to provide adequate sedation in brain trauma patients. Neurological parameters were respected with this regimen, avoiding the risk of secondary patient hemodynamic destabilisation during the waking periods.

P425

Inhalational sedation during transport to the intensive care unit

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Introduction Inhalational ICU sedation is increasingly applied since the introduction of AnaConDa® (Sedana Medical, Sweden). This anaesthetic-conserving device (ACD) retains exhaled sevofluorane (SEV) and resupplies it during inspiration [1]. A syringe pump delivers liquid SEV into the device. Since January 2004 we have used the ACD as a standard practice. Our patients anaesthetised with SEV in the OR and scheduled for ICU sedation with SEV only need propofol on transport. Could this be avoided when using the ACD during transport?
Methods Forty-one patients after major abdominal surgery were included in this quality assurance project. In 20 patients the ACD was inserted into the anaesthesia circuit to take up warmth, humidity and SEV for 15 minutes and used for transport. SEV infusion was started in the ICU after gas monitoring. Twenty-one patients scheduled for propofol sedation served as controls. During transport all patients were ventilated with Oxylog2000 (Dräger, Germany), vital parameters were monitored, and the Ramsay Score (RS) was assessed at five time points. If necessary, propofol injections of 0.5 mg/kg were given. Statistics were *t* test for parametric data (mean ± standard deviation), U test for nonparametric data (median (interquartile range)), SPSS 11.04.
Results The age, weight, duration of anaesthesia (ACD/controls 7.3 ± 2.0/6.3 ± 2.2 hours), total sufentanil (124 ± 75/118 ± 57 μg) and transport time (16.3 ± 2.7/17.0 ± 2.7 min) were not different between groups, and neither were heart rates, mean arterial pressures and RS at five time points during transport. ACD patients needed less propofol injections (0 (0–1)/3 (2–4), $P < 0.001$)

and reached the ICU with a similar RS (5 (4.5–5)/5 (4.75–5)). End-tidal SEV concentrations were similar in the OR (1.3 ± 0.2/ 1.2 ± 0.2 vol%), but different when arriving in the ICU (0.6 ± 0.2/ 0.2 ± 0.1 vol%, $P < 0.001$).

Conclusions AnaConDa® effectively retains SEV in patients and permits inhalational sedation during >15 minutes transport. Hemodynamic stability and depth of sedation are as good as the standard regime with Propofol. Less SEV exhaled by the patients during transport also means less contamination of the workplace.

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P426

Pharmacokinetics of single intravenous bolus administration of propofol in preterm and term neonates

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Background The aim of this study is to describe maturational aspects of propofol pharmacokinetics following single intravenous bolus administration in childhood.

Methods Seventy propofol blood–time profiles were collected in nine neonates (mean weight 2.4, range 0.91–3.8 kg) by arterial blood samples up to 24 hours after administration of a single intravenous bolus of propofol (3 mg/kg over 10 s) before elective chest tube removal. Concentration–time curves obtained for every individual neonate were interpreted by two-stage analysis as two-compartment and three-compartment open models. These newly collected observations following intravenous bolus administration of propofol in preterm and term neonates ($n = 9$) were combined with individual pharmacokinetic estimates in toddlers ($n = 12$) and young children ($n = 10$) [1,2]. Data were reported by the median and range. The Wilcoxon test or linear correlation were used to analyse the pharmacokinetic findings in neonates, toddlers and young children.

Results The blood–concentration curves obtained for every individual patient were interpreted by two-stage analysis as a three-compartment open model in a cohort of 31 patients with a median weight of 11.2 (range 0.91–24) kg and a median postmenstrual age of 108 (range 27–405) weeks. The median clearance was 36.8 (range 3.7–78.1) ml/kg/min, the median apparent volume of distribution at steady state (V_{ss}) was 7.6 (1.33–15.6) l/kg and the median final serum elimination half-life was 377 (range 27–1134) minutes. Median clearance was significantly lower in neonates compared with toddlers and older children ($P < 0.01$) and these differences remained significant after allometric scaling (ml/kg 0.75/min). A significant correlation between V_{ss} and postmenstrual age ($r = 0.61$, 95% CI 0.32–0.8, $P < 0.004$) was observed.

Conclusions Propofol disposition is significantly different in neonates compared with toddlers and young children, reflecting both ontogeny and differences in body composition. Based on the reduced clearance of propofol, accumulation during repeated administration and longer recovery time are more likely to occur in neonates.

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P427

Remifentanil vs conventional sedation in The Netherlands: a pharmacoeconomic model analysis

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Introduction The goal of this study was to compare the duration of mechanical ventilation (MV), the length of stay (LOS) and the direct medical costs of remifentanil-based sedation (RS) vs conventional sedation (CS) in ICU patients requiring MV.

Methods A Markov model was developed based on UltiSAFE, a recent Dutch open-label randomized controlled study that included patients with an expected MV time of 2–3 days. Study medication was either CS (morphine or fentanyl combined with propofol, midazolam or lorazepam according to Dutch guidelines) or RS (remifentanil, combined with propofol when required). The LOS on the ICU, the time at which the patient was eligible for weaning or extubation and the actual time of weaning and extubation, plus all study drugs with all adjustments in dosage, were recorded. The model describes the patient flow on the ICU. Three states were defined: MV before weaning, MV after weaning has started before extubation, post-MV before discharge. At every hour, patients either stay at the current state, move to the next state or die. Transition probabilities and the costs of the study drugs were derived from UltiSAFE, whereas all other direct medical costs on the ICU were estimated in a separate Dutch monocenter micro-costing study. All costs were measured from the hospital perspective with 2006 as the reference year. The time horizon used in the model was 28 days.

Results From the trial data, it was estimated that the costs of RS on MV before the start of weaning amount to €22 per hour, compared with €15 for the CS treatment. After the start of weaning, these costs decrease to €8 per hour for RS and €2 per hour for CS. The LOS on the ICU was 9.2 days in the CS group vs 8.1 days in the RS group (difference 1.1, 95% CI 0.6–1.5), whereas the length of time on MV was 6.3 days and 5.2 days, respectively, with a difference of 1.1 day (95% CI 0.6–1.6). The average total 28-day costs were €15,911 in the CS group vs €14,855 in the RS group, resulting in RS related cost-savings of €1,056 (95% CI €58–2,054).

Conclusion Compared with CS, RS seems to be the preferred regimen for patients with an expected MV time of 2–3 days. It not only significantly decreases the length of ICU stay and the total costs but also significantly reduces the duration of MV, which is a risk factor for ventilator-associated morbidity.

P428

Assessment and management of pain in children in A&E: are we doing it the right way?

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Introduction Pain management is one of the most important components in patient care. The severity of the pain should be assessed effectively and weight-based analgesia should be given. The BAEM Clinical Effectiveness Committee standard of analgesia for moderate and severe pain within 20 minutes of arrival in A&E should be applied to children in all A&E Departments

Methods A retrospective study. Five casualty cards with soft tissue injury and fractures in children under 16 years old were picked randomly every day from January 2005. The assessment and management of pain was recorded in each case. A validated pain score tool – Alder Hey triage pain score – was introduced April

2005. Five casualty cards were picked randomly every day from May 2005. The assessment and management of pain in each case was recorded.

Results There were 155 patients in each month. In January, none of the patients were assessed for the severity of their pain; 34 patients received analgesia, of which 15 received weight-based and 19 received age-based analgesia. In May, 84 patients were assessed for the severity of their pain with the Alder Hey triage pain score; 63 received weight-based and two received age-based analgesia. The rest had no pain.

Conclusion The Alder Hey triage pain score should be introduced in A&E as it serves as an effective means of assessing pain in children of all age groups. Analgesia should be prescribed based on the weight of the children.

P429

Pain after cardiac surgery

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Background Acute pain is common after cardiac surgery and can keep patients from participating in activities that prevent postoperative complications especially respiratory complications. Accurate assessment and understanding of pain are vital for providing satisfactory pain control and optimizing recovery. This study was performed to find the location, distribution, and intensity of pain in a sample of adult cardiac surgery patients during their postoperative ICU stay.

Methods In a prospective study, pain location, distribution (number of pain areas per patient), and intensity (0–10 numerical rating scale) were documented on 250 consecutive adult patients on the first, second and third postoperative day (POD). Patient characteristics (age, sex, size, and body mass index) were analyzed for their impact on pain intensity. There were 140 male and 110 female patients, with a mean ± SD age of 65.7 ± 13.5 years.

Results The maximal pain intensity was significantly higher on POD 1 and 2 (3.7 ± 2 and 3.9 ± 1.9, respectively) and lower on POD 3 (3.2 ± 1.5). The order of overall pain scores among activities ($P < 0.001$) from highest to lowest was coughing, moving or turning in bed, getting up, deep breathing or using the incentive spirometer, and resting. After chest tubes were discontinued, patients had lower pain levels at rest ($P = 0.01$), with coughing ($P = 0.05$). Age and sex was found to have an impact on pain intensity, with patients <60 years old and male patients having a higher pain intensity than older patients on POD 2 (4.7 ± 2.0 vs 3.2 ± 2.4, $P = 0.02$ and 4.5 ± 2.3 vs 2.9 ± 2.2, respectively).

Conclusions Pain relief is an important outcome of care. A comprehensive, individualized assessment of pain that incorporates activity levels is necessary to promote satisfactory management of pain. We recommend the use of remifentanil infusion for postoperative pain relief in suitable cardiac surgery patients.

P430

Opioid receptor expression on neutrophils: effect of tumour necrosis factor alpha treatment

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Introduction Opioids and endogenous opioid peptides possess immunomodulating properties and are involved in the regulation of immunocyte activity. These effects are mediated by opioid receptors (OR) on peripheral white blood cells that can be detected and quantified by flow cytometry. We investigated OR expression on neutrophils using polyclonal antibodies against δ-opioid, κ-opioid and μ-opioid receptors (DOR, KOR, MOR) to assess spontaneous and TNFα-induced OR expression on neutrophils.

Methods After approval by the local ethics committee and informed consent, 100 μl whole blood samples from 11 healthy volunteers (EDTA served as anticoagulant) was incubated with 10 μl TNF-α (100 ng/ml) for 3, 6, 12 and 24 hours. Samples were washed and incubated with 5 μl fluorescein-isothiocynate (FITC)-labelled polyclonal antibodies against human MOR, KOR and DOR. Rabbit IgG antibodies served as a negative control. After red cell lysis, flow cytometry was performed to quantify OR expression using live gating on neutrophils. The percentage of positive cells as well as mean fluorescent intensities (MFIs) were determined.

Results Stimulation with TNFα increased the percentage of DOR-expressing cells significantly from 2.1% to 12.8% positive cells after 6 hours. After 12 hours of stimulation 28.6%, and after 24 hours even 68.1%, of neutrophils expressed DOR. The MFI increased during TNFα stimulation from 47.6 ± 15.7 to 254.8 ± 110 after 6 hours, staying levelled at this height. After 6 hours of stimulation, the MFI for KOR reached a maximum, rising from 59.5 ± 19.4 to 513.9 ± 162. During TNFα stimulation, the percentage of positive cells increased from 5.4 to 65.0% after 24 hours (17.5% at 6 hours). Fourteen per cent of neutrophils expressed MOR after 6 hours (initially 5.4%) and up to 57.2% after 24 hours. The MOR MFI was measured at 43.4 ± 16.3 to 410 ± 263.6 6 hours after stimulation with TNFα.

Conclusion Our results display that stimulation of whole blood with TNFα amplifies OR expression of all subtypes significantly on neutrophils. We suggest further studies to clarify the specific actions of opioids and their receptors in health and acute inflammation.

P431

Intravenous anesthesia with S-(+)-ketamine for 'on-pump' coronary artery bypass surgery: hemodynamic profile and effect on troponin T levels

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Introduction In patients with ischemic coronary artery disease the 'sympathomimetic' effects of ketamine can cause myocardial damage. However, the S-isomer of ketamine may have various advantages. We studied the cardiovascular stability and safety of intravenous anesthesia with S-(+)-ketamine for coronary artery bypass graft surgery (CABGS).

Methods After approval of the local ethics committee and written informed consent, 315 patients scheduled for elective 'on-pump' CABGS were enrolled in the study. Patients were randomly allocated to three anesthetic protocols: sufentanil–sevofluorane–propofol (SSP), sufentanil–propofol (SP), and S-(+)-ketamine–midazolam–propofol (KMP). Standard invasive hemodynamic monitoring was performed using a pulmonary artery catheter and hemodynamic variables were reported. Measurements were taken after induction of anesthesia, after weaning from cardiopulmonary bypass, and 6 hours postoperatively. Serial plasma troponin T levels were taken: before induction of anesthesia, after surgery, and 6 and 24 hours postoperatively. All cardiovascular adverse events were recorded (such as electrocardiographic signs of ischemia, myocardial infarction, 28-day mortality).

Results Groups (SSP: $n = 106$; SP: $n = 108$, KMP: $n = 101$) did not differ in preoperative data (for example, biometry, cardiac and coronary profile and risk). Intraoperative management was comparable among groups. Tropinin T levels were rather lower in the KMP group, but did not differ significantly between groups at 24 hours after aortic unclamping. Cardiovascular adverse events showed the same low incidence in all groups. Hemodynamic data were comparable; however, the heart rate (HR) and mean arterial pressure (MAP) after induction were significantly higher in the KMP group (HR: 59 ± 11 vs 63 ± 32 vs 66 ± 13 beats/min ($P < 0.01$); MAP: 74 ± 12 vs 81 ± 16 vs 83 ± 16 mmHg ($P < 0.01$)).
Conclusion In our study, KMP anesthesia was safe to use for CABGS. In comparison with SSP and SP anesthesia, no significant rise in troponin T as a marker of myocardial damage was observed. All three regimens resulted in stable hemodynamics. However, the use of S-(+)-ketamine as an induction agent in patients with coronary artery disease may be limited due to its sympathomimetic effects leading to raised HR and MAP, even if supplemented by midazolam or propofol.

P432

Computer management systems and protocols in intensive care units: do we have any benefit?

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Introduction Computer management systems and treatment protocols (CMS/P) have been recommended for their potential to improve patient safety and outcome. Computer management systems require substantial investments in the ICUs. In return, a high-quality, standardised ICU treatment with software-implemented protocols as well as decreased hand-written documentation has been aimed at. The objective of this study was to systematically review the literature on CMS/P to evaluate their impact on outcome benefit.
Methods A Medline search from 1996 to 2006 with the following key words was performed: critical care or intensive care, and protocol, and data management system or computer management system or computerized documentation.
Results The search revealed 21 potential articles. The language was English in 18 of the articles, two in German and one in Japanese. Of those 21, 10 articles were not studying CMS/P. Of those 11 that fulfilled the criteria, computer management systems were studied in four articles and treatment protocols in 11 articles. The combination of ICU treatment protocol and computer management system was studied in four of the 21 articles.
Of those 11, three of the studies demonstrated that the implementation of a protocol to computer management system increases staff compliance to the protocol. The newer studies showed also that the costs were not increased by the computerised protocol. However, no definite benefit in patient survival or ICU length of stay could be demonstrated (11 of 21 studies). The combined absolute reduction rate in hospital mortality was 2% (95% CI 0–4%) in those four (19% of 21) studies. CMS/P increased the ICU length of stay 3.5 days (95% CI 1.6–5.4 days) and decreased the hospital length of stay 5.9 days (95% CI 1.0–10.8 days), in two different studies.
Conclusion Our results could not confirm any definite benefit from computerised data management systems or treatment protocols regarding outcome. The ICU personnel adherence to treatment protocols seems to increase when implemented into the computerised data management systems. Further research on this topic is needed to justify the investments in computer management systems.

P433

Decreasing the incidence of ventilator-associated pneumonia using the FAST-HUG evaluation

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Introduction Ventilator-associated pneumonia (VAP) is a leading cause of morbidity and mortality in critically ill patients. We implemented a performance improvement project over 2 years to reduce VAP incidence in the medical ICU (MICU) and surgical ICU (SICU).
Methods From 1 January 2004 to 31 December 2005 a prospective intervention was undertaken. Results were compared with historic controls (2003). In year 1 we introduced aggressive oral care using chlorhexidine mouthwash, an early extubation strategy, changing respiratory equipment only when visibly soiled or malfunctioning, and aggressive enforcement of hand-washing and barrier protection methods. At the end of year 1 we augmented the project with the addition of the FAST-HUG (feeding, analgesia, sedation, thromboembolic prevention, head of bed elevation, ulcer prophylaxis, and glucose control) evaluation. During year 2 FAST-HUG was emphasized daily on patient rounds by the intensivists. The CDC VAP definition was used; the Friedman test and Wilcoxon signed ranks test were used for data analysis.
Results The VAP rates in the MICU and SICU for the control period, 1 January–31 December 2003, were 13.41 and 19.37 VAPs/1,000 ventilator-days, respectively. The MICU VAP rate declined to 3.02 VAPs/1,000 ventilator-days and the SICU rate declined to 8.16 VAPs/1,000 ventilator-days over 2 years. The greatest declines occurred during year 2 (Table 1).

Table 1 (abstract P433)

	2003	2004	2005	*P* values
MICU	13.41	10.14	3.02	NS[a], <0.05[b,c]
SICU	19.37	16.45	8.16	NS[a], <0.05[b,c]

NS, not significant. [a]2003/04. [b]2004/05. [c]2003/05.

Conclusion Daily FAST-HUG review on ICU rounds, with aggressive oral care, an early extubation strategy, and aggressive infection control practices, decreases VAP rates.

P434

Significance of postmortem computed tomography in death diagnosis: investigation of the characteristics in patients with cardiopulmonary arrest on arrival

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Introduction Autopsy is a very useful method in analysis of the cause of death. However, the number of those actual enforcements of autopsy has been getting less and less recently. Now, autopsy imaging is very important as an alternative method to autopsy. We evaluated the characteristics in patients with cardiopulmonary arrest on arrival and studied the usefulness of postmortem computed tomography (PMCT) in death diagnosis.
Patients and methods We analyzed consecutive patients with cardiopulmonary arrest on arrival from October 1997 to November 2006. Total number of patients was 127. We studied the multiple

factors in sex, age, trauma or nontrauma, whether or not PMCT, cause of death and final diagnosis. We especially compared the two groups: PMCT(+) and PMCT(–).

Results Seventy patients (55.1%) were men, and 57 (44.9%) were women. Autopsy was done in only three patients. The number of trauma cases was 21 (16.5%) and nontrauma was 106 (83.5%). PMCT was done in 20 patients (15.7%) and it was possible to decide the final diagnosis in 16 (80%). Among 20 patients, there were six trauma cases and we could diagnose the cause of death in all of them. On the other hand, PMCT was not done in 107 patients (84.3%) and we could estimate the cause of death in just 43 (40.2%).

Conclusions We must make more effort to decide the cause of death. Reliable death diagnosis could lead to more effective cardiopulmonary resuscitation. Our date obviously indicated that PMCT was a very effective and powerful method for death diagnosis, especially in trauma cases.

P435

Simulated critical care calls: a simple way to teach complex skills

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This abstract outlines the use of simulated critical care telephone calls into the education of trainees. We hope others may consider it for their centres.

The Capital Health Region provides advanced healthcare for 2 million people, but spread over 9,800 km. We therefore rely heavily on transportation of critically ill patients to a single urban centre. In addition to geographic and climatic factors, bed pressures complicate how we triage, stabilize, transport and receive those patients. A major strategy is the 'Critical-Care-Line': a 24-hour telephone service with teleconference capabilities and contact numbers. However, experience suggests it takes practice to become proficient with its use.

Given the importance of optimal communication, we arrange simulated calls. Senior trainees are paged during a normal workday by the Critical-Care-Line: just as they will be once in independent practice. The facilitator then assumes the role of a referring doctor in a small town. Peer-reviewed cases are used that include pertinent teaching points. Applicable staff at the teaching centre are briefed of this exercise and asked to act as they normally would. For example, emergency physicians, internists, senior nurses and administrators are notified that they may be brought into the call, depending on whether the trainee decides to involve other services (for example, if he/she decides a patient requires further work-up before deciding upon ICU or if he/she decides to bring the patient to emergency if no ICU bed is currently available). All calls are recorded to aid debriefing.

This method allows us to ascertain how trainees ask focused histories, offer practical advice based upon the variable skill set of referring physicians, and deal with complex ethical decisions (for example, if a family wishes to override a patient's previous wish; or how aggressively to treat the terminal patient for whom no prior discussions have occurred). It allows us to test the trainees' knowledge, but more importantly we can determine how well that knowledge is applied in everyday practice.

In Canada, the Royal College of Physician and Surgeons has decreed that trainees become not just medical experts, but also proficient communicators, collaborators, and managers [1]. These goals, while laudable, have been very difficult to capture without novel approaches such as the one outlined. This simple and cost-free addition to our training has been very well received. Initial success means it will now be expanded throughout acute care specialist training.

