

Preoperative Evaluation and Arrangements for Multiorgan Donation: General Principles and Contraindications

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Key Points of Coordinator Roles

- Promote and facilitate the entire donation process.
- Provide support to families regarding organ and tissue donation respecting individual and cultural differences.
- Be involved in the process of consent for donation.
- Ensure that donation proceeds in line with national legislation, policies, and procedures.
- Obtain all information to allow transplant centers to assess the suitability of potential donors.
- Assist in the optimization of organs for transplant through appropriate donor management.
- Maximize the placement of organs for transplant.
- Train donation services' team members.

- Collect data for organ donation-related audits.
- Facilitate and support the education of healthcare professionals and the general public.

Modified from Akyol M. and Tswen Wen VL. [1]

3.1 Organizational Problems: Donor Coordinators

In Italy, the United States, and the majority of Europe, the management of the patient after brain death, but before organ donation, has traditionally become a task under the responsibility of transplant coordinators.

Donor coordinators often have many years' experience in nursing or other similar health disciplines, but they are usually not physicians. Intensivists in the intensive care unit tend to decrease the time caring for patients after brain-stem death to provide more support to those who are still living [1].

Intensivists use their resuscitative skills to continue to provide care to a patient who they cared for before the declaration of brain death, and each donor can be a potential source of organs for a number of patients on transplant waiting lists. When managing donors, evidence-based care

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should be applied to allow the best care for donor stabilization to optimize organ condition.

The lack of standardization of donor management is one of the reasons for failure to retrieve as many organs as possible [2]. For this reason, protocols for the organization and management of patients after brain death should be developed and implemented by all organ procurement organizations [3].

Donor coordinators have become an important role during the last 15 years, and they have contributed to the successful maximization of the number of potential donors in Spain and worldwide [4].

Coordinators may be affiliated with transplant centers or be part of an independent organization. Transplant coordinators who remain affiliated with transplant units and serve a dual role as donor and recipient coordinators may fulfill each role equally effectively, and this model may have important benefits. However, in terms of one of the most important outcome measures—maximizing the potential from deceased donation—international experience and the balance of evidence suggest that a superior framework involves dedicated donor coordinators based in potential donor hospitals. In some of the countries with the highest deceased donation rates, such as Spain, Portugal, and Italy, there are donor coordinators based in every hospital in the country [5]. They play an important role in increasing and maintaining donation awareness and provide education and support to the staff of potential donor hospitals. Donor coordinators will often help approach the donor family, participate in acquiring consent or authorization for donation, provide help with donor management in the critical care unit, and support the donor family during the process of donation. Donor coordinators will also liaise with legal authorities to facilitate donation and ensure that surmountable legal obstacles do not prevent organ donation. Donor coordinators will then inform organ retrieval teams and coordinate the retrieval process. The responsibility for transporting retrieval teams to donor hospitals and organs to their destinations may rest with the donor coordinator, with the transplant units, or be shared between them. The regionalization of donation services, together with a uniform approach to the

travel arrangements, is probably going to improve the quality and safety of the travel services for the donor team [1].

Donor coordinators also share the responsibility for the appropriate documentation of donor details and the submission of information to the National Transplant Database as well as individual transplant units.

The coordinator should check the blood group and examine all the potential donor parameters—blood pressure, heart rate, temperature, urine output, central venous pressure, wedge pressure if a Swan-Ganz catheter is present, diuresis, and mechanical ventilator parameters—and provide warming to maintain a body temperature above 36.5 °C.

3.2 Exclusion Criteria for Infection Transmission from Organ Donors

Brain death predisposes a patient to infections as a result of severe injury to the cellular immune system [6] and hemodynamic instability with consequent bacterial translocation from the bowel [7]. Nevertheless, there is a strong trend toward expanded donation criteria or, as it is commonly stated, using borderline donors. Therefore, positive cultures or a clinical diagnosis of infection is not currently an absolute contraindication for organ donation.

The transmission of infections from the donor to the recipient constitutes a rare complication of transplantation that is frequently associated with significant morbidity and mortality because immunosuppressant drugs decrease resistance to infection [8, 9].

Most donor infection transmissions are expected, because laboratory screening allows the knowledge of donor infective status before transplantation. Infections, including cytomegalovirus (CMV) and hepatitis B virus (HBV), may occur and are monitored and treated with preemptive therapy and universal prophylaxis [10]. In other cases, the accepting center should match the risk of disease transmission with the risk tolerance and medical status of the recipient.

In addition to laboratory screening, it is mandatory to stratify risk from the donor medical and social history and a careful physical assessment [10]. In the United States, risk stratification considers donors either at increased risk or without identified risk for the transmission of infectious diseases; in Europe, a classification system was initially developed in 2002 by the Italian National Center for Transplantation (CNT) [11] and the CNT/European risk system [12] defined the risk for the transmission of infectious disease. According to this classification, donors are defined as follows:

1. *Unacceptable risk* includes absolute contraindication, with the exception of some life-saving transplantation procedures in the absence of other therapeutic options on a case-by-case basis.
2. *Increased but acceptable risk* includes cases where transmissible organisms or diseases are identified during the evaluation of the donor, but organ utilization is justified by the specific health situation of the recipient or the severity of their clinical condition.
3. *Calculated risk* (criteria referring to protocols for elective transplants) includes all cases where, even in the presence of transmissible diseases, transplantation is allowed for recipients with the same disease or with a protective serological status; this risk also applies to donors with documented bacteremia and/or bacterial meningitis provided that the donor was on targeted antimicrobial treatment for a minimum duration of 24–48 h.
4. *Not assessable risk* includes cases where the evaluation process does not allow an appropriate risk assessment for transmissible diseases.
5. *Standard risk* includes cases where the evaluation process did not identify a transmissible disease.

