Acute lung injury/Airway

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ACUTE RESPIRATORY DISTRESS SYNDROME(ARDS): RESULTS OF A SURVEY IN GERMAN PAEDIATRIC INTENSIVE CARE UNITS

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Background Acute respiratory distress syndrome (ARDS) is a therapeutic challenge in pediatric intensive care in view of the high mortality. In 1992 about 50 German paediatric hospitals founded a working group aiming on collaborative clinical research in this field.
Aims and methods The aim of both a prospective and retrospective survey conducted in German pediatric intensive care units in 1993 was to accumulate data on the epidemiology, risk factors, natural history and treatment strategies in a large group of pediatric ARDS patients who were treated in the three year period from 1991 to 1993.All patients had acute bilateral alveolar infiltration of noncardiogenic origin and a pO2/FiO2 ratio < 150mmHg. The influence of sex, underlying disease and single organ failure was analyzed using the Fischer´s exact test, the influence of additional organ failure on mortality was tested with the Cochran-Mantel-Haenszel statistics.
Results 112 patients were reported giving an incidence of 7 cases per 1000 admissions to pediatric ICUs. Median age was 24 month. In 43% of the cases, ARDS was associated with a pulmonary, in 39% with a systemic underlying disease. In 20% immunocompetence was impaired. Mortality was 46% and not dependent on age, sex and triggering event. The number of associated organ failures, however, strongly influenced mortality. Mortality in immuno- compromised patients was 81%.
The Analysis of treatment modalities employed in the patients revealed a lack of uniform therapeutic strategies. On the other hand, the patients were exposed to interventions not yet supported by controlled trials.
Conclusions The observation of the lack of uniform treatment strategies led to the elaboration of recommendations on ventilator therapy and patient monitoring within the working group. The data gathered in this survey provide the basis for the design of prospective multicenter studies urgently needed to evaluate innovative treatment modalities in pediatric ARDS.

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ARDS TRIGGERED BY RSV INFECTION IN INFANTS

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Recurrent apnea and respiratory failure due to severe lower respiratory tract disorders such as bronchiolitis or pneumonia are the most common reasons for mechanical ventilation during respiratory syncytial virus (RSV) infection. Acute respiratory distress syndrome (ARDS) has been described as a complication of severe RSV infection.[1] In contrast to the low mortality rates associated with RSV infection (< 5%), mortality rates in the range of 40-70% have been reported in pediatric patients with ARDS. However, studies on ARDS are usually lumped in respect to causation and the disease course of RSV induced ARDS has not been previously studied.

We examined the lung function abnormalities of 37 infants with RSV induced respiratory failure requiring assisted ventilation. Measurements included respiratory mechanics, maximal expiratory flow-volume curves and lung volumes. ARDS was defined clinically using the criteria which were recently proposed by the American-European Consensus Conference on ARDS[2]: acute disease onset, PaO_2/FiO_2 ratio $\leq$ 200 mm Hg, bilateral infiltrates on chest radiograph and absence of clinical evidence of left atrial hypertension. We calculated the Murray lung injury scores modified for use in pediatric patients[3] from total respiratory system compliance, radiographic findings, ventilator settings and blood gas results. We identified 10 infants with severe restrictive lung disease that fulfilled the clinical criteria for classification as ARDS. All had lung injury scores above 2.5 which is the recommended cut-off for a diagnosis of ARDS. Twenty-seven infants had obstructive disease consistent with a clinical diagnosis of bronchiolitis. The ARDS patients were significantly younger, had a longer time of assisted ventilation ($p < 0.05$) and a greater proportion of infants with preexisting illnesses ($p = 0.023$, Odds ratio = 6.67) when compared to the patients with obstructive disease. With the exception of one immunodeficient patient, none of these infants died. Given the low mortality despite a clinical picture of severe lung injury, there is evidence that RSV induced respiratory failure may represent a relatively benign cause of ARDS in pediatric patients.

[1] Bachmann DCG, et al. J. Intensive Care Med 1994; 20: 61-63
[2] Bernard GR et al. Am J Respir Crit Care Med 1994; 149:818-824
[3] Stretton M, et al. Am Rev Respir Dis 1992; 143: A248

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Acute Hypoxic Respiratory Failure in Paediatric Intensive Care.