Reference

1. **Royal College of Physicians and Surgeons of Canada, CanMEDS framework** [http://rcpsc]

P436

Required time for certain intensive care unit procedures

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Critical Care 2007, **11(Suppl 2):**P436 (doi: 10.1186/cc5596)

Introduction A significant amount of time is spent in an ICU for procedures and the care of critically ill patients.

Methods We prospectively collected data regarding demographics and time in seconds required for ICU procedures. Time was recorded as the total time (preparation and action, Time A′) and actual time (intervention only, Time B′).

Results We investigated 60 patients (43 males) of mean age 53.6 ± 3.3 years, severity of illness APACHE II score = 16.5 ± 0.3, SAPS II = 46.4 ± 0.7 and mean ICU stay of 18.6 ± 2.9 days. The time required for ICU procedures is shown in Table 1.

Conclusions A significant amount of time is spent in an ICU for certain procedures. The length of time required is related to complications, failures, physicians' level of training, and presence of assistance. ICU staff personnel should be adequately trained to decrease time, complications and thus the ICU stay and costs.

P437

Intra-observer and inter-observer variability of clinical annotations of monitoring data

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Introduction In order to evaluate new methods for alarm generation from monitoring data, a gold standard of alarm evaluation is

Table 1 (abstract P436)

Procedure	*n*	Time A′	Time B′	Failure at first attempt (%)	Number of required efforts
Central line placement	120	1,791 ± 52.6	1,023.6 ± 40.3	10.4	2.6 ± 0.3
Arterial line placement	251	491.4 ± 38.5	240.6 ± 26.8	30.4	2.3 ± 0.2
Tracheal tube change	78	910.1 ± 43.7	46.4 ± 4.4	5.5	1.4 ± 0.1
Tracheostomy change	96	565.2 ± 26.8	34.3 ± 2.5	7.1	1.1 ± 7.1
Transfer for CT	76	3,375.5 ± 174.5	1,912.1 ± 87.3	0.0	1.0

needed. Nearly all clinical studies into monitoring alarms used clinician judgement and annotation as the reference standard. We investigated the intra-observer and inter-observer variability between two intensivists in the classification of monitoring time series.
Methods A total of 3,092 time series segments (heart rate and blood pressures) of 30 minutes each from six critically ill patients were presented to two experienced intensivists (MD1 and MD2) offline and were visually classified into clinically relevant patterns (no change, level shift, trend) by the physicians separately. One intensivist (MD2) repeated the classification 4 weeks after the first analysis on the same dataset.
Results MD1 found clinically relevant events in 36%, and MD2 in 29% of all time series. In 16% of all cases both intensivists came to different classifications. In 10% even the direction of change was classified differently. MD2 classified 10% of all cases differently between the first and second analysis. Even if level changes and trends were treated as one universal pattern of change, intra-individual variability (MD2 first analysis vs MD2 second analysis) was still 5% and inter-individual variability (MD1 vs MD2, only unequivocal classifications) was 10%.
Conclusion Although this study is small with only two observers who were investigated, it clearly shows that there is a significant intra-individual and inter-individual variability in the classification of monitoring events done by experienced clinicians. These findings are supported by studies into image analysis that also found high intra-individual and inter-individual variability. High inter-observer and intra-observer variability is a challenge for clinical studies into new alarm algorithms. Our findings also show a need for reliable classification methods.

P438

Robust regression methods for intensive care monitoring

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Introduction Alarm generation of modern patient monitoring systems still predominantly relies on simple threshold methods. This leads to an unacceptably high rate of false positive alarms. Many false positive alarms are generated by measurement artefacts and measurement noise. One approach to address this problem is to alarm on the underlying signal (that is, the noise-free time series of the physiological variable), instead of the raw measurement.
Methods Monitoring time series were simulated. Against these data four robust regression methods were evaluated: least trimmed squares (LTS), least median of squares (LMS), repeated median (RM), and deepest regression (DR). Moreover, online monitoring series from critically ill patients during multiparameter monitoring were also compared.
Results LTS and LMS showed comparable behaviour, as did RM and DR. LMS and LTS provided only 20% efficiency, DR 61% and RM 70% (least squares regression = 100%). RM and DR had smaller standard deviations and smaller mean-squared errors than LMS and LTS under different noise distributions (standard deviation of online estimates based on sliding windows of size $n = 21$ for simulated standard normal errors: LMS: 0.875, LTS: 0.887, RM: 0.500, DR: 0.533). Analyses with clinical monitoring data also showed that LMS and LTS preserve sudden level shifts but are unstable and perform poorly with trend changes; RM and DR blur shifts but yield more stable estimations.
Conclusion All four methods allow one to extract the underlying signal from physiological time series in a way that is robust against measurement artefacts and noise. However, there are significant differences between the methods. Overall, repeated median regression seems the best choice for intensive care monitoring since it is not only the most stable but also the fastest method.

P439

ISIS program: a new tool for medical research at the bedside in critical care units

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Introduction The goal of this program is to develop an experimental tool able to record, store and analyse data issued from critical care patients. Due to technical limitations and medical constraints, information systems able to manage such data flow are difficult to deploy.
Methods Data recording is done through a laptop connected to the medical devices, allowing analogical and digital signal transmission through a high-speed network. Several servers are dedicated to specialised tasks: mass storage, model generation, artificial intelligence (AI), telecommunications, and security. A 3 Teraflops supercomputer is dedicated to intensive computation when necessary. Twenty applications are dedicated to elective tasks, most of them running using the Linux operating system.
The 'Aiddiag' data-acquisition software is a standalone application adapted to patient data recording from the biomedical devices and caregiver's inputs. It has a friendly designed user-interface touchscreen at the bedside and was adapted according to caregivers' feedback. Data are also stored in a repository and a selective secondary extraction is possible. Online and offline analysis by the AI engine is allowed. Software had to consider time specifications and uses distributed computation to achieve high workload tasks. We complied to the French legal patient data management constraints.
Results After 2 years, our system is fully deployed. It recorded more than 2,500 patient-hours over a 3-month period. Signal loss is less than 1%. Our tool allows recording of more than 40 digital signals, eight analogical signals sampled at a rate of 1 kHz, and caregiver comments and actions. CPU resources of the laptop are available for supplemental AI developments during data acquisition. Transfer of data to the repository is either a hotplug-automated process or delayed with 5 days of buffering in the laptop. Automated artefacts' cleaning allows time-series analysis (GARCH method) to extract behavioural models after intensive computation. The AI engine is used for medical guideline implementation (that is, severe brain trauma care algorithms) and later comparison with caregiver's behaviour. Remote use of our system is possible and schedulable, allowing other research teams to work on the data. Limitations have been detected during intensive calculation. Fine-tuning of the network will suppress these limitations.
Conclusion ISIS is the first program to achieve an easy-to-use recording tool able to build a very large medical repository. Data analysis methods and AI-controlled automated complex medical guidelines are under evaluation.

P440

Inter-rater agreement in the triage of calls to a paediatric interhospital transfer service

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Introduction As a result of centralisation of PICU services in the United Kingdom, transfer of critically ill children has become common over the past decade. It is not uncommon to receive multiple retrieval requests simultaneously, thus a tool to prioritise the urgency of this would be beneficial. Our aim was to develop such a tool and assess its inter-rater repeatability.
Methods The tool was developed by three senior medical staff of the South Thames Retrieval Service (operating from the PICU at Evelina Children's Hospital, London with 1,000 calls per annum from 24 district general hospitals, resulting in 600 retrievals). A modified Delphi method was used, which comprised an iterative process including a literature review, knowledge of the underlying conditions and a review of retrievals performed by the service over the previous 7 years ($n = 3,669$). Inter-rater agreement was assessed using the weighted kappa statistic, and was measured between various pairings of junior and senior medical staff ($n = 28$ combinations) on 50 retrieval episodes.
Results The final tool comprised five categories (three levels of severity each) allowing for a range of scores from 0 to 15 (Figure 1). Three levels of urgency were defined: semi-urgent (score <8), urgent (score 8–10), immediate (score >10). Overall the tool showed a good to very good strength of inter-rater agreement (kappa scores ranging from 0.65 to 0.88; Figure 2). There were no obvious differences between levels of staff seniority.
Conclusion The score showed acceptable agreement, fullfilling the first step of validation.

Figure 1 (abstract P440)

Category	Score		
	1	2	3
Presenting condition	Seizure Prenatal cardiac diagnosis	Respiratory disease Respiratory physiological derangement Metabolic disorder Post-op Previous trauma (<7days)	Shock Sepsis Blood lactate>4mmol/l Trauma Raised intracranial pressure Upper airway obstruction
Underlying condition	Cerebral palsy Chronic developmental delay Pre-existing metabolic disorder	Diabetes Asthma Ex-premature Sickle cell disease Chronic respiratory disorder	Known cardiac disease Suspected cardiac disease Oncology Known airway abnormality
Severity of illness	Mild	Moderate	Severe
Volume resuscitation	<20ml/kg	20-40ml/kg	>40ml/kg
Physiological response to resuscitation	Normalisation of variables	Partial response (within 20% normal range)	Minimal response (>20% outside normal range)

Figure 2 (abstract P440)

Criteria for assessment	Mean Kappa score	Standard error
Presenting condition	0.883	0.103
Underlying condition	0.838	0.112
Severity of illness	0.654	0.122
Volume resuscitation	0.778	0.111
Response to resuscitation	0.729	0.112
Total score	0.71	0.87

P441

Reduction in retrieval mobilisation time over a 5-year period (South Thames Retrieval Service)

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Critical Care 2007, **11(Suppl 2):**P441 (doi: 10.1186/cc5601)

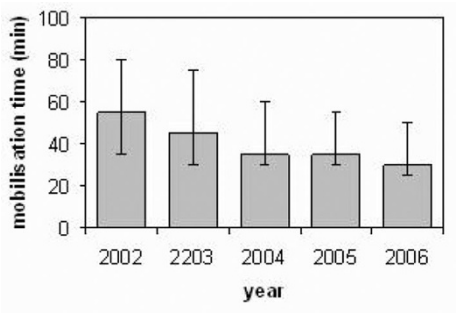
Introduction The South Thames Retrieval Service (STRS) is a specialised paediatric intensive care retrieval service, integrated into the Evelina Children's Hospital, the lead centre in the South Thames Region, London. Over the last 5 years a number of initiatives have been adopted to reduce mobilisation times (the time from retrieval acceptance and activation to departure from the lead centre) and improve service delivery to surrounding district general hospitals (DGHs). The aim of this study was to evaluate whether these initiatives led to a reduction in mobilisation time between January 2002 and December 2006.
Methods The STRS covers 24 DGHs within an 80 mile range serving a population of 1.6 million children in the South Thames region of Greater London. All calls to the service were logged on a detailed database. Retrieval requests for potential PICU patients were triaged and coordinated via a retrieval-specific telephone line. Once accepted, the onsite retrieval team was mobilised and dispatched via a dedicated ambulance to the DGH. Mobilisation includes assimilating and checking pre-packed equipment bags (ventilators, drugs, intubation kit, monitors, and so on) and organising a team of at least one retrieval nurse, doctor and ambulance driver. Details of each retrieval request to the STRS, including the time of the call, were captured on a database containing the patient demographic and clinical details. The interval between accepting the patient for retrieval and team departure from the unit was termed the 'mobilisation time' (minutes). Data were analysed over two time periods, before ($n = 976$ retrievals) and after 2004 ($n = 1,785$), coincident with a dedicated ambulance and driver on site. Nonparametric tests were used for continuous data (Kruskall–Wallis test or Mann–Whitney test) and the chi-squared test for categorical 2 x 2 comparisons.
Results A total of 2,761 retrievals (median age 12 months, 78% ventilated) were performed and included for analysis during the study period, 33 were excluded (missing mobilisation times ($n = 30$) or elective transfers ($n = 3$). Figure 1 shows the process introduced to improve mobilisation times with a dedicated onsite ambulance service in 2004. There was a significant reduction in

Figure 1 (abstract P441)

Year	Process
2002	Control drugs stored and itemised separately from PICU store
	Refrigerated drugs separately packaged in individual transport boxes
2003	New initiative to focus staff awareness of mobilisation times
	Dedicated retrieval nurse identified on each shift
2004	Ambulance and driver on site
2005	Ambulance redesigned to accommodate more equipment
2006	Retrieval doctor allocated for each shift, separate to PICU cover
	Transport ventilators assembled and checked at start of each shift
	Full retrieval kit stored in ambulance

Processes introduced to improve mobilisation times.

Figure 2 (abstract P441)



Median retrieval mobilisation times.

mobilisation time from 2002 to 2006 from 55 minutes (IQR 35–80) to 30 minutes (IQR 25–50), $P < 0.0001$ (Kruskall–Wallis) (Figure 2). When comparing pre-2004 and post-2004 time periods, the median mobilisation time was significantly lower after 2004 with a fall from 45 minutes (IQR 30–70) to 35 minutes (IQR 27–55). There was also a significant increase in the incidence of sub-30-minute mobilisation times, which almost doubled after 2004 with the availability of an onsite dedicated ambulance service (14.3% to 25.9%, $P < 0.0001$).

Conclusion There has been a significant decrease in the mobilisation time of the STRS over the last 5 years. Although the presence of an onsite ambulance service in 2004 had a significant impact on reducing retrieval mobilisation times, a number of other factors and initiatives contributed to steadily reducing mobilisation times over the study period.

P442

Ambulance transport is associated with a higher mortality than private transport following major penetrating trauma in a semi-urban environment

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Aims The use of private transportation has been associated with improved outcomes in urban trauma patients. The need for patient stabilization at the scene needs to be balanced with the need for early operative intervention, and therefore the need for rapid transportation to hospital. Our aim was to assess the relationship between the mode of transport to hospital and outcome in a semi-urban trauma environment.

Methods Data were collected prospectively on 1,396 patients admitted to a Level 1 South African trauma unit over a 1-year period. The Revised Trauma Score was used to assess injury severity and physiological derangement at the time of admission, and to allow comparison between the groups. Mortality was defined as death within 30 days.

Results The mortality in the blunt trauma patients ($n = 527$) was higher in the ambulance transport group, but this was not statistically significant. However, the mortality in the penetrating trauma patients ($n = 808$) was significantly higher in the ambulance transport group ($P = 0.020$, chi-square; Table 1) despite similar Revised Trauma Scores (Table 1).

Table 1 (abstract P442)

Penetrating trauma	Private transport	Ambulance
Alive	98.8% ($n = 254$)	95.6% ($n = 527$)
Dead	1.2% ($n = 3$)	4.4% ($n = 24$)

Conclusion The use of ambulance transportation is associated with a 3.7-fold increase in mortality following penetrating injury. This may be related to longer times in the field resulting in delay to definitive care in hospital.

P443

The use of a track and trigger system on general medical wards

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Introduction Many groups have advocated identification of critically ill medical patients by abnormal or deteriorating physiological parameters. In Southend Hospital a track and trigger system has been used since 2005 to alert nurses to abnormal physiological parameters in order to trigger urgent medical review of the unwell patient. It is recognised that the respiratory rate is a particularly useful predictor of significant deterioration and should be measured with every set of observations. This audit aimed to assess the use of the track and trigger system on the medical wards and ensure that deteriorating critically ill patients are promptly reviewed.

Methods Patient observation charts were reviewed for a specified 24-hour period. Data were gathered on the frequency and type of observations taken. For patients who met criteria to trigger a review, further data were abstracted about the nature of the deterioration and the promptness of the review.

Results One hundred and sixty patient-days of observations were evaluated over seven medical wards. Twenty-nine patients met the trigger criteria and in 16 cases this represented a deterioration. Doctors were called in two cases. Observations were recorded with different frequency on different wards. One ward managed to record the respiratory rate with every set of observations.

Conclusions Documented deteriorations in physiological observations did not trigger medical review. This may be a communication failure or failure to recognise recorded observations as abnormal. For this process to work well relevant observations must be recorded regularly and accurately. The respiratory rate was not consistently recorded between wards and the frequency of measurement of observations was variable. Further education and training is needed to improve recording of the respiratory rate and work needs to be done to establish why doctors were not called appropriately. Concerns about the volume of work generated by the system are unfounded. A positive predictive value of 55% is acceptable and 29 'triggers' in a 24-hour period are manageable.

P444

Design and implementation of needs-specific critical care response teams

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Introduction Following the severe acute respiratory syndrome epidemic in Ontario Canada, the Canadian Resuscitation Institute

was commissioned by the Ministry of Health and Long-term Care to facilitate the improvement of inhospital emergency preparedness through a System-Level Training Initiative. Objectives for the program were to reduce mortality and improve efficiency of ICU resource use through early identification of patients at risk of deterioration and the provision of rapid resuscitation to abort avoidable ICU admissions. The program was designed to train nonphysician responders (primarily nurses and respiratory therapists) supported by remote physician oversight, especially in centres where ICU-trained physicians were not available.

Methods Following an educational needs assessment of learners, a multicomponent critical care response team (CCRT) training course was developed. The 2-day course consisted of a series of small group, interactive, case-based seminars, high-fidelity simulation training, and the publication of a CCRT Provider Manual and Quick Reference Cards. A database for monitoring the effectiveness and impact of the CCRTs was also developed.

Results Beginning in October 2005, 24 CCRT physician instructors were trained in one of two streams: (i) simulator instructors with skills in constructive feedback and assessment of crisis management skills; (ii) instructors who further refined the case-based seminars and edited the Quick Reference Cards. Acquisition of equipment, liaisons with participating hospitals and creation of the CCRT database were completed in the spring of 2006. Since June 2006, 12 CCRT courses have been run, and 263 participants have been trained as CCRT Providers (87% nurses, and 13% respiratory therapists). Local hospital implementation and preceptored programs occurred over a 12-week period before CCRTs we made available full time (24/7).

Conclusions It has been demonstrated that unmet needs in critical care education and training for allied healthcare professionals can be identified and corrected through the development and implementation of a multidisciplinary course designed to facilitate creation of CCRTs in the Province of Ontario. Evaluation of the effectiveness of these teams is ongoing.

P445

Multicentre evaluation of the impact of the introduction of outreach services in the United Kingdom

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Background Critical care outreach services (CCOS) have been introduced in the United Kingdom with aims to: avert or ensure timely admission to critical care; enable discharge from critical care; and share skills with ward staff. We aimed to assess the impact of the introduction of CCOS at the critical care unit level, as characterised by the case mix, outcome and activity of critical care unit admissions.

Methods An interrupted time-series analysis was carried out using data from 108 units participating in the Case Mix Programme that had completed a survey on CCOS provision. Individual patient-level data were collapsed into monthly time series for each unit (panel data). Population-averaged panel-data models were fitted using a generalised estimating equation approach. Various outcomes reflecting the stated aims of CCOS were considered for three groups of admissions: all admissions to the unit; admissions from the ward; and unit survivors discharged to the ward. The primary exposure variable was the presence of a formal CCOS with secondary exposures of CCOS activities, coverage and staffing, identified from the survey data.

Results Of 108 units in the analysis, 79 (73%) had a formal CCOS introduced between 1996 and 2004. For admissions from the ward, the presence of a CCOS was associated with significant reductions in: the proportion of admissions receiving cardiopulmonary resuscitation during the 24 hours prior to admission (odds ratio 0.84, 95% confidence interval 0.73–0.96); the proportion of admissions between 22:00 and 06:59 (0.91, 0.84–0.97); and the mean ICNARC physiology score (absolute reduction 1.2, 0.3–2.1). No significant effects of CCOS on outcomes including hospital mortality and readmission to critical care were identified for patients discharged to the ward.

Interpretation The results of this study were mixed. While some differences in the characteristics of patients admitted to critical care units were found to be associated with the introduction of CCOS, there was no evidence for an impact on the outcomes of patients discharged from critical care. It was not possible to identify any clear characteristics for an optimal CCOS.

P446

Influence of ABO blood group polymorphism on mortality in intensive care unit patients

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Introduction Blood groups may be related to differences in inflammatory responses [1]. We looked at blood group as a risk factor for ICU mortality in general and for patients with sepsis.

Methods Data were retrospectively collected from all 11,553 patients that were admitted from 1997 to 2005 to our medical/surgical ICU.

Results ICU mortality and SAPS II score for different blood groups are shown in Table 1. *P* values are given for the difference between blood groups A and O. No differences were found for age, gender, and reason for admission. No influence of rhesus blood group type was seen on mortality.