The following laboratory tests must be performed prior to organ evaluation [13] (Table 3.1):

Positive culture results or a clinical infection diagnosis should not lead to an absolute contraindication of organ donation. Many reports show that even Gram-negative bacteremia donors can

Table 3.1 Obligatory laboratory screening tests for the donors

Test	Interpretation of a positive reaction
HBsAg	Organs are usually not accepted
Anti-Hbc	All organs can be used for recipients who are HBsAg, Anti-Hbc or Anti-Hbs positive Livers can be used for recipients without HBV markers, but lifelong antiviral treatment and surveillance is required Non-liver organs can be used for recipients without HBV markers; a single dose of Hepatitis B Immuno Globuline (HBIG) prior to revascularization should be given, and short-term antiviral treatment should be considered. If the donor is also anti-HBs positive, HBIG is not required
Anti-HBs	In combination with anti-HBc reactivity, see above If anti-HBc test is negative, all organs can be used (no risk, anti-HBs reactivity most likely due to previous immunization of donor)
Anti-HCV	Organs are usually not accepted but may be accepted if donor is HCV-positive
Anti-CMV IgG	Organs are accepted
Anti-HIV	Organs are not accepted

provide favorable outcomes in kidney, liver, and heart transplantations [14, 15]. Decisions regarding organ retrieval from donors with active or suspected infections are affected by the recipient status/urgency and by the availability of other organ donors. The recipient, furthermore, should be adequately informed for consent.

The evaluation of a large series of donors [16, 17] showed the presence of bacteremia in approximately 5 % at the time of organ retrieval, but no case of transmission of the isolated microorganism from donor to recipient was documented; bacteremia in the donor did not worsen the clinical outcome of solid organ transplant recipients. Cerutti et al. studied 610 consecutive liver transplants in a 5-year period at the Liver Transplant Center in Torino (Italy) [18]. In the study, one or more cultures were positive in 293 of 610 donors (48 %). Samples collected before harvesting were positive in 82 of 610 donors (13 %), and samples collected at harvesting and from preservation

fluid were positive in 256 of 610 donors (42 %). Culture-positive donors were significantly older and presented longer lengths of ICU stay than culture-negative donors.

Donors with hepatitis B or C, previously considered as absolute contraindications, can now have their livers harvested and implanted in recipients infected by the same viruses provided only minimal histologic changes (Ishak fibrosis and portal inflammation) are present in the graft [19].

Cytomegalovirus (CMV) carried within organs can determine CMV infection in recipients, especially in those who are CMV negative at the time of transplantation. Routine prophylaxis against CMV in these cases is mandatory and has markedly reduced CMV mortality and morbidity [20].

3.3 Donor Heart Exclusion Criteria

Improvement in the medical and surgical treatment of cardiac diseases has enhanced the longevity of the population and led to a constant increase in heart failure cases; after the clinical introduction of cyclosporine in the early 1980s, heart transplantation has represented the treatment of choice for end-stage heart failure. Through June 30, 2013, 116,104 cardiac transplants have been performed in more than 416 hospitals worldwide [21]. The notable increase of patients listed for heart transplantation has demanded a consequent modification of standard and traditional donor criteria [22] that were introduced in the early years of the cardiac transplant programs. Moreover, the increase in organ demand caused a shortage of available hearts, producing, in turn, the adoption of more severe recipient criteria that limit the number of patients in transplant lists [23, 24]. For this reason, certain donor criteria have been expanded to raise the available donor pool, considering and accepting the so-called marginal donors. In this case, we emphasize that attention should be oriented toward an individual evaluation of the recipient/donor,

recognizing the patient hemodynamic status/urgency and not only the expanded criteria. Each potential recipient should be accurately evaluated, avoiding transplantation in patients with serious generalized disease, e.g., a septic status. Clinical judgment is needed to decide which marginal donor is adequate for our patient transplantation.

When wall motion abnormalities are found at echocardiography and the left ventricular ejection fraction is <0.45 , even though the donor is stable with inotropic support, before the organ is refused, hemodynamic and metabolic management should be performed [25, 26]; stress echocardiography can be helpful in recognizing hearts eligible for donation.

Stress Echocardiography Dipyridamole stress echocardiography, performed in brain-dead potential donors with left ventricular resting global or discrete wall motion abnormalities, identifies hearts with severe morphologic abnormalities that were not considered for donation from eligible donors who showed an improvement in regional wall motion during stress (viability response) and normal function and coronary anatomy following transplantation [27].