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An audit of patients with severe acute hypoxic respiratory failure (AHRF) receiving high-frequency oscillatory ventilation (HFOV) in our unit (n=32, mortality 75%) revealed that sub-groups with severe underlying disease (n=14, mortality 100%)and those with multiple organ failure (≥ 2 systems failing, n=7 mortality 100%) accounted for **all** the deaths beyond the neonatal period. We therefore hypothesized that in a modern paediatric intensive care unit (PICU):
a) children greater than one month of age with AHRF do not die in the absence of severe, pre-existing disease or multi-organ dysfunction syndrome,
b) respiratory parameters alone will predict outcome poorly in AHRF.
Method Prospective study of all admissions to our tertiary PICU. Data including the respiratory parameters (oxygenation index [OI], alveolar-arterial oxygen tension gradient [A-aDO2], PaO2/FiO2 ratio) were collected hourly from the bedside charts throughout admission. Patients were included in the study if AHRF was present at admission either alone or in combination with other organ dysfunction. AHRF was defined as the acute (<48hour) onset of respiratory dysfunction with a PaO2/FiO2 ratio.< 200 for six consecutive hours during the first 24 hours of admission (with no evidence of left atrial hypertension). X-ray review defined a sub-group of patients with Acute Respiratory Distress Syndrome (ARDS) by the presence of bilateral interstitial infiltrates.
Results To date 59 children (ages 1-168 months, weight 1.2-70 kg) have been admitted in AHRF. 18 of these also had ARDS. The overall mortality was 23.7% (14/59), and greater in the ARDS group than the non-ARDS group (10/18, 55.5% Vs, 4/41,9.7%, p< 0.01). It was not possible to predict survivors from non-survivors on the basis of the severity of the respiratory failure alone. The A-aDO2 on the day of admission (best in 24 hours) was not significantly different between survivors and non-survivors: (mean, ± sd)(174 mmHg ±108, Vs 304 mmHg ±156). All non-survivors were immunodeficient (n=8), previously extremely premature infants (<28/40),(n=3) or suffering from chronic metabolic or gastrointestinal disease (n=3). No previously normal child died.
Conclusion The severity of respiratory failure does not allow prediction of outcome in our patients. We believe that this reflects that modern PICU is so effective at providing respiratory support that pre-existing pathology alone determines prognosis. This suggests that an abnormally regulated host response or abnormal persistence of a pathogen may be required to induce lung injury of sufficient severity that the resulting respiratory failure cannot be supported in a modern PICU.

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ARDS IN CHILDREN: THE EFFECT OF CHANGING FROM PRONE TO SUPINE

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Introduction: Postural changes (supine to prone) is a therapeutic intervention that could be useful in children with adult respiratory distress syndrome.
Objective: To determine the effects of postural changes in the oxygenation of young children with ARDS.
Methods: A prospective study was performed in eleven subjects aged 6 to 120 months (mean=33) with the diagnosis of ARDS receiving ventilatory support. (mean PEEP and FiO2 of 9 and 0.75 respectively). Postural changes was performed every 8-12 hours, during a period of time ranging from 5 to 16 days. Arterial blood gases were determined before and 30-60 min after the postural change. No modification in the mechanical ventilation other that changes in the FiO2 were performed. The oxygenation was determined by the index PaO2/Fi02 (P/F). To study the differences between the oxygenation mean, before and after the postural changes the Wilcoxon test for paired samples was used.
Results: 184 changes were performed (104 from supine to prone and 80 from prone to supine). A 9% increased P/F ratio was obtained after the change from supine to prone. Although, not all the patients receiving postural changes improved their P/F. Six of them (Group I) showed an improve in the P/F when changed from supine to prone, returning to their base line when positioned from prone to supine. No improvement on the P/F was observed in the remaining 5 subjects (Group II) after postural changes (Table 1). During the maneuver no complications were observed. Two patients had a pneumothorax, not related with the postural change.
Conclusions: Postural changes (supine to prone) is an easy way to improve oxygenation in some children with ARDS.

	Change to prone				Change to supine			
	P/F Supine	P/F Prone	ΔP/F	p	P/F Prone	P/F Supine	ΔP/F	p
All patients	98	107	9%	<0.001	104	100	-4%	ns
6 patients	81	95	18%	<0.001	94	83	-12%	<0.05
5 patients	114	120	6%	ns	116	117	-1%	ns

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SURFACTANT APPLICATION IN CHILDREN WITH ACUTE RESPIRATORY DISTRESS SYNDROME