Table 1 (abstract P446)

ABO blood group	A	B	AB	O	*P* value
All patients	$n = 4,787$	$n = 1,168$	$n = 479$	$n = 5,119$	
ICU death (%)	9.5	10.2	10.9	11.2	<0.01
SAPS II	32 ± 16	33 ± 17	34 ± 18	33 ± 17	NS
Severe sepsis	$n = 265$	$n = 73$	$n = 34$	$n = 318$	
ICU death (%)	24.9	28.8	26.5	32.4	0.05
SAPS II	49 ± 18	49 ± 18	54 ± 19	51 ± 18	NS

Conclusion Blood group O is associated with a higher ICU mortality rate than blood group A. The relative risk increase for ICU mortality was 18% for all patients and 30% for patients with severe sepsis.

Reference

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P447

Contribution of genomic variations within human β-defensin 1 to incidence and outcome of severe sepsis

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Sepsis, a systemic inflammatory response to infection, is a common clinical syndrome in the ICU. Human β-defensin 1 (DEFB1) is a

multifunctional mediator in infection and inflammation, which has been largely explored in *ex vivo* studies. The lack of fully representative genetic animal models increases the importance of analyzing the impact of defensin gene polymorphisms on the courses of infectious and inflammatory diseases such as sepsis. This study was designed to investigate whether DEFB1 genomic variations are associated with incidence and outcome of severe sepsis. Six reported polymorphisms were detected in 211 patients with severe sepsis and 157 control individuals using diverse analytic methods. Linkage disequilibrium (LD), haplotype frequency, and statistical power for this association study were analyzed. The −44G-allele and −44G-allele carrying genotypes were significantly associated with incidence and outcome of severe sepsis. There was enough statistical power ($1 - \beta > 0.8$ at type I level of 0.05) to demonstrate a significant contribution of the −44G allele to severe sepsis. The −20G allele and GG genotype were associated with susceptibility to severe sepsis, while the −1816G-allele and −1816G-allele carrying genotypes influenced the outcome of severe sepsis. SNPs −20A/G, −44C/G and −52A/G were in strong LD. Haplotype −20A/−44C/−52G showed a protective role against severe sepsis, whereas haplotype −20G/−44G/−52G served as a risk factor for fatal outcome of severe sepsis. The present findings have important implications in the understanding of the role of DEFB1 in the pathophysiology of severe sepsis, and DEFB1 genomic variations may offer a new means of risk stratification for patients with severe sepsis.

P448

TNFα promoter single nucleotide polymorphisms may influence gene expression in patients with severe sepsis

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Introduction We examined the association of TNFα promoter single nucleotide polymorphisms and haplotypes with gene expression in terms of mRNA levels and with outcome in a cohort of patients with severe sepsis.
Methods Sixty-two Irish Caucasian patients presenting with severe sepsis were enrolled. Blood sampling was carried out on day 1 and on day 7. Mononuclear cells were isolated and TNFα mRNA quantified using the technique of quantitative real-time polymerase chain reaction (QRT-PCR). DNA was extracted and assayed for four TNFα promoter polymorphisms. Haplotypes were inferred using PHASE software.
Results Twenty-seven patients died. Patients carrying an A allele at position −863 produced more TNFα mRNA on day 1 than C homozygotes ($P = 0.037$). There was a trend for patients homozygous for the G allele at position −308 to produce more TNFα mRNA on day 1 than those carrying an A allele ($P = 0.059$). Carrier status for haplotype 1 (with A at position −863 and G at position −308) was associated with greater TNFα mRNA levels on day 1 ($P = 0.0374$). Carrier status for haplotype 4 (with C at position −863 and A at position −308) was associated with a nonsignificant decrease in TNFα mRNA levels on day 1 ($P = 0.059$). When directly compared, haplotype 1 was associated with significantly greater levels of TNFα mRNA than with haplotype 4 on day 1 ($P = 0.02$). Patients homozygous for the A allele at position −308 were more likely to succumb to severe sepsis than those carrying the G allele ($P = 0.01$).
Conclusion These results contradict previous *in vitro* functional studies on the TNF2 allele. This may be secondary to the method of quantification of *in vivo* gene expression with QRT-PCR providing more accurate and sensitive data when compared with prior ELISA-based assays. Indeed, the extrapolation of functionality from *in vitro* functional genetic tests after lipopolysaccharide stimulation may be of questionable value. We conclude that genotypic analysis does have a place in risk stratification in sepsis and that genetic variants at positions −863 and −308, or sites in linkage disequilibrium with these variants, may influence TNFα production.

P449

IL-1/tumor necrosis factor receptor gene expression characterizes sepsis in critically ill systemic inflammatory response syndrome patients

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Introduction The classic response to isolated endotoxin challenge entails secretion of IL-1 and TNFα. The purpose of this study was to longitudinally characterize the cytokine response to sepsis in critically ill systemic inflammatory response syndrome (SIRS) patients.
Methods Uninfected, critically ill trauma patients with SIRS were evaluated daily for sepsis. Patients were divided into two groups: pre-septic = SIRS patients who developed sepsis, and uninfected SIRS = SIRS patients remaining uninfected. Plasma samples and whole blood (PAXgene) obtained at study entry and daily for 3 days prior to sepsis were analyzed for differential gene expression between groups (Affymetrix Hg_U133 2.0 plus microarray, false discovery rate < 0.5%, $P < 0.005$) and quantitative plasma protein TNF and IL-1 levels (Immunoassay, Luminex™, elevated if > 3 SD above the mean for normals). Gene expression data are the median fold change between groups (uP = pre-septic > uninfected).
Results Gene expression on 90 patients and protein measurements on 142 patients were available. Protein levels of both subtypes of TNF and IL-1 were not elevated at any time point in either group. IL-1α was noted to have differential gene expression 24 hours before sepsis. No differences were noted in gene expression for TNFα, TNFβ, or IL-1β. Differential gene expression for only two TNF family members (TNFSF10 and TNFSF13b) was noted. However, differential gene expression for TNF and IL-1 receptors and IL-1 receptor antagonist was prominent (Table 1).

Table 1 (abstract P449)

Gene symbol	Fold change	Gene symbol	Fold change
TNFRSF1A	1.30 up	IL1R1	1.50 up
TNFRSF10D	1.21 up	IL1R2	2.52 up
TNFRSF25	1.19 down	IL1RN	1.48 up

Conclusion Compared with critically ill uninfected SIRS patients, sepsis increases IL-1α but not TNFα gene expression and does not increase TNF and IL-1 protein levels. Interestingly differential gene expression for TNF and IL-1 receptors exists, suggesting receptors, more than ligands, are important in differentiating sepsis from uninfected SIRS.

P450

A novel score based on age and cardiac biomarkers predicts outcomes in severe sepsis and septic shock

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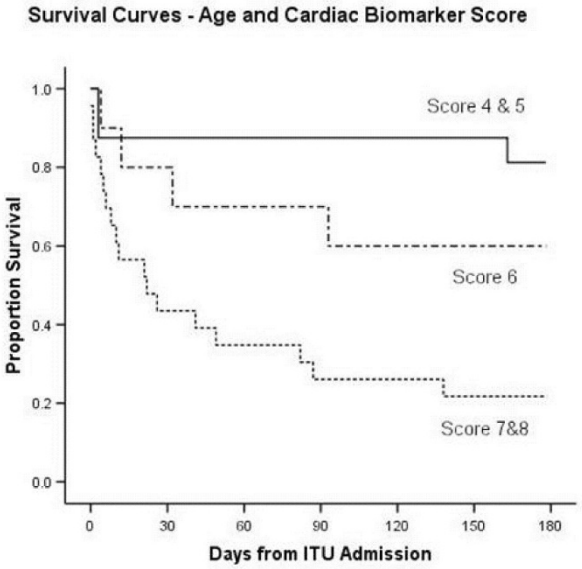
Background Myocardial dysfunction is common among critically ill septic patients. Elevated levels of cardiac biomarkers are predictors of mortality in acute coronary syndrome and in unselected critically ill patients. Our aim was to evaluate the role of the cardiac markers NT-proBNP, Troponin T (TnT) and myoglobin as predictors of inhospital and 6-month all-cause mortality in patients admitted to a general adult ICU with severe sepsis/septic shock.
Methods Serial plasma samples were taken for five sequential days on all patients admitted with severe sepsis/septic shock. Samples were analysed for NT-proBNP, TnT and myoglobin.
Results Samples were analysed on 49 patients. Elevated myoglobin was the only predictor of ICU mortality. Age, myoglobin and NT-proBNP levels predicted hospital mortality. Predictors of 6-month mortality were age, peak TnT, peak myoglobin and peak NT-proBNP levels. The APACHE II score did not predict mortality. A score was established dependent on TnT (<0.1 = 1, ≥0.1 = 2), age (<65 years = 1, ≥65 years = 2), BNP (<10,000 = 1, >10,000 = 2), and myoglobin (<750 = 1, >750 = 2). Patients were placed into tertiles (score = 4&5, 6, 7&8) to produce survival curves (Figure 1, $P < 0.01$).

Figure 1 (abstract P450)



Conclusion In critically ill patients with severe sepsis/septic shock a score based on age and increased plasma levels of cardiac biomarkers can help risk-stratify patients and predict short-term (<6 months) outcome.

P451

The calculated ion gap: a novel predictor of mortality in the critically ill surgical patient

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Critical Care 2007, **11(Suppl 2):**P451 (doi: 10.1186/cc5611)

Introduction Early identification of critically ill surgical patients who are not fully resuscitated improves outcome. Current markers of clinically occult hypoperfusion, such as lactate, have serious limitations. Increased oxidative stress as a consequence of inadequate cellular respiration results in elevated levels of unmeasured anions. We evaluated these anions as a novel marker of outcome.
Methods We prospectively evaluated 109 consecutive patients admitted to a surgical high-dependency unit (HDU). Regional Ethics Committee approval was obtained. Serum electrolytes, albumin, phosphate and lactate were measured on admission and days 1 and 2. We derived the calculated ion gap (CIG) using our simplified modification of the Stewart–Figge equations.
Results The CIG on day 1 predicted mortality ($P = 0.001$, analysis of variance). A CIG > 10 mmol/l correlated very strongly with mortality. The mortality in patients with a CIG < 10 mmol/l ($n = 86$) was 4.7%. The mortality in patients with a CIG > 10 mmol/l ($n = 23$) was 26.1% ($P = 0.006$, chi-square test). There were no differences in CIG with respect to mortality on admission or day 2 ($P = 0.273$ and 0.104, respectively). The mean hospital stay was significantly longer in patients with a CIG > 10 mmol/l (46.6 vs 18.7 days, $P = 0.015$, *t* test) (Table 1).

Table 1 (abstract P451)

	Day 1 CIG < 10 mmol/l	Day 1 CIG > 10 mmol/l	*P* value
Inhospital mortality	4.7% ($n = 86$)	26.1% ($n = 23$)	$P = 0.006$ (χ^2 test)
Length of hospital stay	18.7 days	46.6 days	$P = 0.015$ (*t* test)

Conclusion We describe the CIG for the first time in the critically ill surgical patient, and quantify it using simple bedside calculations derived from routine blood investigations. Failure to normalise the CIG by day 1 after admission to the HDU is an excellent marker for mortality and length of hospital stay, and should be used to guide resuscitation.

P452

Lactate levels from arterial, central venous and peripheral venous blood in severe sepsis and septic shock patients

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Introduction Serial lactate measurements are reliable and may be useful as a prognostic marker in critically ill patients. Differences in its levels, depending on the sample site, can lead to misinterpretation and inadequate treatment. The primary objective of this study is to evaluate the relationship between lactate levels in different compartments of the body, such as peripheral venous, central venous and arterial blood in patients with severe sepsis and

septic shock. Secondarily, we aimed at evaluating the impact of them in patient management

Methods This transversal study included patients with severe sepsis or septic shock with a central venous line in place. Blood from a peripheral venous puncture, central venous line and arterial line were collected, at the same timepoint each 12 hours. Peripheral lactate collection was performed carefully with the left superior limb garroted for a maximal of 2 minutes. Data were analysed by linear correlation test, and a Bland–Altman test was done to verify the degree of agreement between values from different samples. A P value <0.05 was considered significant.

Results Fifteen patients were enrolled, with a mean age of 57.8 years (eight males and seven females), APACHE II score of 15.3 ± 5.0 and SOFA score of 7.13 ± 3.39. A total of 129 samples were available for analysis. The linear correlation between arterial and central venous lactate levels showed an $r^2 = 0.66$ (95% CI: 0.71–1.12). However, Bland–Altman had a mean ± standard deviation bias of 1.25 ± 5.0. Results were similar for arterial and peripheral venous lactate with an $r^2 = 0.85$ (95% CI: 0.97–1.27) and a bias of −2.44 ± 5.0. Clinical agreement between arterial and central venous blood was 90%, arterial and peripheral blood was 71% and central venous and peripheral blood was 64%.

Conclusion Lactate from central venous blood can replaced arterial samples. However, peripheral samples are not clinically reliable.

P453

Lung nitroxidative stress as a prognostic factor in ventilated septic patients

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Introduction During sepsis and mechanical ventilation, nitric oxide (•NO) is produced by lung cells. We study whether pulmonary •NO production is a prognostic factor in mechanically ventilated septic patients.

Materials and methods We studied 50 patients with sepsis within the first 48 hours of sepsis. Operating room patients served as control a group (ORCG). Nitrite and nitrate (NO_x^-) and 3-nitrotyrosine (3NT) in plasma and bronchoalveolar lavage fluid (BALF) were analyzed by the Griess/vanadium chloride method and ELISA, respectively. Results were expressed as median and interquartile range. Receiver operator curves were constructed to compare the predictive value of NO_x^- values in BALF at admission with other variables. Kaplan–Meier analysis was used to compare survival between high and low BALF NO_x^- levels at admission. A P value less than 0.05 was considered significant.

Results At study admission in the sepsis group, nonsurvivors had higher levels of BALF NO_x^- than survivors: 20 (17–33) μM, 27 versus 72 (46–91) μM, 23, $P = 0.0001$. At day 7, BALF 3NT was higher in nonsurvivor septic patients than in survivors: 1,666 (30–3,173) pmol/mg protein versus 291 (13–1,908) pmol/mg protein. BALF NO_x^- had the highest area under the receiver operator curve for mortality (0.812, $P = 0.001$) in relation to other variables. Septic patients with BALF NO_x^- above 36 μM had a relative risk for mortality of 4.23 and an OR of 15.84. The difference between the low bronchoalveolar •NO group (BALF $[NO_x^-] < 36$ μM at admission) versus the high bronchoalveolar •NO group (BALF $[NO_x^-] \geq 36$ μM at admission) in ICU mortality was significant: 19% versus 78% (log rank 18.19, $P = 0.00001$).

Conclusion During sepsis there is enhanced lung •NO production that is associated with ICU mortality.

P454

Brain natriuretic peptide and left ventricular area variation with fluid challenge in septic shock: an echocardiographic study (preliminary results)

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Introduction Myocyte stretch is the main stimulus of brain natriuretic peptide (BNP) synthesis and release. During septic shock, important variations of volemia can occur and a correlation has been described between the cardiac index and the BNP level [1]. However, the relation between the echocardiographic left ventricule area and the BNP level has never been described. The aim of our study was to evaluate BNP and left ventricule area variations after an acute fluid loading in septic shock.

Methods Mechanical ventilated patients with septic shock, and without anterior cardiac disease, were included in our study. A fluid challenge was performed with colloid (500 ml) in 30 minutes. A BNP blood sample was drawn before and 1 hour after fluid loading. The primary endpoint was BNP variation after fluid challenge. Median values (25–75th percentiles) were compared with the Wilcoxon test ($P < 0.05$). The end-diastolic left ventricule area was recorded before and 1 hour after fluid challenge. Linear regression of BNP variation and left ventricular area variation was determined and r^2 was calculated.

Figure 1 (abstract P454)

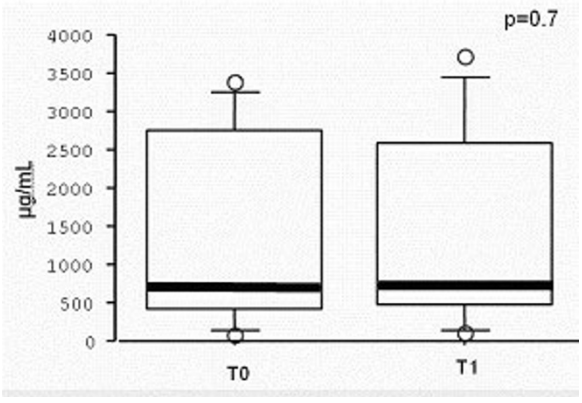
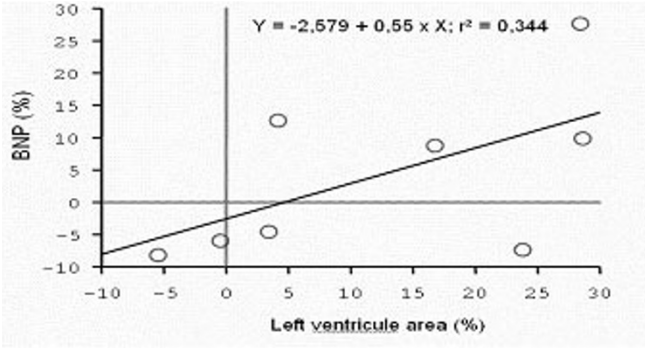


Figure 2 (abstract P454)



Results Eight patients (median age 68 years; six males/two females; SOFA score = 12) were enrolled in our study. The initial BNP level median increased from 695 (417–2,738) to 715 (478–2,596) μg/ml after a fluid loading ($P = 0.7$) (Figure 1).We did not find a statistically significant relationship between BNP variation and left ventricule area variation after fluid challenge ($P = 0.13$) (Figure 2).

Conclusion There is no increase in BNP level in patients with septic shock after fluid challenge. To our knowledge, this preliminary study is the first to evaluate the relationship between BNP and left ventricule area variation in patient with septic shock. Although no statistical significance between left ventricule area variation and BNP variation after fluid challenge, there is a trend to correlation between these two parameters. More patients have to be included to confirm this result.

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P455

Atrial natriuretic peptide reduces the ischemia/reperfusion-induced renal injury in rats by enhancing sensory neuron activation

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Introduction Although carpertide, a synthetic α-human atrial natriuretic peptide (ANP), reduces ischemia/reperfusion (I/R)-induced tissue injury, the precise therapeutic mechanism(s) remains to be elucidated. Calcitonin gene-related peptide (CGRP) released from sensory neurons reduces I/R-induced liver injury by inhibiting neutrophil activation through an increase in the endothelial production of prostacyclin (PGI_2). In the present study, we examined in rats whether ANP reduces I/R-induced renal injury by enhancing sensory neuron activation.

Methods The right renal vessels were clamped in rats for 45 minutes after left nephrectomy. ANP (0.3 μg/kg/min) was continuously infused from 30 minutes before ischemia to 60 minutes after reperfusion. We attempted to determine whether ANP promotes CGRP release from cultured dorsal root ganglion neurons isolated from adult rats *in vitro*.

Results Intravenous infusion of ANP reduced I/R-induced increase in serum levels of blood urea nitrogen and creatinine at 24 hours after reperfusion. ANP inhibited I/R-induced increases in renal tissue levels of TNF and myeloperoxidase at 3 and 6 hours after reperfusion, respectively. ANP significantly enhanced I/R-induced increases in renal tissue levels of CGRP and 6-keto-$PGF_{1\alpha}$, a stable metabolite of PGI_2, at 1 hour after reperfusion. ANP-induced increases in renal tissue levels of CGRP were significantly inhibited by pretreatment with SB366791, a specific vanilloid receptor-1 antagonist. ANP-induced increases in renal tissue levels of 6-keto-$PGF_{1\alpha}$ were significantly inhibited by pretreatment with SB366791, CGRP(8-37), a CGRP receptor antagonist, and indomethacin. Reduction of I/R-induced increases in serum levels of blood urea nitrogen and creatinine and those in renal tissue levels of TNF and myeloperoxidase in rats treated with ANP were completely abrogated by pretreatment with SB366791, CGRP(8-37), and indomethacin. ANP significantly increased CGRP release from dorsal root ganglion neurons *in vitro*.

Conclusions These results strongly suggested that ANP might reduce I/R-induced renal injury in rats by inhibiting neutrophil activation through enhancement of sensory neuron activation.

P456

Mid-regional pro-atrial natriuretic peptide is a strong predictor of outcome in an unselected cohort of critically ill patients

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Introduction Atrial natriuretic peptide (ANP) is a strong predictor of outcome in patients with heart failure, various other cardiovascular diseases and in patients with systemic inflammatory response syndrome and sepsis. Furthermore, ANP is elevated in patients with kidney disease. We aimed to test the prognostic potency of the precursor molecule mid-regional pro-atrial natriuretic peptide (MR-pro-ANP) in an unselected cohort of critically ill patients.