Age and Ischemic Time In the early phases of transplant programs, donors older than 40 were excluded from the donor pool. However, donor shortage promoted the acceptance of donors up to 50 or 60 [28–31]. Using hearts from older donors, the outcome depends on other factors, chiefly ischemic time, which, when longer than 3–4 h, is associated with increased early mortality [32–37]. Lamour et al. [38] found that a 40-year-old recipient with congenital heart disease who received a 50-year-old donor heart with 3-h ischemic time had a 15 % probability of death within 1 year, compared with a 40 % probability of death within 1 year if that donor's ischemic time was 5 h. As indicated by the International Society of Heart and Lung Transplantation guidelines for the care of heart transplant recipients [37], donors younger than 45 may be acceptable even with undesirable characteristics such as prolonged ischemic time, recipient comorbidities, and previous recipient operations with hemodynamically

destabilizing bleeding. Hearts from donors between the ages of 45–55 should safely implant when the projected ischemic time is ≤ 4 h and the potential recipient does not have comorbidities or surgical issues; donor hearts >55 years should be accepted carefully and balance the pros and cons for the recipient (Table 3.2).

Advanced age is a risk factor for death from any cause [39] and from early graft failure [40]. It is well known that at the beginning of the heart transplantation program, the donor upper age limit was 35 years, but after almost 50 years, this limit has progressively increased such that 50–55-year-old donors are now routinely considered. Nonetheless, serious well-known concerns about older donors are related to the transmission of coronary artery disease (CAD), hypertensive heart disease, or valvular degeneration from the donor heart. Many single-center analyses report that older donor hearts have not affected posttransplant survival [41–46].

Conversely, large multi-institutional studies [32, 33] and the International Heart and Lung Transplantation Registry [47] reported increased mortality in heart transplant recipients receiving older donor hearts. These differences are probably due to the smaller number of patients and short follow-up time in individual studies. Lietz et al. [48] found a direct correlation between increasing donor age and the risk of transplant-related coronary artery disease. At the first annual

coronarography, they found that when compared with donors younger than 20, the third, fourth, and fifth decades of donor life increase the risk of CAD by 2.2-, 2.4-, and 2.6-fold, respectively.

Furthermore, the International Society for Heart and Lung Transplantation (ISHLT) registry data and other independent investigators [14–16] have suggested that an ischemic time >4 h may increase the risk for death in recipients receiving hearts from donors older than 50 years. Lietz [48] revealed that ischemic time >4 h and donor death resulting from cerebrovascular accident significantly contributed to poor early posttransplant outcomes. At the same time, it is important to consider that end-stage heart failure presents a significant risk of death while awaiting heart transplantation. The UNOS registry data (in the period 1991–1996) reveal that patients with blood group O have a median waiting time of 332 days; the median waiting time for patients >18 years old was 230 days [49]. Bennett et al. [50] outlined that despite the high risk resulting from the heart transplant, there was a clear long-term survival benefit for status I recipients who received older donor hearts. The data described by Lietz [48] are significant: in patients in status 1 (see Table 3.3), 6-month mortality of 70 % was observed when on a waiting list, and the risk of death was 8.5 times higher than that of status 1 patients who received an allograft from donors >40 years old, with a resulting 14 % 6-month mortality; when an older donor heart was implanted, mortality increased 1.6 times but was not statistically significantly different from recipients who received hearts from younger donors.

Table 3.2 Old donor heart criteria and extended criteria to increase donor pool

Donor heart allocation standard vs. extended criteria	
Standard criteria	Extended criteria
Age <55 years	Age >55 up to 70 years
No known cardiac disease. Ischemic time <120 min (Donor in the same center)	Ischemic time > 360 minutes
No high doses inotropes: Dopamine at a dose of 20 $\mu\text{g}/\text{kg}/\text{min}$ or similar doses of other adrenergic agents (norepinephrine $\leq 0.2\mu\text{g}/\text{kg}/\text{min}$) despite aggressive optimization of preload and afterload	High-dose inotropes >0.2 $\mu\text{g}/\text{kg}/\text{min}$ Donor comorbidities

Table 3.3 There are four United Network of Organ Sharing (UNOS) status classifications based on condition

<i>Status 1A or urgent need:</i> requires intensive care hospitalization, life-support measures, certain cardiac supporting intravenous medications with a Swan-Ganz catheter, or mechanical-assist device(s)
<i>Status 1B:</i> dependent on intravenous medications or a mechanical-assist device—in the hospital or at home
<i>Status 2:</i> stable on oral medications and able to wait at home
<i>Status 3 or inactive list:</i> inactive due to a change in condition—patients do not lose time they have already accrued

Heart donors older than 70 should not be accepted; in our experience, two transplants utilizing 70-year-old donors were followed by early graft failure despite a short ischemic time.

In conclusion, if an older donor heart is transplanted, it is mandatory to avoid other known risk factors, e.g., a prolonged ischemic time.

Infections According to the guidelines of the ISHLT, hearts from donors with severe infections can be accepted if (1) the donor infection is community acquired and donor death occurs rapidly (within 96 h); (2) repeat blood cultures before organ procurement are negative; (3) pathogen-specific antimicrobial therapy is administered to the donor; (4) donor myocardial function is normal, and at the surgical inspection, endocarditis is absent [37] (Aug. 4, 2010).