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Background: Surfactant deficiency or functional defectiv surfactant can often be demonstrated in acute respiratory distress syndome (ARDS). In ARDS of adults the application of exogenous surfactant has been shown to be beneficial in initial studies, but to date, there exists no experience with respect to effect, timing and dosing in children.
Objectives: Retrospective evaluation of children with ARDS treated with exogenous surfactant in the PICU (1992 through 1995) in a single institution with regard to effect of surfactant as well as dosis and timing.
Results: A total of 18 children with ARDS were treated with bovine surfactant (Alveofact®), 17 cases were evaluable in detail. The median age was 2.49 years (range 2 weeks to 11 years). In 9 cases ARDS was associated with pneumonia, in 4 cases with lung hemorrhage; in 4 case isolated ARDS following surgery. The first surfactant application was performed with a median latency of 16 days (range 2.6 to 67.5 days) after first symptoms of ARDS with a median dose of 79 mg/kg (range 18-133 mg/kg). In 17 patients 56 doses of surfactant were applied. During the hour before therapy, the median PaO_2/FiO_2-ratio was 73; the $AaDO_2$ averaged 571. Within 30 min. after application of exogenous surfactant the PaO_2/FiO_2-ratio increased to 113 with a successive decrease over a period of 8 hours; the $AaDO_2$ improved to a median of 483 . Accordingly, an increase in PaO_2 and oxygen saturation and a decrease in ventilation parameters could be observed (decrease of the oxigenation index (OI) from a median of 30.5 before surfactant treatment and 18.2 within 1 hour after therapy).
Six of 17 treated patients survived (7 of the 18, respectively). 13 of the 56 surfactant doses were applied in 2 surviving patients.
Conclusions: The application of exogenous surfactant in children with ARDS caused a significant improvement in oxygenation, which declined over a period of 8-12 hours. The effect could often repeatedly be reproduced, in one case after 11 applications. The increase in oxygenation often allowed the reduction of FiO_2 and/or the inspiratory pressure. No side effects were observed after exogenous surfactant application. In many cases the application of surfactant was too late after first symptoms of disease (median latency 16 days). ARDS mostly due to pneumonia seemed to respond less well to surfactant therapy.

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ARDS and ECMO; preliminary data from a randomized clinical trial. J Fackler, C Steinhart, D Nichols, D Bohn, M Heulitt, T Green, L Martin, K Newth, M Klein, J Ware.

Many suggest ECMO be considered experimental for ARDS and undertaken only with careful data collection and reporting. A multicenter pediatric RCT is in progress to determine whether 1) ECMO and/or 2) permissive hypercapnia, offer significant advantage for the treatment of ARDS.

Methods: All patients aged 2 wk to 18 yr (without congenital heart disease) are eligible for study. Data collection begins when a patient receives at least 50% oxygen and a PEEP of 6 cm H_2O for 12 hours (stage 1). If the predicted mortality reaches 60% within 7 days (stage 2), eligible patients are asked for written consent for randomization. Patients are excluded from randomization with significant chronic lung disease, immune compromise, cardiac disease; or profound *acute* central nervous system damage. The prime outcome variable is survival. At the studies onset, 400 pts were estimated to be required so that 65 pts were randomized per arm.

Results: 131 patients are enrolled from 9 centers. Data are complete on 85. 66 patients never reached Stage 2 (i.e. 60% mortality). 47 patients improved and 19 died. Of the latter, 13 had randomization exclusion criteria even if Stage 2 was reached. 19 patients reached Stage 2. 11 had exclusions from randomization and all died. Eight patients (4 survivors) were eligible for randomization; consent was obtained in no case. Two patients received ECMO. Overall survival is 60% (51/85). In patients without randomization exclusions, survival is 77% (34/44). Morbidity in survivors (discharge - admission POPC or PCPC score $\geq$2) was seen in none of the 4 Stage 2 surviviors and 15% (7/41) of those who reached only Stage 1.

Conclusion: The RCT requires completion.

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THREE-DIMENSIONAL IMAGING FOLLOWING CHEST CT (3D-CT) IN THE DIAGNOSIS AND MANAGEMENT OF PEDIATRIC INTRATHORACIC AIRWAY OBSTRUCTION.

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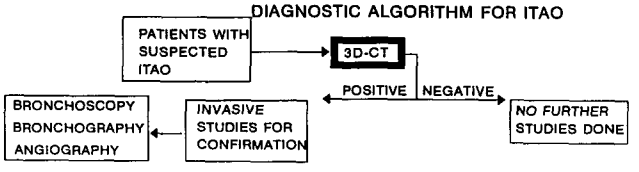
Introduction: The common noninvasive diagnostic efforts to identify possible obstruction of the intrathoracic airway, are of limited value. Invasive procedures such as bronchoscopy and bronchography may also be noncontributory and entail risks. We evaluated the usefulness of 3D-CT in the diagnosis and management of pediatric patients with suspected intrathoracic airway obstruction (ITAO).

Methods: We used a diagnostic algorithm (see diagram) in patients with suspected ITAO resulting in respiratory distress. Three-dimensional imaging of the tracheobronchial tree was reconstructed, following high speed spiral CT scan, by specific computer software (Advantage Window Computer Work Station, General Electric, Milwaukee, Wisconsin). Non-ionic contrast medium was injected, in some patients, to delineate the intrathoracic large vessels.



Results: Eight patients were studied. In 5 patients the 3D-CT revealed intrathoracic airway abnormalities. These patients underwent further invasive studies which confirmed the following diagnoses: 2 patients had bronchomalacia, 1 had bronchial stenosis due to a dilated pulmonary artery and 2 patients had subglottic stenosis extending to the thoracic cavity. Three patients had no significant disruption in the configuration of the tracheobronchial tree and thus did not require invasive diagnostic procedures.

Conclusion: Computer reconstruction of three dimensional images of the tracheobronchial tree is a safe and reliable diagnostic tool for ITAO.