Methods Between August 2004 and February 2006, a total of 294 patients (191 males, age 63.8 ± 14.7 years) admitted to our ICU were studied. The mean SAPS2 and APACHE II score were 52 ± 23 and 24 ± 11, respectively. Two hundred and three patients (69.1%) were on intravenous inotropic support, 30 patients had additional mechanical circulatory support (23 intraaortic balloon counterpulsation (7.8%), eight extracorporeal membrane oxygenation (2.7%), three left ventricular assist device (0.9%)). Two hundred and five patients (69.7%) were mechanically ventilated, and 59 patients (20.1%) presented with acute renal failure. Plasma samples for determination of MR-pro-ANP were obtained on admission in all patients. As MR-pro-ANP values were not normally distributed, log MR-pro-ANP values were used for analysis.

Results Two hundred and thirty-five patients (79.9%) survived to ICU discharge and 59 patients died (21.1%). Log MR-pro-ANP plasma levels were significantly higher in patients who died than in ICU survivors (2.76 ± 0.39 pmol/l vs 2.50 ± 0.38 pmol/l, respectively, $P < 0.0001$). In the Kaplan–Meier analysis of 28-day survival, patients with log MR-pro-ANP plasma-levels above the median had significantly lower survival rates compared with patients with log MR-pro-ANP plasma levels below the median ($P = 0.02$).

Conclusion Our data show that elevated plasma levels of MR-pro-ANP at ICU admission are associated with an adverse outcome in an unselected cohort of critically ill patients.

P457

Clinical meaning of brain natriuretic peptide in the intensive care unit

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Introduction The aim of this study is to evaluate differences in brain natriuretic peptide (BNP) dosage (vn < 100 pg/ml) during the weaning procedure, in patients with heart disease (HD) vs patients without HD, admitted to the ICU.

Methods Ten patients with HD (group A) and 33 patients without HD (group B) were studied by BNP dosage in three specific steps: (1) admission to the ICU; (2) before the extubation (performed if patients, after the end of mechanical ventilation and 1 hour of connection to T-tube, were considered suitable for extubation); and (3) 24 hours after extubation. Necessity of noninvasive ventilation or reintubation after the extubation was considered as weaning failure. Data are shown as the mean ± standard error of the mean;

nominal variables were analyzed with the chi-square test and the risk ratio (RR) with 95% confidence interval (IC95) was performed; intragroup ordinal variables were analyzed with the Wilcoxon test (W), intergroup ordinal variables were analyzed with the Mann–Whitney test (MW). The receiver operative characteristic test was used to discriminate the BNP cutoff value with sensibility, specificity and respective IC95, between group A and group B. $P < 0.01$ is taken as statistically significant.

Results Weaning failure in group A occurred in 50% of patients vs 12% of group B patients ($P < 0.01$ chi-square test; RR = 4.13, IC95 = 1.36–12.49). BNP value differences in group A are not significant (step 1: 662 ± 147 pg/ml; step 2: 769 ± 171 pg/ml; step 3: 843 ± 167 pg/ml), while BNP value differences in group B are statistically significant (W) (step 1: 130 ± 21 pg/ml; step 2: 236 ± 41 pg/ml, $P < 0.01$ vs step 1; step 3: 375 ± 75 pg/ml, $P < 0.001$ vs step 1 and $P < 0.01$ vs step 2). There are statistically significant differences between group A and group B in every step ($P < 0.01$ MW). The BNP cutoff value to discriminate group A from group B is 274 pg/ml with sensibility 90 (IC95 = 55–98) and specificity 79 (IC95 = 61–91).

Conclusions Risk of weaning failure is increased four times in patients with HD. BNP values of group B patients are higher than normal people probably because the heart of ICU patients is submitted to different kinds of stress; therefore the BNP cutoff value to consider for discrimination of patients with HD from patients without HD in the ICU should be higher. BNP production in ICU patients with good performance of the heart is the right protective response to stress performed by therapy adopted during the ICU stay, this response is absent in patients with HD because their hearts already work in safety mode.

P458

Combining various severity of illness scoring systems to improve outcome prediction: pilot experience in the critically ill obstetric population

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Introduction No perfect severity score exists to predict ICU mortality, thus the search for new systems is still a preoccupation.

Hypothesis Use of many severity of illness scores simultaneously improves mortality prediction.

Patients and methods An open prospective observational study as part of the APRiMo project [1]. The study period was January 1996–September 2004. Inclusion criteria were critically ill obstetric patients and ICU length of stay >24 hours. Exclusion criteria were those of the used scores. The main outcome of interest was the survival status at ICU discharge. The database was divided into two samples: development and validation datasets. Development database patients were chosen randomly ($n = 414$) and the remaining patients composed the validation dataset ($n = 229$). A multivariable logistic regression model was developed to predict mortality associating the Acute Physiology and Chronic Health Evaluation II score [2], Simplified Acute Physiology Score II [3], Admission Mortality Prediction Model (MPM-H0) and Day 1 Mortality Prediction Model (MPM-H24) [4]. Discrimination and calibration were assessed by goodness-of-fit C-hat statistics and area under the ROC curve. The developed model was then tested in the validation dataset. Good discrimination was retained if C-hat statistics $P > 0.1$ and good calibration if area under the ROC curve > 0.8.

Table 1 (abstract P458)

	Development	Validation
Hosmer–Lemeshow C-hat statistics test	0.868	0.42
ROC	0.936	0.945
Nonsurvivor prediction	28/46 (60.9%)	18/28 (64.3%)
Survivor prediction	364/368 (99%)	199/201 (99%)

Results Six hundred and forty-three patients enrolled. The overall mortality rate was 11.51%. The new model predicted accurately 99% of survivors and more than 60% of nonsurvivors.

Conclusion The 'multiscore' model seems to refine prognosis. This is partly due to mixing of new evaluated parameters. Testing the latest developed generations of scores and also organ dysfunction systems could be interesting.

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P459

Validation of logistic organ dysfunction score prediction compared with APACHE II score prediction hospital outcome in Thai patients

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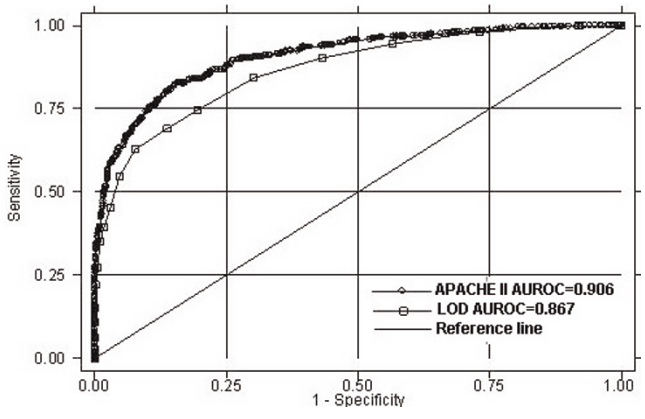
Critical Care 2007, **11(Suppl 2):**P459 (doi: 10.1186/cc5619)

Introduction To assess the performance of the logistic organ dysfunction (LOD) score and Acute Physiology and Chronic Health Evaluation II (APACHE II) score in a mixed medical–surgical ICU of a tertiary referral university hospital in Thailand.

Figure 1 (abstract P459)



Methods The data were collected prospectively on consecutive patients admitted to the ICU of Songklanagarind Hospital over a 24-month period from 1 July 2004 until 30 June 2006.
Results A total of 1,962 patients were enrolled, with 432 deaths (22%) prior to hospital discharge. Both systems provided overprediction of hospital mortality. LOD and APACHE II scores predicted hospital mortality of 25.4 ± 26.5 and 29.6 ± 27.8, respectively. Both models showed excellent discrimination. The receiver operating characteristic curves of both systems are shown in Figure 1. The area under the receiver operating characteristic curve (AUROC) of LOD was 0.867 (95% CI = 0.846–0.886) and the AUROC was 0.906 (95% CI = 0.889–0.923) for APACHE II. Both models presented a poor calibration in overall population. However, the LOD score had good discrimination and calibration in subgroups of nonoperative patients (AUROC 0.854, the Hosmer–Lemeshow goodness-of-fit H statistic 11.67, $P = 0.166$) and patients that exclude coronary artery disease and cardiac surgery (AUROC 0.860, the Hosmer–Lemeshow goodness-of-fit H statistic 10.03, $P = 0.263$).
Conclusion The LOD score showed good accuracy to predict hospital mortality in subgroups of nonoperative critically ill patients and excluded coronary heart disease and cardiac surgical critically ill patients in Thailand.

P460

Could we use the admission Acute Physiology and Chronic Health Evaluation II score for outcome prediction in critically ill obstetric patients?

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Introduction The APACHE II score (APII) has widespread use in ICUs for research and benchmarking. Physiological data for calculation of the APII score derive from worst values in the first 24 hours after ICU admission.
Hypothesis Mortality prediction by the APII system depends on data sampling. Use of ICU admission data (first hour) could be accurate to predict mortality.
Methods An open prospective data-sampling part of the APRiMo study. Included were critically ill obstetric patients, with ICU length of stay (LOS) ≥6 hours. Admission (H1: first-hour worst physiological data) and H24 (worst 24-hour physiological variables including H1 collected data) were used to generate, respectively: the admission APII score (H1-APII) and H24-APII. The formulae to calculate individual mortality for H1 and H24 APII were those validated for H24-APII as stated by Knaus and colleagues [1], adjusting for admission diagnosis. We compared both scores by discrimination and calibration statistical tests. $P < 0.05$ was the threshold for statistical significance.
Results The study period was January 1996–September 2004. We included 541 patients, overall mortality was 10.5%. Mean H1-APII and H24-APII scores. respectively. were 7.6 ± 6.1 and 8.6 ± 7, with derived mean predicted mortality, respectively, of 8.63% and 9.86%. The H24-APII score was higher than the H1-APII score in 135 patients (25%), among those patients 32 died (24% of patients with worsened APII) vs 6.16% if H1 = H24 ($P < 0.01$). Running a multiple logistic regression with mortality as the dependent parameter, we found that worsening of the APII score over time is not significantly associated with mortality ($P = 0.791$), whereas the H1-APII score ($P < 0.001$) and ΔAPII score (H24-APII minus H1-APII score) ($P = 0.04$) are correlated with mortality. Respective ORs are 1.28 and 1.45. Overall discrimination ability assessed by receiver operating characteristic curves was good for H1-APII (0.78) and H24-APII (0.784) ($P = 0.834$).
Conclusion To avoid variation in APII mortality prediction caused by variable sample rates, the admission APII is reliable. Customizing mortality formulae could improve performances of APII-H1.
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P461

Two-day intensive care unit outcome prediction score: a trial to improve outcome prediction in critically ill obstetric patients

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Critical Care 2007, **11(Suppl 2):**P461 (doi: 10.1186/cc5621)

Introduction The critically ill obstetric population median ICU stay is 4 days, thus general severity of illness scores are supposed to be accurate in mortality prediction. A literature review makes us sceptical.
Objective Development of a new prognostic model based on association of one of the generalistic severity scores (SAPS II, APACHE II), one of the organ dysfunction scores (LOD, MODS, SOFA) and evolution of these scores during the first 2 days of ICU hospitalization.
Methods An open prospective analysis part of the APRiMo study [1] ranging from January 1996 to September 2004. Inclusion criteria were critically ill obstetric patients with an ICU length of stay > 24 hours. Exclusion criteria were those of the used scores. The main outcome of interest was survival status at ICU discharge. The database was divided into two samples: a development sample by random choice of 450 patients, and the remaining patients in the validation dataset. Multivariable logistic regression models were developed. We chose among different developed models the best performer as assessed by Hosmer–Lemeshow (HL) goodness-of-fit statistics (calibration) and the area under the receiver operating characteristic curve (AUROC) for discrimination. Accuracy of the developed model was verified on the validation dataset using the same statistical tests. Results are expressed as the mean ± standard deviation unless stated elsewhere. Data were computed on SPSS 11.5 Win-XP version.
Results Six hundred and forty patients included. Age 31 ± 6 years, length of stay 5 ± 5 days, SAPS II 27 ± 16, SOFA score 5 ± 4, LOD score 2 ± 1.7. The overall mortality rate was 13.3%. The best model was the one combining SAPS II and LOD scores. The LOD score and SAPS II alone discriminated well but calibrated poorly in outcome prediction. Discrimination was optimal for the new developed model in both development and validation datasets, with AUROC respectively of 0.87 and 0.85. Calibration was good in the developed and validated datasets, respectively $P = 0.176$ and 0.34. The developed model predicts death accurately in 2/3 cases.
Discussion and conclusion The SAPS II and LOD scores are complementary. Development of dynamic models in time helps to refine prognosis prediction.
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P462

The correlation of the Sequential Organ Failure Assessment score with intensive care unit outcome

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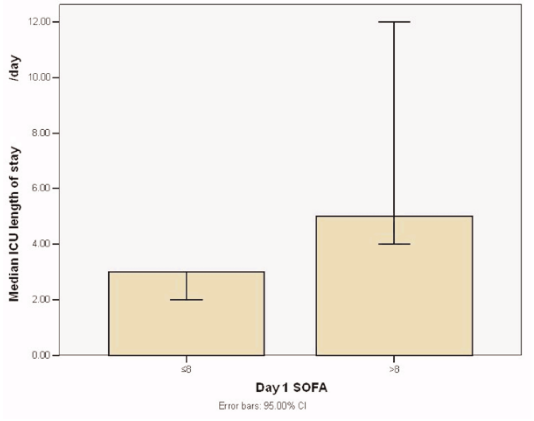
Methods We conducted a prospective observational review of 100 consecutive patients admitted to our ICU. We collected data relating to daily maximum organ dysfunction scores. Outcome was defined in terms of length of ICU stay and ICU mortality.
Results We included 100 patients (62 males), mean age 60.9 years. Of these admissions, 45 were elective surgical, 22 emergency surgical, 33 medical. The median Sequential Organ Failure Assessment (SOFA) score on admission was 4.50 (IQR 4). The median maximum SOFA score was 5.00 (IQR 5). The median length of ICU stay was 3.0 days (IQR 3). The overall ICU mortality rate was 14.0%. For patients with a maximum SOFA score ≤8, mortality was 5.1% – vs 45.5% for those whose maximum SOFA score was >8 ($P < 0.001$). Sixty-four per cent of patients scored their maximum SOFA score on admission. In patients whose SOFA score increased after admission, the mortality was 24.3%. Logistic regression analysis showed the maximum SOFA score bore a stronger correlation with mortality than admission SOFA score. See Figure 1.
Conclusion Maximum and admission SOFA scores are of prognostic value in the intensive care setting; allowing patients with increased risk of mortality and prolonged stay to be identified.

Figure 1 (abstract P462)



Median length of ICU stay in patients with an admission SOFA score >8 vs those whose admission SOFA score was ≤8 ($P = 0.001$).

P463

Sequential Organ Failure Assessment score as an outcome predictor in malarial multiorgan dysfunction syndrome

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Introduction Acute severe malaria is one of the leading causes of multiorgan dysfunction syndrome (MODS) in a developing country like India, and is associated with significant mortality. The outcome of malarial MODS predicted in various studies is extremely variable and dependent on many patient parameters.
Objective We prospectively evaluated the correlation of the APACHE II score, parasite index, procalcitonin (PCT) levels, number of organ dysfunctions/failures and Sequential Organ Failure Assessment (SOFA) score with the outcome of severe malaria.
Methods Eleven patients with acute severe malaria with MODS were treated in our ICU in the last 5 months. All these patients were treated with artesunate and/or quinine as per the WHO antimalarial treatment schedule, along with standard ICU care. The APACHE II and SOFA scores were calculated on admission. PCT levels were measured semiquantitatively on admission. The parasite index was confirmed by two pathologists.
Results Nine out of 11 patients survived without any residual organ damage, and the remaining two died due to MODS (Figure 1). Both these patients had five organ dysfunctions on admission, and their SOFA scores were 18 and 20, respectively. They had a low parasitic index of 1% and 2.5% and their PCT levels were 0.5–2 and >10 (semiquantitative method), respectively. Their APACHE II scores were 16 and 10.
Conclusion The pretreatment APACHE II score, parasite index, PCT levels and number of organs involved have variable correlation with mortality and are not consistent predictors of outcome. A higher SOFA score on admission is a more reliable predictor of mortality in malarial MODS.

Figure 1 (abstract P463)

Pt No.	PARASITE	APACHE II score	SOFA score	No. of O.D.	PCT	P. I.	OUTCOME
1	P.Vivax	17	10	5	>10	10%	Survived
2	P.Falciparum	6	9	4	>10	15%	Survived
3	P.Falciparum	5	4	2	>10	1%	Survived
4	P.Falciparum	12	13	5	2 – 10	20%	Survived
5	P.Falciparum	9	8	2	2 – 10	2.5%	Survived
6	P.Falciparum	5	8	2	0.5 – 2	1%	Survived
7	P.Falciparum	12	9	5	>10	2%	Survived
8	P.Falciparum	5	5	2	2 – 10	0.5%	Survived
9	P.Falciparum	10	8	3	0.5 - 2	4%	Survived
10	P.Falciparum	16	18	5	0.5 - 2	2.5%	Died
11	P.Falciparum	10	20	5	>10	1%	Died

Pt.No.- Patient Number; APACHE II- Acute Physiology And Chronic Health Evaluation II ; SOFA- Sequential Organ Failure Assessment; No. of O.D.- Number of Organ Dysfunction; PCT- Procalcitonin levels ; P.I.- Parasite Index

P464

Model calibration and discriminatory ability: a comparison of four derived variables from the SOFA score and the SAPS II

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Introduction We sought to compare four derived variables from the SOFA score and the SAPS II in ICU patients in terms of discriminatory ability and model calibration.
Patients and methods Four hundred and fourteen patients were included; they were evaluated on admission and every 48 hours thereafter until ICU discharge or death. Readmission and patients with an ICU stay shorter than 48 hours were excluded. The TMS score was calculated by summing the worst scores for each of the organ systems. Organ failure was defined by a SOFA score ≥3.

Figure 1 (abstract P464)

	AUC (area under the curve)	CI 95%	% Correctly classified*
SAPS II	0,804	0,758-0,849	77,3
Domax	0,855	0,817-0,892	78,8
SOFAmax	0,887	0,854-0,920	80,9
DeltaSOFA	0,771	0,722-0,821	72,7
TMS	0,871	0,836-0,906	78,0
SOFAi	0,771	0,723-0,819	74,2

*Classified as + if predicted mortality ≥0.5. Domax, the maximum number of organ failures during ICU stay.

ΔSOFA was defined by TMS minus admission SOFA (SOFAi). The maximum SOFA was defined by the worst SOFA value during the ICU stay. Logistic regression modeling techniques were used to describe the association of derived SOFA variables and SAPS II with mortality. ROC curves were used to assess the model's discriminatory ability and we examined the model calibration using the Hosmer–Lemeshow goodness-of-fit test. $P < 0.05$ was considered significant.

Results Diagnostic categories were: trauma 21.3%, postoperative 19% and medical 59.7%. Global mortality was 34.3%. Survivors had lower average SAPS II (28.1 ± 14 against 48.6 ± 19, $P < 0.01$), SOFAi score (3.7 ± 3 against 7.2 ± 4, $P < 0.01$), SOFAmax score (4.6 ± 4 against 10.8 ± 3, $P < 0.01$), ΔSOFA (1.6 ± 6 against 4.2 ± 3, $P < 0.01$), DoMAX (1.6 ± 6 against 4.2 ± 3, $P < 0.01$) and TMS (5 ± 3 against 11.4 ± 4, $P < 0.01$), and the difference was statistically significant. Results regarding model calibration and discriminatory ability are presented in Figure 1.

Conclusion The SOFAmax score had the best model calibration and could be used to compare different patient populations in terms of mortality.

P465

Sequential Organ Failure Assessment score trends and sepsis survival in a Brazilian university hospital intensive care unit

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Introduction Sepsis is associated with progressive organ failure. We sought to describe Sequential Organ Failure Assessment (SOFA) score daily trends in septic patients and tried to correlate those trends with survival.

Methods Patients with severe sepsis or septic shock admitted for at least 5 days in a seven-bed medicosurgical ICU of a Brazilian university hospital were studied. The daily SOFA score for each patient was calculated during the first 5 days of admission. Relevant data were prospectively acquired from March 2003 to May 2006 and the latter retrieved from a electronic database. ICU survivors were compared with nonsurvivors using the Mann–Whitney U test. Day-to-day changes were verified within each group using Friedman's test. $P \leq 0.01$ was elected as the significance limit. Medians and interquartile ranges (IQRs) were used to describe the sample.