Drug Intoxications Cocaine abuse increases the risk of acute myocardial infarction by increasing blood epinephrine and norepinephrine levels that in turn increase systemic blood pressure, heart rate, and myocardial oxygen demand. In the vessels, these effects create a deficiency of endothelium-derived relaxation factor with increased risk for intravascular thrombosis and decline of cardiac contractility [51, 52]. Direct toxic effects on the myocardium have been described, such as scattered foci of myocyte necrosis, and in some studies, contraction band necrosis, myocarditis, and foci of myocyte fibrosis [53]. These abnormalities may lead to cases of cardiomyopathy. Because intravenous (IV) cocaine is more toxic to the heart compared to non-IV cocaine, ISHLT recommends not accepting hearts from IV cocaine abusers [37, 54]. However, hearts from donors with a history of non-IV cocaine abuse appear to be safe in terms of the early postoperative period [37].

Alcohol Abuse Alcohol alters energy stores in the heart, reducing the effectiveness of calcium uptake by the sarcoplasmic reticulum [55] and reducing sodium-potassium adenosine triphosphatase (ATPase) activity, and it interferes with calcium-troponin binding, thus collectively

reducing myosin-actin interaction. Early survival and graft function are inferior in the recipients of hearts from donors with a history of alcohol abuse [56, 57]. Nevertheless, there are reports where grafts from alcohol abusers did not show a survival disadvantage [58] or even had a protective effect [59]. In our personal experience at Divisione Cardiochirurgia Policlinico San Matteo Pavia, at least two hearts from alcohol abusers had early graft failure.

Carbon Monoxide Poisoning Carbon monoxide competes with oxygen to form carboxyhemoglobin (HbCO) instead of oxyhemoglobin; it has 210 times the affinity of oxygen for hemoglobin. Therefore, in an atmosphere of 21 % oxygen and 0.1 % carbon monoxide, the blood leaving the lungs will be approximately 50 % saturated with oxyhemoglobin and 50 % saturated with carboxyhemoglobin. At the cellular level, there is a leftward shift of the oxyhemoglobin dissociation curve with reduced oxygen delivery to the tissues and an impairment of mitochondrial cellular respiration due to the competition of carbon monoxide with oxygen for cytochrome a3 [60]. Because the myocardium is vulnerable when deprived of its oxygen, the consequent myocardial injury may determine a primary graft failure in the immediate postoperative period.

Reports on the outcomes of hearts from donors with carbon monoxide intoxication have yielded conflicting results [37, 61, 62]. As recommended by ISHLT [37], before accepting a graft from a donor who died from carbon monoxide poisoning, the graft should be carefully evaluated by ECG and echocardiogram with a minimal elevation of cardiac markers and minimal inotropic requirements; furthermore, the ischemic time should be short with a favorable donor to recipient weight ratio and low pulmonary vascular resistance.

Other Poisonings Grafts from donors with other types of poisonings, including cyanide [63–65], methanol, and ecstasy [66], have been transplanted with satisfactory outcome. In these cases also, cardiac clinical tests should be carefully evaluated.

Cardiac factors:

- Intractable ventricular arrhythmias represent a definitive contraindication.
- Valvular heart disease. A bicuspid aortic valve is not contraindicated if the valve function is maintained [37]. A moderate aortic insufficiency, not diagnosed prior to organ retrieval, may cause improper myocardial protection during cardioplegic infusion. Most valvular pathologies in the donor graft are considered a contraindication to heart transplantation; however, there are reports indicating successful bench repair or posttransplant repair/replacement for aortic and mitral valves [67–70].
- Coronary artery disease. Coronary artery disease in the transplanted heart represents a major concern for physicians involved in heart transplant programs. Coronary disease can be unrecognized, due to the lack of coronary angiography in the donor, or known. In both cases, there is a subsequent risk of early graft failure. Considering patients with early graft failure, the prevalence of coronary disease was 22.8 % [71]; moreover, some reports indicate that a transmitted coronary disease may accelerate graft vasculopathy [72, 73]. Grauhan [74] showed that when donor grafts with more than single-vessel disease are used, the risk of early graft failure is elevated; the risk is 6.3 % in donors without coronary disease, 7.5 % in donors with single-vessel disease, and 42.3 % in grafts with double- and triple-vessel disease. In contrast, Marelli et al. [75] reported the transplant of donor grafts with coronary disease in patients who were urgent cases or who would otherwise not have been offered heart transplants due to associated medical risk (alternate recipients, see below); 59 % of the patients received a concomitant coronary bypass procedure. The study reported that in the patients listed in status I, actuarial survival at 2 years was 50 vs. 81.3 % in the “alternate” recipients.
- Donor left ventricular hypertrophy. This is an important risk factor determining early graft failure, particularly when left ventricular donor wall thickness is >14 mm [76].
- Cardiac tumors. At echocardiography, a myxoma can be diagnosed. A right atrium myxoma can be bench removed, and there is only an embolic risk in the pulmonary circulation (lungs should not be evaluated in this case). When a myxoma is situated in the left atrium, there is a high risk of coronary embolism at the moment of cardiac harvesting when the aorta is clamped [77].
- Hemodynamic instability. It is well known that donor hemodynamic instability represents an important contraindication to heart retrieval. Hemodynamic instability appears primarily after the “catecholamine storm” when vasoplegia and hypotension may irreversibly compromise donation. For this reason, there is increasing evidence that the moderation of pathophysiological changes by active management in an intensive care unit can increase available grafts for transplantation, also recruiting donors considered marginal [78–80]. This active management is realized through the following approaches:
 - Swan-Ganz catheter insertion for cardiac index and wedge pressure measurements; central venous pressure alone is not a sufficient diagnostic tool for fluid administration monitoring.
 - If vasopressor drugs are needed, vasopressin at 2.4 units h⁻¹ may reduce catecholamine administration; high doses of norepinephrine, > 0.2 µg/kg/min should be avoided. Canadian guidelines recommend vasopressin as a first-choice drug [81].
 - The management of electrolyte disturbances in the Eurotransplant region from 1997 to 2005 increased recipient mortality when donor sodium concentrations were <130 or >170 mmol/L⁻¹ (BJA).
- Alternate recipient list. An alternate recipient list was proposed by Lacks [82] to transplant heart recipients at high risk and without standard criteria. These patients are coupled to marginal donor organs refused by other centers. The most frequent donor risks for the alternate recipient list were high inotropic doses, left ventricular hypertrophy, and hepatitis C seropositivity. A significant mortality was reported in the alternate recipient list [83–85],