Results One hundred and seventy-six patients were studied (71 males (56%), median age 51 (IQR 36–67) years, 78 (44%) with severe sepsis, median length of ICU stay 10 days (IQR 7–16), median admission SOFA 6 (IQR 4–9), median APACHE II score 19 (IQR 13–26), ICU mortality 27.84% (49/176 patients)). The SOFA score and its components scores along the five admission days distinguished the survivors from the nonsurvivors. Considering the SOFA score and its respiratory, neurologic and circulatory components, survivors presented lower scores as the days passed ($P < 0.001$). Mortality was increasingly higher for those patients who persisted with a SOFA score ≥ 7 as the days passed.

Conclusion In the sample studied, the persistence of an elevated SOFA score and its components during the first 5 days of admission predicted a higher mortality. Survival appears to be related to early organ dysfunction recovery. The SOFA score and SOFA-related variables' day-to-day changes in a population of septic patients may have an important prognostic implication and some patterns of daily evolution may distinguish those patients with a more ominous outcome.

P466

Cumulative lactate load correlates with cumulative Sequential Organ Failure Assessment score and survival in intensive care unit patients

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Background Changes in lactate levels are used as a prognostic marker in critically ill patients. However, the relation between the time course of arterial blood lactate clearance and important outcome parameters such as ICU length of stay (LOS), incidence of organ failure and survival rate has not been established.

Methods Case records from all ICU patients admitted between 2002 and 2004 were retrospectively identified in the ICU database. The Sequential Organ Failure Assessment (SOFA) score was calculated daily to assess the time course of organ failure. All lactate levels were extracted and the total cumulative lactate load (area under the curve above the upper normal level of 2.2 mmol/l; cum-lactate), and total cumulative SOFA score (cum-SOFA) were calculated and related to ICU LOS and final hospital survival. Values are the median (interquartile range).

Results Observations in 1,711 ICU admissions were analyzed, age was 69 (57–77) years, cum-lactate was 420 (94–419 min·mmol/l) and cum-SOFA was 11 (4–38). Cum-SOFA was higher in patients with hyperlactatemia (cum-lactate > 0) during the ICU stay ($n = 782$; 24 (7–71)) than in those without (5 (3–20); $P < 0.001$). Cum-SOFA correlated with cum-lactate and with ICU LOS, and cum-lactate correlated with ICU LOS (all $P < 0.001$). In patients who died in the hospital ($n = 329$), cum-lactate (1,180 (203–3,427) min·mmol/l) and cum-SOFA (30 (10–95)) were higher than in hospital survivors ($n = 1,382$; 298 (73–1,154) min·mmol/l, and 22 (5–67); both $P < 0.001$). In emergency admissions, cum-lactate (484 (113–2,031)) and cum-SOFA (27 (8–78)) were higher than in planned admissions (131 (37–454)) and (4 (3–28); both $P < 0.001$), respectively.

Conclusion In ICU patients, the cumulative area under the lactate curve correlates with the ICU LOS, cumulative SOFA score, and inhospital mortality. The prognostic value of cum-lactate requires prospective evaluation.

P467

Sequential Organ Failure Assessment score and procalcitonin serum concentrations in patients with systolic heart failure early after cardiac surgery

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Introduction Previously we investigated the clinical course of patients with good left ventricle ejection fraction (EF) by assessing the Sequential Organ Failure Assessment (SOFA) score and procalcitonin (PCT) level early after cardiac surgery. In this study we included patients with systolic heart failure (HF), prospectively collecting data: B-type natriuretic peptide (BNP), PCT, and SOFA score.
Methods Two hundred and seventy-five patients (subjected to coronary artery bypass grafting, valve reconstruction or combined operations) were divided into three groups: echocardiographically estimated EF > 30% for the PCT group (group A, $n = 102$), the control group (group B, $n = 103$), and patients with EF < 30% for BNP analysis (group C, $n = 70$). PCT was measured preoperatively, 6 hours, 24 hours and 48 hours postoperatively. The SOFA score was assessed daily as SOFA1, SOFA2, SOFA3. BNP was measured preoperatively in patients with HF.
Results PCT serum concentrations are presented in Table 1. In groups A, B, and C, SOFA1 was 1.31 ± 1.67 vs 1.62 ± 1.65 ($P > 0.05$), and 4.73 ± 2.57 ($P < 0.05$). SOFA2 was 0.97 ± 1.56 vs 1.34 ± 1.67 ($P > 0.05$), vs 4.69 ± 2.47 ($P < 0.05$). SOFA3 was 0.63 ± 1.11 vs 1.13 ± 1.68 ($P = 0.0178$), and 4.04 ± 1.81, respectively. The ICU stay was 5.74 ± 11.49 days in group A, 6.97 ± 11.61 days ($P = 0.04476$) in group B, and 3.5 ± 1.11 days in group C. The postoperative hospital stay was 12.08 ± 11.28 days vs 12.93 ± 10.73 days vs 12.25 ± 2.5 days ($P > 0.05$) in group A vs group B vs group C. Inhospital mortality was 3% vs 3% vs 2.8% ($P = 0.8038$) in the three groups.

Table 1 (abstract P467)

	–24 hours (preoperative)	6 hours (day of operation)	24 hours (first post-operative day)	48 hours (second post-operative day)
Group A	0.23	0.33	0.34	0.56
Group C	0.25	0.75	1.07	0.88

Discussion We have found that the SOFA3 score had a predicting value in the mortality rate as well as PCT concentrations measured 48 hours after surgical intervention.

P468

The relationship between mortality and its time of day in intensive care unit patients

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Introduction It has been known that a lot of factors are effective on mortality in ICU. In terms of ICU organization it has also been known that staff might be effective on mortality and morbidity. The aim of our study is to compare the cases in terms of significant time periods that are followed and lost in the ICU.
Methods Intensive care medical records between 2002 and 2005 of 242 patients (151 males and 91 females) who attended our ICU for 48 hours or more and proceeded mortally were analyzed retrospectively. Patients were subdivided into three groups according to the time at which mortality occurred: Group 1 08:00 a.m.–16:00 p.m., Group 2 16:00–24:00 p.m. and Group 3 00:00–08:00 a.m. Patients were also subdivided into two groups according to the days on which they died being the weekend and a weekday. The age, gender, primary diagnosis, ICU stay and mechanical ventilator times, APACHE II, Glasgow Coma Scale and SOFA scores, and mortality ratios of patients were taken and compared according to the time period.
Results No statistically significant difference among the three groups was found in terms of age, gender, primary diagnosis, ICU stay and mechanical ventilator times, and APACHE II, Glasgow Coma Scale and SOFA scores. Also no statistically significant difference was found between mortalities during the weekend and a weekday.
Conclusion A well-organized ICU can work functionally during the night-time, change of shifts and weekend. In this situation, for optimal performance, the structure and management of organization come into prominence. Our results show that in ICU patients mortality is not related to time of day when optimum situations are provided.

P469

Simple prediction of mortality in case of readmission to the intensive care unit

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Introduction Mortality of patients readmitted to the ICU is significantly higher than the mortality of patients treated once in the ICU. A simple method to predict mortality of patients readmitted to the ICU could help to select the most seriously ill readmitted patients.
Methods Adult patients that were admitted to all three ICUs of the same hospital twice or more times during the same stay in the hospital during a 3-year period were retrospectively selected. The sex and age of surviving and nonsurviving readmitted patients were compared. The mortality rate of patients readmitted into the ICU during 24 and 48 hours was compared with the mortality rate of all readmitted ICU patients. The mortality of patients that were readmitted more than once into the ICU was compared with the mortality of patients that were readmitted once. The duration of stay in other departments before readmission into the ICU of survivors was compared with duration of stay in other departments of nonsurvivors.
Results A total of 13,343 patients were admitted. Eight hundred and fifty-six patients were readmitted, 172 readmitted patients died in the hospital (hospital mortality – 20.09%). The readmission rate of men was higher in comparison with women (550 vs 306 patients). The mortality of readmitted men was lower than the mortality of readmitted woman; 77 men (17.2%) died vs 95 (25.1%) women ($P = 0.00001$). The age of 565 patients was lower than 70 years. The mortality of readmitted patients with age lower than 70 years was lower than the mortality of patients older than 70 years; 103 (18.2%) patients younger than 70 years died vs 70 (24%) patients older than 70 years ($P = 0.00001$). Mortality of patients that were readmitted during 24 or 48 hours was bigger than the mortality of all readmitted patients (26.9% and 25.11% vs

20.09%; $P = 0.045$ and $P = 0.097$). The mortality of patients that were readmitted more than once (from a total 160 patients, 41 died – 25.6%) was bigger than the mortality of patients readmitted just once (from a total 696 patients, 131 died – 18.96%) ($P = 0.12$). The length of stay of nonsurviving readmitted patients in other departments before readmission was higher than the length of stay of survivors (mean 7.64 days vs mean 5.71 days).

Conclusion Sex and age older than 70 years of patients readmitted to the ICU, readmission during 24 hours, and length of stay in other departments before readmission could be used for simple prediction of mortality of patients readmitted into the ICU. The amount of single patient readmissions to the ICU cannot be used as a predictor of death of patients readmitted to the ICU.

P470

Comparison of intensive care unit mortality performances: standardized mortality ratio vs absolute risk reduction

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Critical Care 2007, **11(Suppl 2):**P470 (doi: 10.1186/cc5630)

Introduction The aim of this study was to assess the role of absolute risk reduction (ARR) to measure ICU performance as an alternative to the standardized mortality ratio (SMR).

Methods This retrospective study involves patients admitted to three ICUs of a single tertiary medical center from January 2003 through December 2005. Only the first ICU admission of each patient was included in the study. The ICUs were staffed similarly. We abstracted data from the APACHE III database. For each ICU, the SMR and ARR with their 95% confidence intervals (CI) were calculated. ICU performance was categorized as shown in Table 1. When comparing ICUs, if the 95% CI of the SMR or the ARR overlap between the units, the performances were considered similar. If there was no overlap, the differences in performance were considered statistically significant.

Results During the study period, 12,447 patients were admitted to the three ICUs: 4,334 to the medical ICU, 3,275 to the mixed ICU and 4,838 to the surgical ICU. The predicted mortality rates were 19.5%, 16.0% and 9.0% and the observed mortality rates 14.8%, 9.7% and 4.3% for the medical, mixed and surgical ICUs, respectively. The SMR and ARR in mortality for each ICU are presented in Table 2.

Conclusions ICU mortality performances assessed by SMR and ARR give different results. The ARR may be a better metric when comparing ICUs with a different case mix.

Table 1 (abstract P470)

Performance	SMR, 95% CI	ARR, 95% CI
Poor	>1	<0
Average	Includes 1	Includes 0
Good	<1	>0

Table 2 (abstract P470)

ICU	SMR, 95% CI	ARR, 95% CI
Medical	0.76, 0.70–0.82	4.7%, 3.1–6.3
Mixed	0.61, 0.54–0.68	6.3%, 4.7–7.9
Surgical	0.48, 0.41–0.	4.7%, 3.7–5.7

P471

Prediction of the tacrolimus blood concentration in liver transplantation patients with support vector regression during an intensive care unit stay

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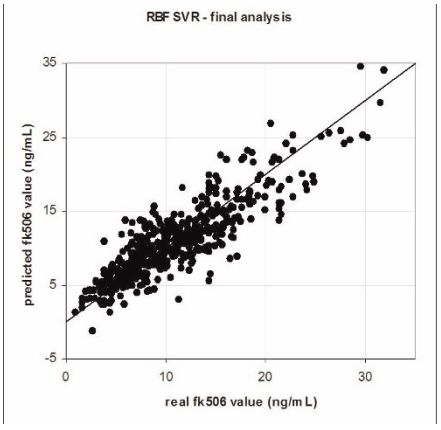
Introduction The tacrolimus blood concentration has wide intra-individual and inter-individual variability, especially in the initial phase after transplantation in the ICU. To insure clinical effect and to avoid side-effects, it is crucial to monitor concentrations very carefully. Prediction models can save time and resources, enabling clinicians and nurses to improve clinical care. The performance of linear and nonlinear support vector machines (SVM) as prediction models for the tacrolimus blood concentration in liver transplantation patients is compared with linear regression analysis.

Methods Five hundred and twenty-three tacrolimus blood concentration levels, together with 35 other relevant variables from 56 liver transplantation patients between 2002 and 2006, were extracted from Ghent University Hospital database (ICU Information System IZIS) (Centricity Critical Care Clinisoft; GE Healthcare). Multiple linear regression, and support vector regression with linear and nonlinear (RBF) kernel functions were performed, after selection of relevant data components and model parameters. Performances of the prediction models on unseen datasets were analyzed with fivefold cross-validation. Wilcoxon signed-rank analysis was performed to examine differences in performances between prediction models and to analyze differences between real and predicted tacrolimus blood concentrations.

Results The mean absolute difference with the measured tacrolimus blood concentration in the predicted regression model was 2.34 ng/ml (SD 2.51). Linear SVM and RBF SVM prediction models had mean absolute differences with the measured tacrolimus blood concentration of, respectively, 2.20 ng/ml (SD 2.55) and 2.07 ng/ml (SD 2.16). These differences were within an acceptable clinical range. Statistical analysis demonstrated significant better performance of linear ($P < 0.001$) and nonlinear ($P = 0.002$) SVM (Figure 1) in comparison with linear regression. Moreover, the nonlinear RBF SVM required only seven data components to perform this prediction, compared with 10 and 12

Figure 1 (abstract P471)



components needed, respectively, by multiple linear regression and linear SVM.
Conclusion Performance of SVM with linear and nonlinear kernel function was excellent and superior in comparison with the multiple linear regression model in predicting the tacrolimus blood concentration.

P472

Effects of the clinical characteristics of the organ donor on the long-term results of the transplant and survival of the patient, with particular reference to kidney transplants

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Introduction To assess the role of the single clinical parameters of the donor on the outcome of the transplant and the variability of this in relation to the state of an optimal or borderline donor.
Methods One hundred and fifty-one receiving and deceased donor brace subordinates to kidney transplant. Clinical parameters investigated for every donor were: age, arterial hypertension (≥140/80 mmHg), diabetes, blood values of creatinine. It was chosen to classify as marginal all the donors with age >55 years, and/or hypertension, and/or diabetes, and/or with blood values of creatinine >1.5 mg/dl, and/or whose death has happened because of one whichever pathology that has determined cerebral anoxia. Based on such parameters the donors' borderline was 72/151 (47.7%), while the optimal was 79/151 (52.3%). The mean age of the donors was 47.5 years (range 14–81 years). The population of the 151 receiving optimal and marginal kidneys was constituted of patients judged suitable for the transplant with typical risk factors for a standard population of subjects on dialysis. The mean age of receiving patients was 46 years (range 21–71 years). We have classified receiving based on the outcome of the transplant to 5 years, as: patients alive with transplanted kidney still working, deceased patients, and patients re-entered to haemodialysis.
Results Eighty-seven per cent ($n = 69$) of kidneys transplanted from optimal donors, in fact, have turned out working, 4% ($n = 3$) have re-entered haemodialysis within 5 years from the surgery, and only 9% ($n = 7$) have deceased in the same period. Regarding marginal kidney receiving, it has been possible to demonstrate that 72% ($n = 52$) of such subjects maintained a good function of the transplant, 11% ($n = 8$) re-entered haemodialysis, and 17% passed away within 5 years of the transplant.
Conclusions The difference between the survival of the two receiving groups is not such to justify the exclusion of marginal donors from the 'pool' of potential kidney donors. Considering that, the use of marginal donors can be a valid system in order to supply the lack of organs. Moreover the histological examinations, executed on patterns captured with wedge biopsy before the transplant, can be an effective strategy finalized for the expansion of potential kidney donors.

P473

Upregulation of the endothelin axis in alveolar macrophages following brain stem death in a murine model

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Introduction Outcomes post lung transplantation continue to improve, but early pulmonary dysfunction dictates long-term morbidity and mortality. Ischaemia reperfusion injury is a precipitant of poor postoperative outcome in lung transplantation and may cause primary graft dysfunction (PGD). A number of processes are thought to contribute to PGD. Relatively little is understood of the role of brain stem death (BSD) in subsequent organ dysfunction. We wished to examine the effect of BSD on the endothelin (ET) axis.
Methods Following ethics approval, 14 Wistar–Kyoto rats were anaesthetised, with tracheostomy and arterial and venous cannulation. A 200 µl Fogarty's balloon catheter was inserted via a burr hole into the subdural vault. The balloon was inflated in the experimental group but not the control group. Four hours of positive pressure ventilation were followed by euthanasia and organ retrieval. Lung tissue was stained for H&E for morphology, and alveolar macrophages (AM) were identified by anti-CD68 staining. AM were stained with a monoclonal anti-ET-1 antibody, as well as the polyclonal anti-ET-A and ET-B.
Results All animals survived the experiment. There was a significant increase in the ratio of AM to neutrophils ($P = 0.002$). The ET-1 content on the AM was significantly increased in the experimental group (27.57 ± 5.26 vs 7.01 ± 1.75, $P < 0.0001$).
Conclusions In this model, BSD was associated with an increase in the ratio of AM to neutrophils, and there was significant upregulation of the endothelin axis on these AM, as evidenced by raised levels of ET-1, ET-A and ET-B. There may be a role for endothelin blockade in the BSD organ donor. This may increase the yield of organs that can be accepted for transplantation and improve early graft function in the recipient.

P474

Prognosis factors in lung transplant recipients readmitted to the intensive care unit

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Introduction The short-term survival after lung transplantation has improved gradually. Despite this the peritransplant period is of high risk. Factors influencing the readmission of lung transplant recipients to the ICU are diverse, but respiratory failure and sepsis are the predominant causes. The objective of our study was to identify outcome predictors and prognostic factors for survival among lung transplant recipients on readmission to the ICU.
Materials and methods A retrospective study of all lung transplant recipients achieved during a 10-year period (from 1997 to 2006). Data collection included the age, gender, reason for and type of lung transplantation. Variables specific to individual ICU admissions included the admission diagnosis, length of stay, duration of mechanical ventilation, interval time from transplantation, Acute Physiology and Chronic Health Evaluation (APACHE) II score on ICU admission, and the identification of systemic organ dysfunction. We used Student's t test (or, where appropriate, its nonparametric equivalent) or the χ^2 test for comparisons among the patients who died and the patients who survived their ICU admissions.
Results A total of 144 lung transplants were performed at our institution. Forty-six of them died on the ICU during the immediate perioperative period. Finally, 98 were discharged from the ICU. Twenty-eight patients were readmitted to the ICU after discharge (28.57%). The mean of age was 51.3 ± 11.6 years. The male/female ratio was 23/5. The mean period transcurred between ICU discharge and ICU readmission was 107 ± 162 days. The admission diagnosis was sepsis in 20 cases (71.4%). Seventeen patients died during the ICU stay (60.7%). We found that an

increase in APACHE II score, delay to ICU readmission, need of mechanical ventilation and three or more organ dysfunctions were significantly associated with mortality.
Conclusions Admission to the ICU is common in lung transplant recipients, and it is associated with a high mortality. Sepsis is the main cause of ICU readmission and the most frequent cause of death. Lung transplant recipients with higher APACHE II score and three or more organ dysfunction present higher mortality. The delay on ICU readmission is also associated with higher mortality.

P475

Predictors of intensive care unit readmission within 48 hours after discharge

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Introduction Readmission to the ICU during the same hospitalization is associated with significant morbidity and mortality and results in a longer length of stay and higher costs. There is therefore growing interest to identify reliable predictors for readmission. The aim of our study was to assess the incidence of ICU readmissions, identify predictors of ICU readmission, and determine patient outcome.
Methods We performed a retrospective case–control study. The study population consisted of all patients who were discharged alive from our 28-bed surgical, thoracic–surgical and medical ICU in a university teaching hospital in a 1-year period. A case was defined as a patient readmitted to the ICU within 48 hours after discharge. For each case, three control patients were randomly selected from the study population. The following information was collected: demographic parameters and APACHE II score, parameters of hemodynamic, respiratory and renal function, length of ICU stay, duration of invasive ventilatory support (ventilator time), and time between extubation and discharge. To determine a predictive model, covariate selection was done by the two-sample *t* test, Mann–Whitney test and univariate logistic regression. From significant ($P < 0.10$), plausible and clinically relevant variables, a predictive model was generated using multivariate logistic regression.
Results During a 1-year period 1,635 patients were admitted to our ICU. Of 1,393 patients at risk for readmission, 25 (1.8%) readmissions occurred in 23 patients. Nine of the 23 (39%) readmitted patients died during their hospitalization, while the overall ICU mortality was 10.6%. The most important reason for readmission (68% of the cases) was respiratory deterioration. In the univariate analysis, age, ventilator time during first admission and time between extubation and ICU discharge were significant predictors of readmission. In the multivariate analysis, age (OR 1.1; 95% CI 1.00–1.13; $P = 0.03$) and ventilator time during first admission (OR 1.1; 95% CI 1.00–1.10; $P = 0.03$) were significant predictors, corrected for patient characteristics. Furthermore, patients who were readmitted had a significant longer duration of total (first and second admission) ventilator time (188 vs 106 hours, $P = 0.012$), and total ICU stay (400 vs 127 hours, $P = 0.009$).
Conclusion Patients readmitted to the ICU have significant longer overall ventilator time, ICU stay, and a higher ICU mortality. The ventilator time during first admission (especially beyond 300 hours) is an important predictor of readmission. The time it takes to get patients ready for discharge after extubation also differed significantly. The data suggest that elderly patients who have been ventilated for a long period are at particular risk for readmission and should receive additional care before discharge from the ICU.