although other reports show a survival similar to patients in the standard list [86].

3.4 Donor Lung Exclusion Criteria

Lung transplantation is hindered by donor shortage: less than 25 % of all brain-dead donors are deemed suitable for lung transplantation. Therefore, a very significant number of donor lungs are never used, despite consent. Aspiration, contusion, and infections are important events that occur as a consequence of brain death. The following two important factors play a key role in irreversibly (permanently) deteriorating lung function.

Hemodynamic Instability The mechanism causing the “catecholamine storm” (described above) is responsible for increased minute ventilation, hypertension, tachycardia, and cardiac arrhythmias. There is a net shift of blood volume from systemic circulation to the low-resistance pulmonary circulation, resulting in increased pulmonary venous pressure, which, in turn, causes transudative pulmonary edema. The acute increase in capillary pressure induces barotrauma capable of damaging the capillary-alveolar membrane. The structural damage to the pulmonary endothelium ultimately leads to vascular leakage and persistent protein-rich pulmonary edema [87, 88]. The end result is a neurogenic pulmonary edema.

Activation of Inflammatory and Immunological Pathways After brain death, there is an increase in inflammatory molecules that may threaten the lung function in the pre-donation period. When lung transplantation has been performed, ischemia can trigger the activation of macrophages, which release proinflammatory cytokines and result in an ischemia-reperfusion injury [89].

According to the ISHLT data, the criteria for the “ideal” donor are shown in Table 3.4 [90, 91]. In older donors, early and late survival was decreased, and if older donor age is matched with graft ischemic times longer than 6 h, this effect was pronounced. Moreover, De Perrot (Toronto Lung Transplant Program) [92] did not find a sig-

Table 3.4 The “ideal” lung donor criteria

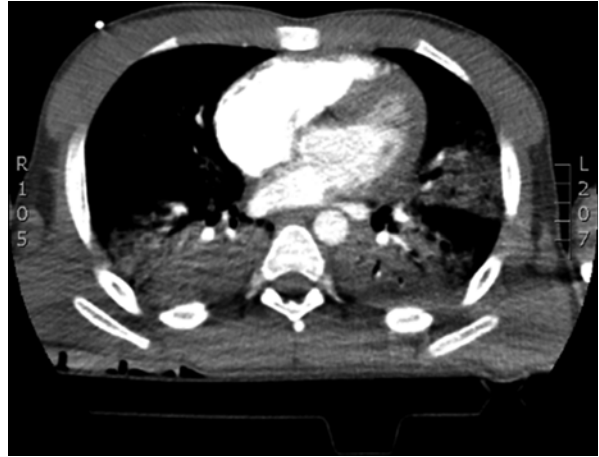
Age <55 years
PaO ₂ >300 mmHg on FIO ₂ 1.0, PEEP 5 cm H ₂ O
Clear chest X-ray
No chest trauma
No evidence of aspiration or sepsis
Tobacco history <20 pack-years
ABO compatibility
Absence of organism on sputum stain
Absence of purulent secretions at bronchoscopy
No prior cardiopulmonary surgery

nificant difference in 30-day mortality related to donor age, although mortality was significantly higher in recipients with pulmonary fibrosis and pulmonary hypertension compared to those with cystic fibrosis or emphysema. In the study, recipients from donors aged 60 or older had decreased 5- and 10-year survival compared with recipients from younger donors; the cause of death was predominantly bronchiolitis obliterans syndrome (BOS) in the older donor group, whereas it was predominantly sepsis in the younger group.

Most transplant centers prefer an ischemic time between 4 and 6 h. Lung preservation with an extracellular solution allows good results with ischemic times greater than 10 h [93, 94].

Gas exchange is considered the most important parameter for assessing lung function. The PaO₂/FIO₂ ratio should be >300 mmHg (obtain PaO₂ value, convert FIO₂ % in decimal value). However, the ratio can be easily modified by secretions, pulmonary edema, atelectasis, and aggressive donor management (recruitment maneuvers, low tidal volume, PEEP of 15 H₂O cm, bronchial aspiration, and bronchoscopy). Direct left and right pulmonary vein blood gas sampling is sometimes very important in reassessing the lungs individually, and partial pulmonary vein oxygen pressure was reported to correlate much more reliably than PaO₂ with the outcome in the recipient. By separate sampling of pulmonary vein PaO₂, it is possible to harvest at least one lung if the PaO₂/FIO₂ ratio is much better than in the sample obtained from the arterial peripheral catheter. Sometimes in young donors gas exchanges may be satisfactory also in case of severe chest trauma, but chest CT can show important massive, bilateral pulmonary

Fig. 3.1 Contrast-enhanced axial computed tomography scan through the thorax of a 19-year-old man after a motor vehicle accident shows massive, bilateral pulmonary contusions and hemothorax. At FIO_2 of 0.40 and 1, the PaO_2 was respectively 131 mmHg and 441 mmHg



contusions, pneumopericardium and hemopneumothorax (Fig. 3.1).

During the harvesting procedure, significant fluid losses are found. Additionally, 8 L of infused fluid are required, and most of this volume is blood, crystalloid, and colloid. If lungs are evaluated for transplantation, it is preferable to administer crystalloid to restrict hypovolemia. It is thought that large amounts of colloid can pass into the extracellular space due to endothelial permeability modification by the inflammatory molecules and can worsen lung function after transplantation by increasing the oncotic pressure. A large quantity of crystalloids may also produce a considerable increase of the central venous pressure and, if prolonged over time, may produce edema of the liver parenchyma and hamper liver graft function after transplantation. Liver edema may also have an adverse effect on bleeding during the splitting procedures of the liver.

At surgery, lungs are directly inspected to check zones of atelectasis, hemorrhagic contusion, edema, nodules that must undergo intraoperative wedge biopsy, and pneumonic infiltration. Then, lung compliance should be evaluated under direct vision by performing the “collapse test”: an endotracheal tube is disconnected from the ventilator, and if the lungs remain inflated or slowly collapse (more than 10 s), this is a sign of interstitial space edema, infection, or emphysema (small airway obstructive disease).

A positive gram stain of tracheal aspirate should not preclude lung donation. The amount

of secretions is much more significantly associated with a negative outcome. The University of Alabama at Birmingham showed that a positive donor gram stain is not necessarily associated with pneumonia development [95].

Alcohol Abuse Donor chronic alcohol abuse has been correlated with an increased risk of primary graft dysfunction. Pelaez et al. showed that donor alcohol abuse may have a great impact on the risk of primary graft dysfunction and that there is a clearly established link between alcohol abuse and ARDS (acute respiratory distress syndrome) [96].

Donor History of Asthma Asthma in the donor has been often considered a contraindication to lung transplantation primarily for the preoperative airway inflammation status that can affect transplantation outcome. Fatal asthma donors predispose the recipient to early and late graft dysfunction, especially refractory acute rejection [97]. However, the use of grafts from carefully selected donors with a history of asthma increases the donor pool and has satisfactory long-term results [97].

Ex Vivo Lung Perfusion Ex vivo lung perfusion (EVLP) was developed in the late 1990s by researchers at Lund University, in Lund, Sweden, who studied non-heart-beating donor lungs with the objective of increasing the number of organs suitable for transplantation [98]. Through experimental studies on pigs, a perfusion solution was developed to prevent edema formation and the

loss of lung function. The solution was designated Steen Solution® (Vitolife; Gothenburg, Sweden). Steen Solution is an extracellular solution for lung preservation composed of electrolytes, dextran, and albumin. A noteworthy feature of the solution is its high oncotic pressure [99]. The first clinical use of EVLP [100] was described in 2001: the donor was a 54-year-old man who had suffered cardiac arrest due to acute myocardial infarction. The transplantation to a recipient patient with pulmonary emphysema was successful. ELVP has been performed by several lung transplant centers worldwide with good results. At the Toronto Lung Transplant Program, from September 2008 to December 2011, 253 lung transplants were performed with conventional preservation lungs. Primary graft dysfunction grade three at 72 h was recorded in 2 % EVLP vs. 8.5 % control ($P=0.14$), and time on mechanical ventilation, extracorporeal life support, ICU stay, hospital stay, and 30-day mortality were not different. Furthermore, similar 1-year survival rates were observed: 87 % for the EVLP group vs. 86 % for the standard group [101].

3.5 Liver Donor Exclusion Criteria

For heart and lung donation, the only absolute exclusion criteria are human immunodeficiency virus infection (HIV), uncontrolled tumor disease, and bacterial or viral infections, as previously discussed. All general clinical conditions, including biochemical, morphological, and functional conditions, must be considered for the donors and their organs to balance the decision regarding whether a liver graft can be used.