P476

Intensive care unit readmissions after lung transplantation: epidemiology and outcome

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Introduction Significant improvement of short-term and long-term survival after lung transplantation (LT) has been observed. Nevertheless, a significant number of patients need to be readmitted to the ICU. The aim of our study was to analyse the epidemiology, outcome and risk factors for LT patients readmitted to the ICU after an initial discharge.
Methods From February 1996 until May 2006 we studied all LT patients from a single centre initially discharged from the ICU who needed to be readmitted. Demographic data included the type and date of LT, best post-LT FEV_1, last pre-ICU readmission FEV_1, admission diagnosis, time from LT to ICU admission, mechanical ventilation (MV) use, rejection episodes and infections. Actuarial survival rates (ASR) were calculated with Kaplan–Meier curves.
Results A total of 103 LT patients were discharged from the ICU, 41 patients (39.8%) were readmitted (males 53.6% (22 patients) with a mean age of 42 years (15–66)). Indications were emphysema in 13 patients (31.7%), idiopathic pulmonary fibrosis in eight patients (19.5%), bronchiectasis in five patients (12.2%), cystic fibrosis in five patients and others in seven patients (17%). Seventeen patients underwent bilateral LT, 11 patients right LT (26.8%) and eight patients left LT (19.5%), while five patients received a heart–lung transplantation. Respiratory failure was the principal ICU admission diagnosis (68.3%), followed by seizures (7%) and septic shock (4.8%). MV was required in 35 patients (85.3%). ICU mortality for readmitted patients was 68.3% with a 1-year, 3-year and 5-year ASR of 67.3%, 62.9% and 47.4%. The survival median was 1,761 days (1,134–2,388). In the MV patients, a 1-year, 3-year and 5-year ASR of 63.1%, 58.9% and 44.2% was found with a median survival of 1,618 days (132–3,104). The time to ICU admission was 1,303 (4–3,096 days). ICU admission timing was not found to be a predictor for early (<30 days; 53.8%) vs late (>30 days: 46.4%), $P = 0.65$. Deceased patients required significantly more MV (71.4% vs 38.5%; $P = 0.044$ (chi-square); OR: 4; 95% CI: 1–15.99). Emphysema was not more prevalent in the deceased patient group, and neither was the pre-ICU readmission FEV1 nor the occurrence of opportunistic infections. Steroid-resistant acute rejection was found to correlate with mortality.
Conclusion ICU readmissions are frequent among LT patients. In our study group, respiratory failure was the more prevalent admission diagnosis. The need for MV was associated with a worse prognosis as well as steroid-resistant acute rejection episodes. Early or late ICU admission after LT has not influenced mortality.

P477

The functional outcome of patients requiring intensive care readmission

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Introduction Rates of readmission to the ICU are often cited as controversial indices of quality of intensive care, adequacy of follow-up and as guides to resource allocation. Nonetheless there are few data on the long-term functional outcome of ICU recidivists: we set out to study this.

Methods With ethical approval, from a prospectively collected database of all ICU admissions from 2004, we identified all readmissions to our ICU from within the hospital. We identified survivors from the database, and contacted them, 2–3 years later, to assess their functional outcome, as the Glasgow Outcome Score (GOS) and Karnofsky score.
Results Of 97 readmissions, 79 (81%) survived the ICU. Most of them (57%) came from the high-dependency unit (HDU), of whom 74% survived. Thirty-three per cent came from other wards and 10% from theatre: 90% of each of these groups survived the ICU. Further data on these groups' interim survival and functional outcomes are presented.
Conclusion Survival rates among those readmitted are high. Those returning from the HDU represent a cohort at higher risk of mortality. The functional status after 2.5 years varies particularly with the timing of readmission, readmission diagnosis and APACHE score at readmission.

P478

One-year survival of patients admitted to the neurological intensive care unit

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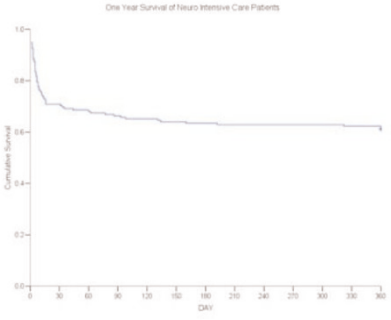
Introduction Patient survival in neurological intensive care units (NICUs) may be obvious; however, there is currently little evidence regarding the longer term outcome of these patients. In this study the 1-year survival of NICU patients has been defined.
Methods Between April 2004 and April 2005, all patients admitted to the NICU requiring ≥24 hours of ≥2 organ system support were identified (n = 175). The year following admission was divided into three phases – early (0–30 days), middle (31–90 days) and late (91–360 days) – and mortality was recorded. Data were analysed using Kaplan–Meier and log-rank analysis.
Results Patients were admitted from many sources; interhospital transfers (n = 90), neurosurgical admissions (n = 26), medical admissions (n = 36), and emergency admissions (n = 15). Reasons for admission included haemorrhage (n = 66), trauma (n = 52) and neoplasm (n = 19). Ninety-one patients (52.0%) spent less than 7 days on the NICU and 84 (48%) required ≥7 days. Overall survival was 70.9% at 30 days and 61.1% at 1 year. There was no significant variation between the young (<60 years) and older (≥60 years) groups (62.6%, n = 115 vs 58.3%, n = 60, $P > 0.5$). Nor was there a difference between those receiving two organ support and those receiving ≥3 organ support (62.1%, n = 66 vs 60.6%, n = 109, $P > 0.5$). Mortality (deaths/30 days) varied dramatically between the early, middle and late phases (29.1% vs 3.2% vs 0.9%, $P < 0.001$).
Conclusions Although mortality is high during the first 30 days of neurological critical illness there is a significant plateau in the survival curve; patients surviving beyond the initial phase tend to survive long term. Larger studies may be beneficial to further evaluate subgroup variation in the survival curve profile.

Figure 1 (abstract P478)



P479

Use of a modified early warning system to predict outcome in patients admitted to a high dependency unit

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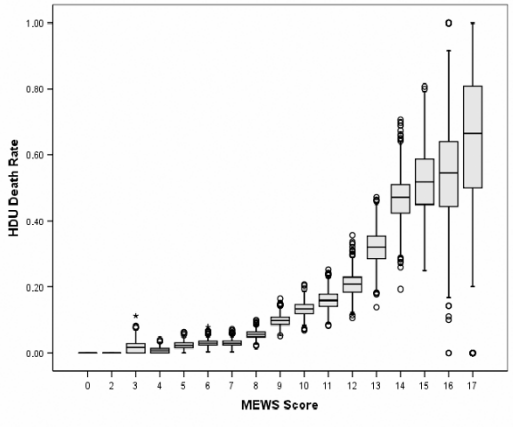
Introduction The modified early warning system (MEWS) is a physiological scoring system that identifies patients at risk of deterioration who require increased levels of care [1]. The use of a patient's MEWS score to predict outcome in a high-dependency unit (HDU) has not been previously described.
Method Approval for the study was granted by the local ethics committee. We reviewed MEWS scores from all patients (n = 2,974) admitted to a six-bed medical and surgical adult HDU in a general hospital from July 2002 to October 2005. The MEWS score was calculated from observations of heart rate, blood pressure, respiratory rate, urine output, conscious level and temperature recorded within 24 hours of admission to the HDU.
Results Of the 2,974 patients reviewed, 2,447 patients had sufficient data. Analysis using logistic regression shows a strong relationship between the probability of death and the MEWS score: the odds of death increase by 1.48 (confidence interval 1.41–1.56; $P < 0.001$) for each unit increase in the MEWS score. However, there is no reason that these data should follow a logistic form and the estimates of uncertainty around the point estimates from logistic regression are poor. More accurate estimates of the death rate for each of the MEWS scores were achieved using a 'bootstrapping' technique (repeated sampling, with replacement, from the dataset) 1,000 times (see Figure 1). The median death rate (%) for each MEWS score was: 3 = 1.5%; 4 = 0.7%; 5 = 2.2%; 6 = 3.0%; 7 = 3.0%; 8 = 5.6%; 9 = 9.7%; 10 = 13.3%; 11 =

Figure 1 (abstract P479)



Distribution of bootstrapped estimates of death rates by MEWS score (median, interquartile and observed range).

15.9%; 12 = 20.9%; 13 = 32.0%; 14 = 47.2%; 15 = 51.9%; 16 = 54.6%; 17 = 66.7%. MEWS scores of 2 or less ($n = 19$) had no deaths.

Conclusion The MEWS score can be used as a useful predictor of outcome in a HDU.

Reference

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P480

Changes of the system of postoperative care decreases mortality in a surgical unit

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Introduction In 2005, 10 public health care institutions functioned in the area of Lodz, having in their structure a surgical unit classified as a general surgery unit. They were three university teaching hospitals, three provincial hospitals, three county hospitals and one departmental hospital. Mortality in university teaching hospitals having 167 beds was 1.25%, in provincial hospitals with 191 beds was 2.96%, and in county hospitals with 140 beds was 3.98%. The lowest percentage mortality was noted in the surgical unit of Bolesław Szarecki University Teaching Hospital No. 5 in Lodz (UH No. 5) and it was 0.35%. The authors decided to analyse the causes of such low mortality in this hospital. Two remaining university teaching hospitals, N. Barlicki University Teaching Hospital No. 1 in Lodz (UH No. 1) and WAM University Teaching Hospital No. 2 in Lodz (UH No. 2), were selected for comparative analysis. The selection was dictated by a few reasons. The Medical University in Lodz is the founding body of all hospitals subjected to analysis. These hospitals are only a few kilometres away from each other. The units have a similar number of beds, and well-educated medical and nursing staff. Heads of the hospital departments have all been awarded a professorship. Health benefits are provided on the basis of the same list of benefits as part of contract with the same payer – Lodz Provincial Branch of the National Health Fund.

Methods The study is a retrospective analysis of mortality in general surgery units located at three university teaching hospitals: UH No. 1, UH No. 2 and UH No. 5. The study comprised 25,921 patients treated in these units from 1 January 2003 to 30 June 2006. The available statistical material was analysed. In the first stage the statistical data were analysed by the Provincial Centre of Public Health in Lodz. The obtained information concerned the number of treated patients, the number of patients transferred, discharged or dead, the number of man-days, mean bed use, mean hospitalisation time, mean number of patients per bed and mortality. The second stage focused on explaining the reasons for significantly lower mortality among patients hospitalised in the surgical unit of UH No. 5. Among others, the structure of the hospitalised patients in each of these units was analysed, the quantity and range of a contract signed with the unit financing the benefits and internal principles of these units functioning.

Results Mortality in the general surgery unit of UH No. 5 was 0.40% within the period from 1 January 2003 to 30 June 2006. In the general surgery unit of UH No. 1 and of UH No. 2, mortality was respectively 2.70% and 2.13%.

Conclusions Changes of the system of postoperative care consisting of taking over postoperative care by physicians and anaesthesiological nurses, intensive monitoring of postoperative patients, and immediate transfer of patients with life hazard to the ICU decreases significantly the mortality in a surgical unit.

P481

Organizational culture and climate in step-down units

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Critical Care 2007, **11(Suppl 2):**P481 (doi: 10.1186/cc5641)

Introduction The purpose of this study was to examine organizational culture and climate (OCC) in step-down units (SDUs). Organizational culture is defined as the norms, values, beliefs and expectations shared by those who work in a given unit. Organizational climate is the perception of unit culture by its workers. In ICUs, organizational culture is an important determinant of the quality of care delivered. In an attempt to alleviate ICU demand and expenditures, many centers have opted to provide graded levels of critical care with the creation of SDUs. There is a paucity of literature specifically examining OCC in SDUs.

Methods A prospective descriptive analysis of OCC in four SDUs (18 beds) with an open model of care in a tertiary regional referral centre. We administered a modified version of the previously validated Shortell ICU nurse–physician questionnaire to all healthcare professionals (HCPs) and physicians caring for patients in the SDUs in May 2006. We measured opinion regarding patient safety culture, organizational practices, perceived effectiveness of practice, and job satisfaction. Responses were converted to item scores, which reflect negative to positive opinion (0–100). Scores were aggregated for each survey construct and for an overall SDU rating.

Results Surveys were completed by 68 HCPs and 69 physicians. Aggregated mean ± standard deviation item scores of HCP and physician opinions were (presented as assessment area, HCPs, physicians, *P* value): overall OCC in SDUs, 54.8 ± 19.9, 57.0 ± 20.3, $P = 0.52$; patient safety culture, 52.2 ± 21.2, 50.9 ± 21.0, $P = 0.72$; within-group relationships, 66.5 ± 16.0, 63.7 ± 18.2, $P = 0.33$; between-group relationships, 53.8 ± 22.2, 62.4 ± 21.7, $P = 0.02$; overall leadership, 52.2 ± 19.6, 54.8 ± 18.7, $P = 0.42$; conflict management, 55.2 ± 20.1, 61.3 ± 20.1, $P = 0.08$; effectiveness of care, 54.7 ± 16.8, 55.8 ± 19.3, $P = 0.72$; and job satisfaction, 67.5 ± 19.0, 77.9 ± 20.3, $P = 0.002$. The overall OCC score and most subcategory scores were similar between HCPs and physicians. Physicians had a better opinion of their relationships with other groups and a higher job satisfaction than HCPs.

Conclusions Overall scores of OCC were poor and did not differ between HCPs and physicians with the exception of between-group relationships and job satisfaction. More research is needed to determine the correlation between clinical outcomes and OCC in SDUs and whether improvements in OCC result in better clinical outcomes and job satisfaction.

P482

Patient and family satisfaction with care in step-down units

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Introduction The purpose of this study was to determine the level of satisfaction of patients and families with the care received in step-down units (SDUs). In an effort to alleviate ICU demand, many centers have opted to provide graded levels of critical care in SDUs. However, there is a paucity of literature as to the effectiveness of care delivered in SDUs. Measures of patient and family satisfaction with healthcare are recognized as valuable tools for the assessment of healthcare delivery including adherence to

patient-centered and family-centered quality care. Literature examining patient or family satisfaction in SDUs is limited.
Methods We administered a modified version of the previously validated Family Satisfaction with ICU care survey to patients and families of patients who were cared for in the SDUs (18 beds in four separate units) of a tertiary regional referral center. We obtained self-reported levels of patient and family satisfaction with 27 aspects of care related to SDU experience, communication, and decision-making. Responses were converted to item scores, which reflect poor to excellent satisfaction with care (0–100).
Results A total of 120 patient surveys (60% response) and 99 family surveys (45% response) were completed. Patients had a mean SDU length of stay of 2.5 days, APACHE II score of 9.9 and an SDU mortality of 2.4%. The highest levels of satisfaction with care were (mean ± standard deviation item score; presented as aspect of care, patients, families, *P* value): overall care (aggregate score), 81.1 ± 21.5, 80.1 ± 22.3, NS; concern and caring received from SDU staff, 87.9 ± 17.1, 90.4 ± 5.0, NS; and nurses' skill and competence, 88.7 ± 16.0, 88.8 ± 16.6, NS. The lowest levels of satisfaction were: frequency of communication with physicians, 71.6 ± 27.8, 62.7 ± 32.2, $P = 0.03$ and decision-making (aggregate score), 67.5 ± 29.9, 62.7 ± 30.5, NS. For the decision-making process, a proportion of respondents felt they were not included (patients, families, *P* value; 40.3%, 42.7%, NS), not supported (31%, 38.6%, NS), and not in control (32.7%, 55.3%, $P = 0.001$). Patients and families were least satisfied with the frequency of communication with physicians and participation in decision-making. Patients and families were similar in their assessments with the exception of the frequency of communication with physicians and control of the care delivered.
Conclusions While most patients and family members were satisfied with care received, these data identify opportunities for improvement. Specifically, attention must be paid to communication and decision-making processes in SDUs.

P483

Abstract withdrawn

P484

Causes and consequences of failure of implementation of management plans in critical care

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Introduction We investigated patient management plans to ascertain the total number made, types of plan, priority, personnel responsible and expected time frame, proportion completed and the causes and consequences of failed plans (on the patient, the family and the critical care service).
Methods Over seven consecutive days, details of all consultant determined management plans were recorded by a dedicated nurse auditor. A plan was defined as an identifiable do-able, short-term action. Data on type, (arbitrary) priority, involved personnel and time frame were noted. The auditor later returned at the end of shift to determine whether plans had been completed in the appropriate time frame (successful plan) or not (unsuccessful plan). For unsuccessful plans, the nurse, senior nurse, senior house officer, fellow and consultant were all independently quizzed on causes and consequences (for patient, family, service) from a predetermined list of possibilities.
Results Of 200 plans, 130 were successful, for three plans data were missing and 67 (34%) plans were unsuccessful. Of unsuccessful plans, 36 were completed late, 22 were never completed and nine had missing data. Thirty-six per cent, 34% and 18% of arbitrarily defined high-priority, medium-priority and low-priority plans were unsuccessful. Most plans were to be actioned by nurse or senior house officer, and 36% and 28% were unsuccessful, respectively. More unsuccessful plans than successful plans were recorded in the computerised notes, 79% vs 67%. Only 40% of data (staff opinions) on perceptions of causes and consequences were gathered. Patient consequences of failed plans included increased ICU stay in 24%, increased morbidity such as risk of inadequate nutrition in 9%, delayed definitive treatment in 7%, delayed weaning in 6%, increased risk of infection in 5% and no impact on patient in 44%. Consequences for family included no impact in 53%, misinformation given in 8%, delayed patient access in 2%, and delayed communication in 2%. Service consequences were bed blocking/increased workload in 20%, delayed admission of another patient in 14%, cancelled elective operations in 4%, and loss of unit capacity and cohesion in 7%.
Conclusions We failed to achieve 100% successful plans. Small numbers and failure to gather more than 40% of staff opinions on causes and consequences of failed plans limit this pilot study. Documentation in (electronic) notes did not improve completion of plans. The process and efficiency of care has an impact on at least aspects of morbidity and length of stay, and deserve further study.

P485

Outcome of very old patients on mechanical ventilation

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Background The population group of 85 years old or more, classified as very old, are the most rapidly growing group in developed countries, although it still represents 0.46% of the Brazilian population. Aging is associated with decreased cardiopulmonary and renal reserve as well as the development of progressive organ failure.
Objective To evaluate outcomes of very old patients in mechanical ventilation.
Patients and methods A prospective cohort study in the medical/surgical ICU of a tertiary-care Brazilian hospital. Two hundred and forty-four patients aged 85 years old or more were selected from 7,410 patients admitted to the ICU from October 2002 to September 2006. Data were extracted from the QUATI (Dixtal-Brazil) database and included sex, age, APACHE II score, ventilation-days, length of stay, incidence of sepsis, tracheotomy, dialysis therapy and hemodynamic monitoring. For statistical analysis we used the chi-square test for evaluated difference of proportion, and considered statistical significance as $P < 0.05$.
Results There were 168 female (68.9%) and 75 male (30.7%) patients. The mean age of the study population and the APACHE II score were 89.55 ± 3.61 years and 17.98 ± 6.3, respectively. Median ventilation-days and length of stay were 6 and 8.14 days, respectively. Tracheotomy was performed in 44.1%, dialysis therapy in 15.2% and hemodynamic monitoring in 19.8%. Only the group above 95 years old had a significant increase of days of ventilation and length of stay: 18.77 vs 10.47 days ($P = 0.01$) and 19.74 vs 12.86 days ($P = 0.07$), respectively. The predicted APACHE II mortality for the studied population was 26.9 ± 17.21% and the present rate to the population studied was 47.7%. Patients in dialysis and with diagnosis of sepsis at admission had poorer prognosis (respectively a 1.6 and 1.52 times likely ratio to die).

Conclusion The percentage of older patients admitted to the ICU is increasing. The need for tracheotomy and dialysis as well as the length of stay are increasing with this population. APACHE scores do not seem to present a good relationship with mortality in this population. Dialysis and sepsis were associated with a significant increase in mortality.