The classical clinical and morphological exclusion criteria of the hepatic donor, which years ago would have absolutely contraindicated donation, have now become relative contraindications. These criteria must only be considered if several contraindications occur simultaneously. Based on different studies, the principal liver viability marker is its gross and microscopic inspection. Less than 40 % steatosis evaluated on liver biopsy is fundamental to assure the normal

function of the implanted graft, but in the absence of other contraindications, a steatosis of 50 % can be considered for the transplantation of the whole liver for special recipients at risk of dropout from the waiting list (HCC patients). Split-liver transplantation, a procedure where one donor liver is divided into two hemilivers for two recipients, is an important tactic for overcoming organ shortage. To date, the principal beneficiaries have been adult/pediatric pairs, and excellent outcomes have been described. However, the criteria for the liver-splitting technique require much more restrictive criteria than for conventional whole livers. Donor eligibility criteria for the split-liver procedure were as follows: age 55 or younger, no cardiac arrest episodes, less than 5 days in intensive care, low inotropic support (dopamine ≤ 5 mg/kg/min, dobutamine ≤ 10 mg/kg/min, and no epinephrine or norepinephrine requirement), $\text{Na}^+ \leq 155$ mg/L, liver enzymes no more than double the normal, and no macroscopic evidence of hepatic steatosis, or less than 20 % hepatic steatosis if a biopsy was taken, because liver biopsy was not routinely performed. Liver-splitting techniques for two adults are still experimental surgical procedures, and they have interesting results when these restrictive criteria are employed for donors and for particular pairs of recipients in which one is of small size [102].

Livers from elderly donors undoubtedly represent a diffuse problem: age limit criteria have become more flexible in recent years due to the worldwide decrease of young donors. The transplant teams have perceived that the most effective method to increase the number of donors is to increase their age acceptance; octogenarian donors can be considered, provided liver biopsy results in the absence of fibrotic changes [103]. Livers from positive HCV donors represent a small percentage of other possible sources. Hepatic donors' acceptance criteria that permit the use of HCV-positive donors without liver disease for HCV-positive recipients are increasing. The short-term results of these transplants do not differ from those obtained in HCV-positive recipients from HCV-negative donors. Recent reviews report studies in liver transplants with HCV-positive donor livers in HCV-positive recipients and showed similar graft

survival, patient survival, and hepatitis C recurrence in the recipient and in an HCV-positive hepatic recipient group in whom livers from HCV-negative donors were transplanted [104]. Although there are fewer data than for kidney transplants, somewhat encouraging results are seen with hepatic grafts from non-heart-beating donors; 5-year survival is slightly greater than 50 % [105].

Several additional contraindications pertaining to the living donor are the same as those stated below for living donor liver transplantation (LDLT). In addition to the contraindications previously mentioned, there are some particular absolute contraindications for a living donor. Donors having macrosteatosis (>20 %) on liver biopsy are rejected. Remnant liver volume cannot be less than 25 %. This is an issue especially when the right lobe graft is large. It is never an issue when the left lateral segment is the proposed graft and is rarely an issue if the left lobe graft is taken. The Human Organ Transplantation Act, in some countries, does not allow unrelated donation; this is to prevent donation under any type of coercion and to avoid any organ trade. The living donor should be between 18 and 55 years of age. A body mass index >30 for the donor is generally associated with a consistent degree of macrosteatosis; donors should be encouraged to reduce weight, and a liver biopsy should rule out liver steatosis >20 %. A liver attenuation index <5 on a plain CT scan is suggestive of steatosis. Such donors are either rejected or, in the absence of other donors, need to reduce weight, and a biopsy should be performed to rule out macrosteatosis >20 % [3]. Donors are also rarely rejected for anatomical reasons. Double artery, double portal vein, or multiple hepatic veins such as a V8 or a V6 can be anastomosed using specific surgical techniques, and these presentations should no longer preclude donation. However, multiple anatomical anomalies, e.g., a portal vein trifurcation with a right bile duct draining the segment IV, double right hepatic arteries in the donor, or multiple right-sided segmental portal vein tributaries draining into the left portal vein, are considered contraindications for LDLT. The majority of biliary anatomy in the donor is acceptable [106].

3.6 Kidney Donor Exclusion Criteria

The successful retrieval and transplantation of kidneys, pancreas, and other organs is dependent on the optimal perfusion of the donor and from all management strategies with particular respect of the hemodynamic stability. Allograft renal function after transplantation may be influenced by donor management. Although the use of dopamine as a renal protective agent in the general critical care population is inappropriate, Schnuelle and colleagues demonstrated in a European multicenter trial that donor pretreatment with low-dose dopamine can reduce the need for dialysis after kidney transplantation [107]. Absolute kidney donor exclusion criteria (Table 3.5) shared by the donors of other organs are the same as those for other organs and include HIV infection, malignant neoplasms (including in the central nervous system), sepsis, disseminated infections uncontrolled with antimicrobial