P486

Outcome of octogenarians versus nonoctogenarians admitted to the intensive care unit with return of spontaneous circulation after out-of-hospital cardiac arrest

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Critical Care 2007, **11(Suppl 2):**P486 (doi: 10.1186/cc5646)

Introduction The aim of this study was to evaluate the outcome of octogenarians (O, age >79 years) versus nonoctogenarians (NO, age <80 years) in relation to predicted outcome (APACHE II predicted mortality, AIIPM) and length of stay in the ICU in days (LOS) after out-of-hospital cardiac arrest (OHCA).
Methods From 1 January 1997 to 1 December 2006, the AIIPM, LOS and hospital mortality were prospectively recorded and the standardised mortality ratio (SMR) was calculated. Patients were categorised in cohorts of AIIPM.
Results Hospital mortality in the NO group was 58.9%, and in the O group was 75.4% ($P = 0.001$, chi-square). The LOS ICU was similar in both groups (Table 1; PM, predicted mortality).
Conclusion In octogenarians admitted in the ICU after OHCA, hospital mortality is higher than in the younger group but still an important proportion survives. Non-octogenarians survived more often than predicted by APACHE II. Despite the higher mortality, ICU treatment after out of hospital resuscitation of octogenarians seems worthwhile.

P487

The costs of intensive care

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Introduction For most countries, there are no good estimates for the costs of intensive care (IC) although it is known that the ICU is a major inpatient cost driver. The aim of this study was to estimate the real costs of IC in two hospitals in The Netherlands using a micro-costing methodology.
Methods The costing study was undertaken at two hospitals in The Netherlands. We conducted a retrospective cost analysis of 200 consecutive patients admitted to a 32-bed mixed adult ICU at an academic hospital during two periods in 2006: 16 April–15 May and 5 June–23 June. For comparison, we collected detailed data at a general hospital that has a 10 bed-adult general ICU for the period 1 January–1 July 2003. The costs were adjusted to 2005 using the general price index. Both times, we applied a micro-costing approach, implying that all relevant resources were identified and valued at a detailed level.
Data on resource use of diagnostics, drugs, fluids, materials, admission and discharge were acquired from the computerized Patient Data Management System in both hospitals. Hotel and nutrition costs were collected from the respective financial departments. These costs were divided by the annual number of patient-days to calculate the cost per day. The NEMS or TISS scores in the academic or general hospital, respectively, were used to estimate nursing time per patient per day. The costs of medical specialists were based on the labour costs and the number of ICU days per year. In the academic hospital, time for consultations of medical staff attributable to each individual patient-day was prospectively collected using patient record forms. These costs we assumed to be comparable in the general hospital in the absence of detailed data.
Unit costs of diagnostics and consumables were derived from the financial hospital databases. Labour costs were based on standardised costs per minute, which equalled the normative income divided by the number of workable minutes per year. Estimates of the costs of inpatient-days and nonpatient-related care were based on the annual account for 2005 of the hospitals. Nonpatient-related care (capital, overhead) was appointed to patients using a marginal mark-up percentage.
Results In the academic hospital the average total costs per ICU day amounted to €1,775, compared with €1,703 in the general hospital. The distribution of the costs by cost component varied.
Conclusions The overall costs per day for IC in an academic hospital were slightly higher than the costs for an ICU day in a general hospital. These derived costs fit nicely to the official reference costs of €1,730 for an ICU day in The Netherlands, which is based on a global top-down approach.

P488

Does the Glasgow Coma Scale correctly diagnose the vegetative and minimally conscious states?

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Introduction Progress in intensive care has led to an increase in the number of patients who survive severe brain injury and, therefore, the number of patients with impaired consciousness.

Table 1 (abstract P486)

	NO				O			
AIIPM	*n*	PM (SD)	SMR	LOS (days)	*n*	PM (SD)	SMR	LOS (days)
0–0.2	29	0.12 (0.07)	1.72	2.1	1	0.17	5.9	0
0.2–0.4	36	0.29 (0.05)	0.96	3.0	8	0.29 (0.07)	2.6	0.25
0.4–0.6	83	0.52 (0.06)	0.93	2.9	19	0.49 (0.06)	1.18	5.6
0.6–0.8	131	0.72 (0.06)	0.88	3.9	43	0.74 (0.06)	0.85	4.1
0.8–1.0	210	0.89 (0.05)	0.81	3.7	71	0.88 (0.05)	0.99	3.0
Total	489	0.69 (0.23)	0.85	3.5 (4.4)	142	0.75 (0.18)	1.0	3.4 (4.4)

Behavioral assessment remains the gold standard to monitor the level of consciousness. However, about one-third of patients diagnosed with a vegetative state are actually conscious (or in a minimally conscious state). We compared the ability of the famous Glasgow Coma Scale (GCS) and other standardized behavioral scales to correctly diagnose the vegetative state in an acute (intensive care and neurology ward) and chronic (neuro-rehabilitation) setting.

Methods Sixty postcomatose patients (that is, GCS > 8) were prospectively assessed using the GCS, the Full Outline of UnResponsiveness (FOUR) and the Coma Recovery Scale-Revised (CRS-R) in randomized order. The mean age was 50 years (range 18–86); 39 were men. Etiology was traumatic in 24 patients.

Results Overall, 29 patients (16 acute and 13 chronic patients) were considered as being in a vegetative state based on the GCS. The FOUR identified four out of these 29 patients (1/16 acute and 3/13 chronic patients) as not being vegetative considering the presence of visual pursuit. The CRS-R identified an additional seven patients (4/16 acute and 3/13 chronic patients) showing visual fixation meeting the criteria for a minimally conscious state set forth by the Aspen Workgroup. Therefore, the GCS diagnosed a total of 38% (11/29) of conscious patients (5/16 acute and 6/13 chronic patients) as being in a vegetative state.

Conclusion Using the GCS can lead one to misdiagnose conscious patients. This misdiagnosis can lead to major clinical, therapeutic and ethical consequences. Using additional sensitive tools such as the CRS-R can avoid this kind of situation.

P489

Intensive care of the elderly in Finland

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Introduction The population is ageing. We wanted to find out how age affects resource consumption and outcome of intensive care in Finland.

Methods We analysed data on 79,361 admissions to 26 Finnish ICUs during the years 1998–2004. We measured the severity of illness with SAPS II scores and the intensity of care with TISS scores.

Results The median age was 62 years; 8.9% of the patients were aged 80 years or older. The hospital mortality rate was 16.2% in the overall patient population but 28.4% for patients aged 80 years or older. In a multivariate logistic regression analysis, old age was an independent risk factor for hospital mortality (Table 1). Overall, the mean length of ICU stay was 3.1 ± 5.3 days; it was 3.2 ± 5.3 days in the age group 75–79 years but only 2.4 ± 3.5 days in the age group 80 years or older. Overall, the mean TISS score per day was 25.8 ± 10.9; it was 27.8 ± 10.7 in the age group 75–79 years and 25.3 ± 9.9 in the age group 80 years or older. If the need for intensive care remains unchanged in each age group, the change in the age distribution of the Finnish population will increase the demand for ICU beds by 25% by 2030.

Table 1 (abstract P489)

Age group (years)	Adjusted OR	95% CI
0–39	Reference	
40–59	2.05	1.8–2.3
60–69	3.17	2.8–3.6
70–74	4.14	3.7–4.7
75–79	5.41	4.8–6.1
80–	7.08	6.3–8.0

Conclusions The hospital mortality rate increased with increasing age. The mean intensity of care and length of ICU stay were lower for the oldest patients than for patients <80 years old. The ageing of the population will probably cause a remarkable increase in the need for intensive care.

P490

One-year survival and functional outcome in critically ill elderly patients

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Introduction The number of elderly ICU patients is increasing [1] but limited outcome data are available. In this pilot study we evaluated survival and quality-of-life indicators in ICU patients aged ≥65 years.

Method Retrospective analysis of admissions between 1996 and 2005 defined the number of elderly ICU patients. Then between 2004 and 2006, consecutive patients ≥65 years admitted to general (631), cardiothoracic (722) or neurological (118) critical care units requiring ≥24 hours of ≥2 organ support were identified. Patients were divided into 'young' (age 65–74 years, $n = 733$) and 'old' (age ≥75 years, $n = 738$). Age, sex, organ support, diagnosis, and referral source were recorded. Patients were followed-up 1 year after discharge. A standard telephone interview of a random sample of survivors (young $n = 15$, old $n = 22$) assessed performance status and the EQ5D health-related quality of life [2]. Data were analysed using Kaplan–Meier and log rank.

Results From 1996 to 2005, 47.3% (4,717) of admissions to the ICU were aged ≥65 years; 24.0% (2,393) were ≥75 years. One-year survival of the young group (51.8%) was significantly ($P < 0.001$) better than the old group (37.9%). However, in those receiving ≥3 organ support (young $n = 197$; old $n = 199$), this significance is lost (42.2% vs 32.6%, $P > 0.2$). Younger elective surgical patients had better survival than older (79.4%, $n = 196$ vs 64.5%, $n = 173$). There was no survival difference between young and old after emergency surgery (52.9%, $n = 57$ vs 50.4%, $n = 85$; $P > 0.5$). There was no difference between 'young' and 'old' groups in the EQ5D weighted health index (0.67 ± 0.30 vs 0.62 ± 0.29, $P > 0.5$) or performance status scores (1.73 ± 0.96 vs 1.72 ± 0.98, $P > 0.5$). The EQ5D scores of survivors were lower than matched population norms (0.64 vs 0.76, $P < 0.01$).

Conclusion Survival is worse in older ICU patients, although initial data suggest no difference in functional outcome. Survivors have lower quality-of-life scores than population norms [3]. Further work is pending.

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P491

The outcome of patients admitted to an intensive care unit with haematological malignancy: a case–control study

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Introduction The outcome of patients with haematological malignancy admitted to the ICU has been reported as between

34% and 75%. Historically, these patients have been regarded as having a poor prognosis once admitted to the ICU. We decided to compare the ICU and hospital mortality of these patients with patients of a similar age and severity of acute illness.
Methods Twenty-four patients were admitted to the ICU from August 2004 to August 2006 with a haematological malignancy. These were case-matched using sex, age (±2 years), APACHE II score (±2) and admission diagnosis with patients admitted to the ICU without a diagnosis of haematological malignancy. Eighteen patients were matched to one case control; however, in six patients, two matches were found. Where it was impossible to differentiate between cases on the grounds of diagnosis, age or APACHE II score they were both included. We compared ICU and hospital mortality between the two groups.
Results Patients with a haematological malignancy had an ICU mortality of 50%, and a hospital mortality of 58%. Control patients had an ICU mortality of 60%, and a hospital mortality of 67% (statistically nonsignificant). The length of time to admission between the two groups was significantly longer in the haematology group at 12.4 days, compared with 2.8 days in the control patients ($P < 0.05$). The level of organ support was the same between the two cohorts.
Conclusion We have demonstrated that, for our unit, there was no statistically significant difference in hospital or ICU mortality between the two groups. In fact, the group with a haematological malignancy had a lower mortality than the control group. The presence of haematological malignancy, of itself, does not appear to increase the mortality risk, when compared with a population of patients without haematological malignancy of a similar age, APACHE II score and admission diagnosis.

P492

Quality of life following prolonged critical illness: insights from a qualitative approach

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Introduction The measurement of health-related quality of life (HRQoL) among survivors of critical illness has become a prominent feature of our outcomes research. Local research experience suggests that existing measures may fail to capture the broad spectrum of morbidity that survivors experience. The purpose of this research is to explore, through predominantly qualitative methods, critical-illness mediated morbidity among survivors of prolonged critical illness; a group in whom this type of morbidity appears to be most prevalent. An important secondary aim is to explore the contribution of the processes of rehabilitation and recovery to perceptions of HRQoL.
Methods Survivors who experienced prolonged critical illness (defined as ≥14 days mechanical ventilation) were identified from the Scottish Intensive Care Society Audit Group (SICSAG) database, Wardwatcher®. Participants were contacted ≤6 months following ICU discharge, and were invited to complete professionally recommended quality-of-life questionnaires (the Short Form 36 and EuroQol-5D) and to participate in a semi-structured interview. Interviews explored everyday experiences of ongoing morbidity and were analysed with regard to their correlation with the domains and scores of the HRQoL questionnaires.
Purposive sampling provided clinically important insights into experiences and perceptions of health and pre-existing morbidity and, importantly, the processes of rehabilitation and recovery; that is, through comparison of (i) patients with/without appreciable pre-existing disease and (ii) patients receiving ward-based rehabilitation with those who receive formalised rehabilitation in dedicated facilities.
Preliminary results Ten of the required 40 interviewees have so far been recruited. Preliminary analysis confirms that survivors experience a range of morbidity not well captured by professionally recommended measures, and that pre-existing disease is an important factor in both coping with new morbidity superimposed by critical illness, and in marshalling support. The process of rehabilitation appears to have important effects on perceptions of recovery, self-management strategies, and perceptions of HRQoL.
Conclusions This qualitative enquiry has already provided, and will continue to provide, new and clinically relevant insights into patients' experiences of morbidity, the processes of rehabilitation, recovery and perceived HRQoL following discharge into the community.

P493

Quality of life before intensive care unit admission is a strong predictor of survival

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Objective To examine whether health-related quality of life (HRQOL) before admission to the ICU can be used as a predictor of mortality
Design and methods A prospective cohort study in an university-affiliated teaching hospital. Patients admitted to the ICU for >48 hours were included. Close relatives completed the Short-form 36 (SF-36) within the first 48 hours of admission to assess the pre-morbid HRQOL of the patient. Mortality was evaluated from ICU admittance until 6 months after ICU discharge. Logistic regression and ROC analysis were used to assess the predictive value for mortality of the first general health question of the SF-36 ('in general would you say the health of your relative is excellent, very good, good, fair or poor'), as well as HRQOL measured by the complete SF-36. The Acute Physiologic and Chronic Health Evaluation (APACHE) II score was used as an accepted mortality prediction model in ICU patients. Three models were constructed including the HRQOL (model A), APACHE II score (model B), or both (model C) to age and gender. Percentages of correct survival/death predictions were calculated.
Results Four hundred and fifty-one patients were included at admission to the ICU. At 6 months follow-up, 159 patients had died and 40 patients were lost to follow-up. When the general health item was used as an estimate of HRQOL, the area under the curve (AUC) for model A (0.719) was comparable with model B (0.721), and slightly better in model C (0.760). The percentage of wrong predictions was lower in model C (survival 27%; death 37%) compared with model A (30% and 41%). Similar results were found when using the complete SF-36.
Conclusions This study shows that the pre-admission HRQOL measured with either the one-item general health question or the complete SF-36 are as good in predicting survival/mortality in ICU patients as the APACHE II score and improves prediction slightly when combined. As the one-item general health question is easily and quickly obtained, assessment of HRQOL before admission to the ICU may facilitate the decision process in determining which patients will benefit from ICU treatment.

P494

Five years experience of critical care bereavement follow-up

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Introduction We believe that by explaining and answering the questions of those relatives that wish it, we can alleviate the grief caused by the death of a relative in critical care. Death is a common outcome of critical illness and relatives are at high risk of problems with complicated or unresolved grief due to the sudden, often unexpected, manner of that death. We describe the establishment and results of a bereavement follow-up service.
Methods All relatives, since January 2001, have been offered bereavement follow-up. Following the death of a patient in critical care, relatives are informed of the bereavement follow-up service. After death, a booklet is given to the next of kin with information about the service. Four to six weeks later a condolence card is sent, which includes a reminder of the follow-up service. We do not offer a counseling service and details of other organizations providing this are given. Appointments are made by telephone. The interview usually takes place outside critical care and is led by a consultant and a specially trained nurse. Relatives are given the opportunity to ask questions. A monitoring form is completed. A letter is sent to the GP detailing the issues discussed.
Results In the 30-bed critical care unit in a teaching hospital, during study period January 2001–November 2006, 8,964 admissions and 1,560 deaths (17.4% of patients) occurred (male:female ratio 1.27:1). The average age of deaths was 64.7 years. Eighty-nine families were seen in bereavement follow-up (5.7% of total deaths) and two families attended for a second visit. The male:female ratio was 2.18:1.0, and the average age of death was 42.9 years. A length of stay before death of 1 week or less occurred in 59.6%. Forty-seven per cent of families were seen between 2 and 4 months after the death of their relative. The issues most commonly raised were specific questions about the patient (56.2%), review of information in the notes (34.8%), complaints (23.6%), clarifying misunderstandings (18%) and contacting other health professionals (21.3%).
Conclusions We describe the results of a bereavement follow-up service for families whose relatives died on the critical care unit at University Hospital of Wales, Cardiff. In total, 5.7% of families took up the service offered. These were usually the families of younger than average male patients, who died with a critical care stay of less than 1 week. We believe that by answering questions still troubling the families 2–4 months after death, we can assist them with their grief. We also believe that this follow-up service by providing further communication can resolve some difficult issues before they develop into formal complaints.

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Quality of life aspects in oncologic patients who survived an intensive care unit admission

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Introduction The number of organ failures in oncologic patients admitted to the ICU is a good predictor of mortality. We propose to analyze the association of this variable and quality of life (QOL) aspects in oncologic patients who survived an ICU admission.
Methods ICU data were prospectively collected from March 2003 to November 2005. Oncologic patients were selected. QOL aspects were evaluated through the analysis of independence to accomplish daily living activities (IADL) after ICU discharge, defined as the patient's ability to walk, eat by mouth, maintain an oriented conversation and bath himself. The number of organ failures was assessed through the SOFA score. Severe organ dysfunction (SOD) was defined if the patient had three or four points in any of the six domains of the SOFA score. According to the number of SOD, patients were divided into two groups: one with two or less SODs and another with three or more SODs. Groups were compared using Fisher's exact test.
Results Seventy out of 793 patients had an oncologic diagnosis. The mean age was 52 ± 19 years, male gender 56%, medical admission 77%, hematological malignancies 47% and mean APACHE II score 20 ± 8. ICU mortality was 53% and inhospital mortality was 71%. Nine (13%) patients were discharged of the hospital with complete IADL. Mortality in the group admitted with three or more SODs was 100%, while in the other group it was 39% ($P = 0.01$, OR 2.5 95% CI 1.8–3.6). During the ICU stay, patients who developed three or more SODs had a higher ICU and inhospital mortality than the ones who did not (89 x 23%, $P < 0.001$, OR 7, 95% CI 1.8–26 and 100 x 53%, $P < 0.001$, OR 2, 95% CI 1.4–2.6) and a smaller proportion of IADL after ICU and hospital discharge (0 x 22%, $P = 0.04$, OR 1.7, 95% CI 1.3–2.2 and 0 x 47%, $P < 0.001$, OR 2, 95% CI 1.4–2.6).
Conclusion Mortality should not be the only aspect analyzed when considering an ICU admission for an oncologic patient. The QOL, including IADL, must be taken into account. A higher number of SODs during the entire ICU stay is associated with higher ICU and inhospital mortality. Beyond this association, a smaller number of SODs may be associated with higher probability of IADL.

P496

Intensive care unit utilization after esophagectomy

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Introduction At our institution, postesophagectomy patients are usually managed in a progressive care unit with ICU admission reserved for those of high acuity. We hypothesized that ICU admission after esophagectomy is predictable and associated with high mortality.
Methods A retrospective analysis of all patients after esophagectomy between January 2000 and June 2004 at a tertiary referral center. Data regarding demographics, preoperative morbidities, perioperative complications, APACHE III predictions, mortality, and lengths of stay were collected.
Results Four hundred and thirty-two patients underwent esophagectomy during the study period: 123 (28.5%) were admitted to the ICU (ICUGP) and 309 (71.5%) were not (NICUGP). Overall mortality was 3.7% (16 of 432 patients). Fifteen of 123 in ICUGP died in hospital (12.2%) compared with one of 309 in NICUGP. For ICUGP, mean (±standard deviation) acute physiology and APACHE III scores were 41.8 (±16.6) and 54.5 (±18.1), respectively. Forty-seven percent of ICUGP had a new (versus pre-existing postoperative) infiltrate on chest X-ray, 21.8% had positive sputum/bronchial culture and 5% positive blood culture within 48 hours of ICU admission. A total 13.8% of ICUGP had 'aspiration' documented in physician notes. The median (IQR) ICU and hospital lengths of stay were 3.6 (1.7–9.9)

and 17.0 (11.3–33.9) days, respectively. Compared with NICUGP, patients in ICUGP were more likely to have developed post-operative arrhythmia (57.9% vs 12.9%, $P < 0.001$), were older, of higher ASA status, and more likely to have diabetes, coronary artery disease, hypertension, a higher cancer stage, and to have received more intraoperative blood products. Of 352 patients originally not sent to the ICU, 43 (12.2%) were subsequently admitted to the ICU. These patients had higher APACHE III scores and were more likely to have 'aspiration' documented, although their mortality was not higher than direct ICU admissions.
Conclusions After esophagectomy, overall mortality is low, but many patients require ICU admission. Postoperative arrhythmias and aspiration pneumonitis are especially problematic.