Table 3.5 Kidney and pancreas exclusion criteria

Kidney and pancreas exclusion criteria: absolute contraindications
HIV (or risk group)
Sepsis or uncontrolled disseminated infection (bacteria, viruses, fungi)
Multiorgan failure
Malignant tumor disease with metastasizing capacity
Creutzfeldt-Jakob, Kuru, Gerstmann-Straussler-Scheinker, fatal familial insomnia
Diabetes type I
Chronic pancreatitis
Pancreatic trauma (only for pancreas)
Patients treated with cadaver-derived pituitary hormones
Chronic kidney failure (structural damage)
Age >80 for kidneys and >45 for pancreas
Arterial hypertension
Diabetes type II
Acute renal failure
Chronic alcohol abuse
Prolonged warm ischemia
Glomerulonephritis and other nephropathies in normal renal function phase
Donors with positive serology for hepatitis B and C viruses unless for patients with hepatitis HBV and HCV

therapy (including bacteria, viruses, and fungi), multiorgan failure, and uncommon diseases such as Creutzfeldt-Jakob and those caused by prions such as Kuru. Donors with hepatitis B and C may be accepted for donation to recipients who are carriers of the same viruses. Thus, kidneys from AgHBs carrier donors may be used in AgHBs(+) recipients. Additionally, the use of renal grafts from donors with HCV-positive antibodies in HCV-positive recipients can be considered without apparently increasing major morbidity or mortality. Chronic renal failure is also an absolute renal donor exclusion criterion.

3.7 Pancreas Donor Exclusion Criteria

The pancreas shares the same donor selection criteria with the kidney, with the specific characteristic that pancreatic donors cannot have a personal background of alcoholism, a personal or familiar background of diabetes, significant alterations in the serum amylase values, or an age greater than 45–50 (Table 3.5). The best indication of the suitability of a pancreas allograft for transplantation is the appearance of the organ at the time of procurement. After completing the surgical maneuvers, the pancreatic parenchyma should be carefully evaluated for its procurement in terms of fat content, edema, or fibrosis and for quality of the vasculature. All aspects of the pancreas should be inspected for injury to the pancreatic parenchyma and for the presence of hematomas, masses, or nodular areas. Most centers avoid transplanting organs with calcifications, extensive fibrosis, fatty infiltration, severe edema, or significant visceral atherosclerosis. Depending from different center policies, pancreas procurement may be cancelled for technical reasons such as abnormal arterial vascularization between the liver and the pancreas, which may occur with a right replacing hepatic artery originating from the superior mesenteric artery and would render a successful and correct split and the transplantation of both organs difficult. Surgical injuries that occur during pancreas procurement may lead to complications after transplantation, impaired function of the allograft, graft loss, or even death of the patient. These injuries may be so dangerous that

the pancreas harvesting must be considered an absolute contraindication. In such cases, pancreatic islet transplantation can be considered. Proper procurement and the constant training of surgeons for pancreatic procurement are therefore very important to maintain high-quality pancreas procurement. Some recent reports show that vascular lesions are observed in 16.7 % of pancreatic grafts and suggest that surgical procedures of pancreas procurement may be improved by better surgical training and the standardization of the surgical technique. Some studies have shown that pancreatic allografts have been frequently refused during back-table inspection, partly because of multiple surgical injuries to the artery, veins, and duodenum [108]. Donor age and procurement by centers not performing pancreas transplantations were both found to significantly increase the probability of pancreas refusal. The quality of pancreas procurement may thus be improved by the specific training of surgeons who specifically perform pancreas transplantations.

3.8 Intestinal and Multiorgan Exclusion Criteria

There are very few absolute contraindications to intestinal donation, and they can be grouped into four broad categories: (1) severe intestinal trauma, (2) malignancy outside of the central nervous system (CNS), (3) active infections, and (4) inflammatory bowel disease (IBD) or the same contraindications for liver procurement in the case of combined liver and intestinal transplantation. Ideal donors are preferably younger (<45 years) and with little or no use of vasoactive drugs.

Patients with short bowel syndrome present with the abdominal cavity retracted, thus requiring smaller donors (30–40 % less of the calculated body surface area). Preference is given to ABO identity. With the development of effective drugs for prophylaxis and the treatment of cytomegalovirus, seropositive donors are accepted and are avoided only for recipients with negative serology. The decontamination of the gastrointestinal tract and the use of antibodies in donor lymphocytes showed no benefits related to infection, rejection episodes, or incidences of graft versus host disease. Typically, in these donors

Table 3.6 Intestinal and multiorgan exclusion criteria

Donor criteria	Exclusion criteria
All donors evaluable at a standard risk	Abdominal trauma especially when operative procedures have been performed
Age <45 years	Asphyxia or CO intoxication
Intensive care <5 days	Resuscitation after long period of hypotension
Enteral nutrition during stay in ICU	Prolonged shock
BMI <25	Blood losses with large RBC transfusion
Size matching with recipient	Alcoholism or drug abuse
Cold ischemia <6 h	Arteriosclerosis
Crossmatch negative	Malignancy outside of the central nervous system (CNS), active infections, or IBD

also liver and pancreas are retrieved. Due to the shared bloodstream, the simultaneous harvesting of these grafts can be a challenge but is possible to perform the procedure without compromising other grafts [109] (Table 3.6).

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