P497

Visiting policies in Italian intensive care units: a national survey

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Introduction Today no published data are as yet available on visiting policies in Italy's approximately 600 ICUs. We carried out a multicentre survey to evaluate visiting policies in Italian ICUs.
Methods An email questionnaire was sent to all 303 ICUs (general and specialized) in the Italian collaborative Gruppo Italiano per la Valutazione degli Interventi in Terapia Intensiva, asking about their visiting policies.
Results The response rate was 84.8% (257/303). The median daily visiting time was 60 minutes (10th percentile: 30 minutes; 90th percentile: 120 minutes); however, 2% of ICUs allowed no visiting whatsoever. A total 54.8% of ICUs surveyed had only one daily visiting slot, and 44% two. Only 1.2% had more than two visiting slots. The number of visitors was restricted in 91.8% of ICUs. The type of visitors (immediate family only) was restricted in 17.5% of ICUs. Children were not permitted to visit in 69.1% of ICUs and 17.5% had a minimum age limit for visitors. In the case of a dying patient, 20.6% of ICUs did not alter the visiting policy; 49% extended visiting hours; 44% increased the number of slots; and 53% allowed more visitors. A gowning procedure was compulsory for visitors in 95.3% of ICUs. No waiting room was provided by 25.4% of ICUs.
Conclusions This is the first survey on visiting policies in Italian ICUs. Despite the widely-held conviction that there is no sound scientific basis for restricting visitors in ICUs [1-3], our findings show a clear tendency in Italian ICUs to apply restricted visiting policies (concerning visiting hours, number and type of visitors), which are only partially liberalized when the patient is dying. Our survey could contribute towards modifying current policies in favour of opening ICUs that are still 'closed' and promoting more appropriate and attentive care for the patient and his/her family.
Acknowledgement We thank Gruppo Italiano per la Valutazione degli Interventi in Terapia Intensiva for their valuable help.
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P498

Communication with patients during ward rounds on the intensive care unit: a prospective, observational, semiblind study

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Introduction It is good medical practice to communicate with patients regarding their condition and proposed treatment. Communication is essential to allow them to express their concerns and exercise their own autonomy, in a situation where they otherwise may have little control. Poor communication may contribute to unnecessary anxiety or depression. The aim of this audit was to observe whether the doctors communicated with patients on ward rounds.
Methods We audited 28 ICU ward rounds. It was noted whether the patient was sedated or not sedated, and whether they had their eyes open or closed. Negative comments were recorded, and defined as comments regarding a patient's poor progress or prognosis made at the bedside during the ward round. We also noted whether the patient was informed that the ward round was in progress, whether they were informed of the plan for the day, and whether any reassurance was offered. The other members of the team were not aware of the audit.
Results Twenty-eight ward rounds were audited, a total of 328 patient reviews. The total number of patients with their eyes open was 171, while 157 had their eyes closed. An adverse comment was made during 8.2% of reviews within earshot of the patient. A negative comment was made on 27 episodes, 13 of these were when the patient was not sedated but had their eyes closed. Four episodes occurred when the patient was not sedated and had their eyes open, while 10 were sedated and had their eyes closed. Of the 171 patients with their eyes open, 74 (43%) were informed that we were the team doing the ward round, while 97 (57%) were not spoken to at the start of the review. Fifty-three (31%) were informed of our management plan for the day and 43 (25%) were offered reassurance. In total, 103/171 patients (60%) with their eyes open were spoken to during the ward round, and we did not speak to 68 (40%).
Conclusion On intensive care ward rounds, patients are often not engaged in conversations or allowed to express their concerns. The majority of patients were not offered reassurance or informed about the treatment plan. Improved communication skills may help to lessen patients' anxiety and unnecessary stress both during their stay on ICU and following their discharge.

P499

Hospital volume and outcome following mechanical ventilation on the intensive care unit

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Introduction The study was undertaken to determine the relationship between hospital volume and mortality in mechanically ventilated adult medical and surgical patients. The regionalisation of adult critical care services has been suggested by healthcare providers and health policy-makers as a means of achieving the ideal balance of providing high-quality care that is both cost-effective and accessible. Recent studies have had conflicting results.

Methods The Birmingham and Black Country Critical Care Network database was retrospectively reviewed over a 10-year period from 1 April 1996 to 31 March 2006. The database included 50,686 patient episodes. After exclusion (incomplete data 9,700 episodes, unventilated patients 19,244 episodes, mechanical ventilation for less than 24 hours 3,814 episodes, interhospital transfers 795 episodes) the final cohort included 9,920 adult medical patients and 7,210 surgical patients. Hospitals were grouped into five volume categories to aid interpretation of the results (<100; 100–149; 150–199; 200–249; ≥250 ventilation episodes/year). The odds ratio and 95% confidence intervals for death on the ICU were calculated in relation to the hospital volume of ventilation.

Results For both medical and surgical patients there was no relationship between the hospital volume of ventilation and death on the ICU. The odds ratio remained insignificant even after adjustment for patient demographics, APACHE II score, length of ICU stay and urgency status. Medical patients' adjusted odds ratio was 0.735 (95% CI 0.604–0.894). Surgical patients' adjusted odds ratio was 0.771 (95% CI 0.559–1.064).

Conclusion There is no relationship between hospital volume and ICU mortality in both medical and surgical patients following mechanical ventilation. The results of this study do not support the argument for regionalisation of adult critical care services in the United Kingdom.

P500

Continuous education in intensive care for physicians in Brazil: for whom and their needs

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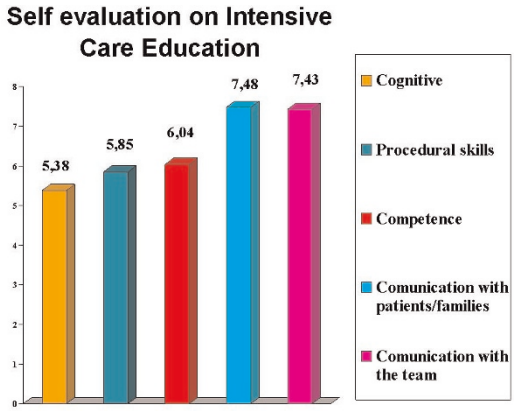
Introduction The postgraduation course had been developed by the Brazilian Critical Care Society (AMIB) to be applied to physicians from all regions of Brazil since 2004. The importance of this 360-hour course is to provide continuous education and to train abilities to make decisions and start treatment. Also, for those who are in ICU practice, to qualify for application of specialist examination. The main objective of this study is to identify who are the doctors that are looking for this course.

Methods An opinion poll was collected from the students on the first day of the class course approaching the following aspects:

1. Profile.
2. He/she is attending the course in order to: prepare for the specialist critical care examination (), improve qualification (), work at an ICU (), any other reason if they do not deal with critical care patients ().
3. If he/she works at an ICU: how long (years) and the role (duty, routine or leader).
4. Partners of AMIB (yes) (no); if they have specialist title recognized by the AMIB (yes) (no).
5. If he/she has other postgraduation or residency program.
6. Self-evaluation related to the critical patient knowledge (scales from 1 to 9, considering 9 the highest grade).
7. Interest in the subjects of intensive care medicine (scales from 1 to 9).

Results From 2004 to 2005 the AMIB started eight postgraduation courses in different regions of Brazil; 250 students were enrolled; 184 had answered the survey. The average age was 35.8 years (24–57); 133 men, 51 women. One hundred and five students are attending the course in order to improve their qualification, 87 are studying for the specialist title examination, 58 to work in the ICU and 47 to acquire new knowledge. They considered their main specialties to be: internal medicine (54), intensive care (15), surgery (10) and anesthesiology (seven). Sixty-five percent work in the ICU (12.7% are leaders, 19.5% daily routine, 86.4% on duty and 6.8% play all three functions), 6% have the specialist critical care title, 15.7% are associated with the Brazilian critical care society, 49.45% have medical residence in another area, 36.4% have other postgraduations. They self-considered around grade 6 for cognitive aspects, procedural skills and competence and near grade 8 for communication and relationship (see Figure 1). Cardiopulmonary resuscitation, mechanical ventilation, haemodynamics and neurointensivism are the most desirable subjects.

Figure 1 (abstract P500)



Conclusions Doctors are mainly from the fourth decade, want to improve their qualification, and are usually working in ICUs. The low number of specialists who works in ICU is a reality and there is a need to expand it. The self-evaluation points to problems with knowledge and ability; however, communications and relationships were well adjusted. The diversity of data will assist the AMIB to provide continuous education and qualify doctors to attend the demand of intensivists in Brazil.

P501

Data completeness in the Finnish Intensive Care Quality Consortium database

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Introduction Benchmarking has been an essential part of intensive care medicine in Finland since 1994. At present, web-based quality/performance reports are shared with the 24 members of the Finnish Intensive Care Quality Consortium (FICQC). Thirteen ICUs collect FICQC data manually and 11 ICUs utilize data collection software (IVT) integrated with the Clinical Information System (CIS). In recent literature, the completeness of data between centralized medical benchmarking registries varies widely [1,2]. We hypothesized that: (1) the completeness of data in FICQC has

increased over the years and (2) the variation between the different units still exists.

Methods We assessed data completeness of a Finnish ICU quality benchmarking database from 1998 to March 2006 containing 93,964 admission records. The data completeness was defined as a ratio of available and required data at ICU admission level. We evaluated the dataset and selected 19 most significant admission scheme variables to be included in completeness ratio calculations.

Results The majority of data (77.5%) was collected with the manual system and the remaining 22.5% with an integration software. The mean admission data completeness ratio (CR) increased from 85.3% at 1998 to 97.9% at 2005 ($P = 0.01$). Between the ICUs, the mean CR varied from 91.6% to 99.6% ($P = 0.01$). The mean CR of the data collected with the IVT was 98.7% and with the manual system was 95.1% ($P = 0.01$). The rate of 100% complete records per patient was 48.7% and it increased from 0.0% in 1998 to 71% in 2005.

Conclusion Data completeness in the FICQC has improved during the study period, although there is still significant variation between ICUs. Improved data completeness and decreased proportion of missing data are most likely due to the increasingly common use of CIS and automated data collection. We conclude that measuring/reporting the amount of missing data is mandatory when data collection and data management procedures for benchmarking are being developed.

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P502

Analysis of critical incidents during the interhospital transport of critically ill patients

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Introduction In this study we created a database to analyse the incidence and types of critical incidents that occurred during the interhospital transfer of critically ill patients. The transfer of critically ill patients presents important risks and the safety of patients has been shown to be facilitated by the development of standard equipment and specialist teams [1]. The West of Scotland Shock team is a designated regional transfer service based in Glasgow. We are involved in the interhospital transfer of patients and not primary retrieval. A recent study looking at critical incidents during the intrahospital transport of the critically ill highlighted the risks posed, and recommended the monitoring of incidents in order to aid the continuous improvement in patient safety [2]. No similar study has been carried out looking at the interhospital transport of the critically ill patient.

Methods The study was a cross-sectional analysis of critical incidents occurring during interhospital transport that were reported to the West of Scotland Shock Team critical incident database set up in September 2005. The information obtained was categorised into: (a) where the incident took place, (b) type of incident, (c) written description of events, (d) outcome (potential or actual harm to the patient) and (e) designation of the staff member reporting the incident.

Results A total of 199 transfers were performed over the 6-month period. Thirty-four critical incidents were reported. Twenty-four (70%) incidents took place before, seven (21%) during and three (9%) after transfer. No patients sustained actual harm, 29 (85%) were perceived by the reporter to have suffered potential harm and the most common cause of this were delays in the transfer. No potential or actual harm was perceived in five (15%) of the incidents. Fifty-three per cent of events were reported by senior house officer grade and 47% of incidents were reported by a specialist registrar. Only one incident was reported by a nurse on the team.

Table 1 (abstract P502)

Causes of all incidents (irrespective of patient outcome)	
Communication problem	10 (29%)
Organisational delay	7 (21%)
Lack of staff	2 (6%)
Equipment failure	9 (26%)
Poor preparation of patient	5 (15%)
Staff injury	1 (3%)

Conclusions Interhospital transport of critically ill patients can pose important risks. In our study no actual patient harm occurred although most incidents had the potential to cause harm. The majority of incidents were caused by system-based factors. This database has allowed us to perform continuous service development and education of staff.

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P503

Maximisation of heart and lung donation in a neurosurgical intensive care unit

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Introduction The number of heart-beating donors in The Netherlands is decreasing. This decrease is only partially compensated for by an increase of nonheart-beating donations, resulting in an increasing shortage of donor organs, especially of donor hearts and lungs. In 2005 compared with 2004 the number of patients waiting for a donor heart increased from 38 to 50 (32%). In lung donation the increase was 37% (from 79 to 108). One approach to reduce this shortage is to maximize the number of organs per donor by optimisation of donor treatment in the ICU.

Methods We investigated the possibilities for improvement of donor management in our ICU by a retrospective study in 37 heart-beating organ donors hospitalised in our ICU from 1993 to 2005. There was no protocol for the treatment of organ donors in our institution.

Results The heart was donated in 18 of 37 patients (49%). Lung donation was possible in only eight of 37 donors (22%). Most hearts and lungs were rejected for transplantation for valid reasons. In some patients there was room for improvement: in two of the three cases where hemodynamic instability impeded heart and lung donation (one dying from subarachnoidal bleeding and one from ischemic cerebral infarction), hemodynamic instability was closely associated with the moment of cerebral death. In three further patients heart donation was not carried out because of wall movement abnormality or electrocardiogram abnormalities. None of

them had previous cardiac disease. All three had disturbances in cardiac rhythm closely related to the occurrence of cerebral death. Two of these three patients also developed neurogenic pulmonary edema. We speculate that in all five patients the instability leading to the decision not to perform heart and lung donation was caused by excessive sympathic stimulation at the time of cerebral death leading to impaired myocardial function and neurogenic pulmonary edema. These disturbances may be reversible within a few hours. Inotropic therapy, judicious fluid administration guided by close hemodynamic monitoring together with a trial of treatment with triple hormonal therapy (corticosteroid, vasopressin and thyroid hormone) might have improved cardiac and pulmonary function, rendering heart and lung donation possible.

Conclusion On the basis of this retrospective study we conclude that donor management in our ICU can be improved. A management protocol with special attention for treatment of disturbance in cardiac and pulmonary function caused by sympathic overstimulation might considerably increase the amount of hearts and lungs donated, contributing to a decrease in organ shortage.

P504

Medical practices during the last 48 hours of life in children admitted to seven Brazilian Pediatric intensive care units

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Introduction During the last decades life support limitation (LSL) practices have been offered more frequently in Latin American pediatric intensive care units (PICUs). We hypothesize that, depending on the Brazilian region, the incidence of LSL and the medical management may differ.

Objective To evaluate the incidence of LSL practices and the medical management during the last 48 hours of life of children admitted to seven PICUs located in regions of Brazil.

Methods A multicenter, observational and retrospective chart review study. The medical chart of all deaths occurring between January 2003 and December 2004 in seven Brazilian PICUs located in Porto Alegre (two), Sao Paulo (two) and Salvador (three) were evaluated. Two pediatric intensive care residents of each service filled a standard protocol searching for: demographic data, mode of death (full reanimation, nonreanimation orders or withdrawn treatment) and medical management during the last 48 hours of life. Student's *t* test, analysis of variance, chi-square test and relative risk were used for comparing the data.

Results There were 561 deaths, 36 being excluded that died with less than 24 hours, 61 with brain death and 36 missing charts. Full cardiopulmonary reanimation was offered to 56.5%, with differences between the northeast and southeast regions ($P < 0.001$). Higher age ($P = 0.02$) and long length of PICU stay were associated with nonreanimation orders. The plan for LSL was recorded in a clear manner in just 52.7%. No respiratory support was observed in 14 dying children. For 66% patients with do-not-resuscitate orders the inotrope drugs were maintained or increased in the last 48 hours.

Conclusions The incidence of LSV has increased among the Brazilian PICUs with a difference between the regions. The nonreanimation order is still the most common practice with scarce initiative for withdrawn life support.

P505

End-of-life care in the critically ill: a description of knowledge, attitudes and practices of physicians and nurses from Karachi, Pakistan

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Introduction As the numbers of people admitted to ICUs are increasing, physicians are faced with obligations beyond attempting to reverse illness and include providing quality end-of-life care. Barriers to this include inadequate understanding of the dying patient and withdrawal or limitation of care. The objectives of this study were to document the comprehensions of physicians and nurses dealing with these situations.

Methods We carried out a cross-sectional survey of clinicians working at three hospitals in Karachi (one private, university hospital, one mixed public and private, tertiary care hospital and one large government-funded hospital). A 13-question instrument was developed to assess recognition of end-of-life in the ICU, knowledge of commonly used terms to describe limitations of care, and attitudes and practices towards withdrawal and limitation of life-support measures and organ harvest for transplantation. After measuring the frequencies for presentation of the data, differences between the three respondent subgroups were compared using a chi-square analysis. Fisher's exact test was used where the individual cell count was <5. A one-way analysis of variance was used to compare differences in age and years of practice. A two-sided *P* value of <0.05 was considered statistically significant.

Results A total of 137 physicians and critical care nurses completed the survey. The average age was 34 years and 58% were males. 'Brain death' was defined as an 'irreversible cessation of brainstem function' by 85% of respondents; 77% relying on clinical examination, 49.6% consulting neurophysicians and 28.3% ordering further testing to confirm the diagnosis. Withdrawal of life support is practiced by 83.2%; most frequently in the setting of absent brainstem and cortical functioning (74.3%), followed by acute, progressive multiorgan failure (39.8%). Physicians are more likely (*P* value 0.000) to withdraw mechanical ventilation, compared with nurses who would withdraw vasopressors (*P* value 0.006). The primary physician is the most frequent caregiver (60.2%) to start a discussion on withdrawal of life support, with 72.6% respondents consulting the Hospital Ethics Committee. Only 13.3% respondents never withdraw life support; 28.3% considered it their responsibility to 'sustain life at all costs' and only 8% gave religious beliefs as a reason. Only 56.6% favored organ harvest for transplantation from cadavers, while 64.6% supported harvest from brain dead individuals. Nurses were significantly more likely to support organ harvest for transplant from heart-beating, brain dead individuals (*P* value 0.025) than cadavers (*P* value 0.000).

Conclusion There are deficiencies and disparities in the understandings of physicians and nurses on the recognition and management of end-of-life in the ICU.

P506

World Resources in Critical Care Study: a survey of critical care research and resources in eight countries

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Introduction Critical care research involves data from many countries, but critical care resources in these countries are unknown. We hypothesized that there are large differences in critical care resources between countries.

Methods We identified original research articles on critical care in three high impact factor journals (*N Engl J Med*, *JAMA* and *The Lancet*) published from 2001 to 2005. A list of the countries where data collection occurred was extracted. Eight countries contributed to ≥10 studies. A collaborator in each country was asked to provide baseline critical care information for their country from 2005, or as close to that date as possible.

Results Sixty-two studies involving data from 51 countries were identified. Eight countries contributed data to ≥10 studies during this time period: the USA (26 studies), France (18), the United Kingdom (14), Canada (13), Belgium (12), Germany (10), The Netherlands (10) and Spain (10). Relevant data on baseline hospital and critical care resources for the eight countries identified are presented in Figure 1 (data from Canada not available). Adult ICU beds ranged from 3.3/100,000 population in the United Kingdom to 24.6 in Germany, and represented a range of 1.4% of all acute care hospital beds in the United Kingdom to 11.0% of all beds in the USA.

Conclusions Many countries contribute substantially to critical care research. However, the underlying critical care resources vary dramatically among these countries.

Figure 1 (abstract P506)

	US	France	UK	Canada	Belgium	Germany	Netherlands	Spain
Total number of adult ICUs (excluding stand-alone CCUs)	5,980*	550	274	NA	135	NA	115	258
Total number of adult ICU beds	71,979	5,707	1,993	NA	NA	20,259	1,367	3,628
Adult ICU beds/100,000 population	24.3	9.3	3.3	NA	NA	24.6	8.4	8.2
Adult ICU beds as a % of all acute care hospital beds	11.0%	2.5%	1.4%	NA	3.8%*	4.1%	2.8%	2.5%
Mean number of adult ICU beds	12.0*	10.4	7.3	NA	17.2*	NA	11.9	14

Baseline critical care resources in eight countries. *Extrapolated from survey data, not full national data.