61 Anesthesia for Organ Procurement

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KEY POINTS

- The shortage of organs available for transplantation is a worldwide problem.
- The discrepancy between the number of patients waiting for organ transplantation and the available organs remains significant, but has narrowed since 2013.
- Most organs in the United States are donated after neurologic death, with a small portion donated after circulatory death and from living organ donors.
- Neurologic-death donors have physiologic alterations that must be actively managed to ensure that the organs are suitable for transplantation.
- Determining neurologic death and circulatory death should follow national guidelines and local institutional protocols.
- The anesthesiologist must have an awareness of the ethical and legal issues related to the declaration of death that precedes organ donation.
- Expansion of the donor pool through the inclusion of extended criteria, such as high-risk donors, addresses the organ shortage and decreases waiting-list mortality.
- The use of extended criteria high-risk organs significantly impacts recipient outcomes and presents challenges to perioperative management.
- Ischemia-reperfusion injury in organ transplantation is unavoidable; however, management strategies can lessen the likelihood of postoperative graft failure.
- Goal-directed donor management can improve the number of organs transplanted per donor.
- Living organ donor kidney transplantation remains an important donor source in the United States, whereas the use of living donors for liver transplantation varies by country.
- New technologies, including machine perfusion after procurement, are promising as a means to mitigate the effects of prolonged preservation time, to increase the donor pool, and to improve transplant recipient outcomes.

Introduction

Organ transplantation requires the donation and successful procurement of a human organ. The success of organ transplantation relies on a functioning donor graft. The majority of organs used for transplantation in the United States are from donors after the declaration of neurologic death (donation after neurologic death, DND). Organs from donation after circulatory (cardiac) death (DCD) and living organ donation are in the minority, however, they remain an important source of donors.[1] Organs procured from these sources have different characteristics and present varying challenges in management. For instance, DND donors often have significant physiologic alterations and hemodynamic instability that is associated with neurologic death. These alterations and instability, if not treated, will lead to organ deterioration and may prevent the organ from being suitable for transplantation. In contrast, DCD donors have an obligatory period of hypotension of varying duration before cardiac arrest. The resulting compromise in perfusion can exacerbate reperfusion injury and lead to an increased incidence of posttransplant biliary dysfunction.

The shortage of organs is a worldwide problem and is the most important obstacle in organ transplantation. The gap between the number of patients waiting for transplant and the available organs has widened (Fig. 61.1). In 2015, more than 119,000 transplant candidates were wait-listed in the United States through the United Network for Organ Sharing. Of these, 33,000 candidates underwent transplant surgery.[2] The majority of candidates were awaiting kidney grafts, with a smaller number awaiting liver, heart, and lung grafts. Many strategies were implemented to decrease the gap between the demand and supply, including public awareness campaigns and updates to the organ allocation system. Organ donation rates and the number of organs transplanted per donor vary substantially across geographic regions. Per 100 eligible deaths in the United States in 2016, the organ donation rate was 72.3, ranging from 52.9 to a high of 93.3 (Israni OPTN 2016 Annual Data Report).[3] To increase the number of organs for transplant, many programs have expanded the donor pool by using extended criteria donors (ECDs). Not surprisingly, the number of organs transplanted per donor varies according to donor category: ECD, DCD, or standard criteria donor (SCD). The number of organs transplanted from DCD donors is similar to ECDs, primarily attributable to the ability of the kidney to tolerate the longer periods of ischemia associated with organ procurement after DCD. The use of

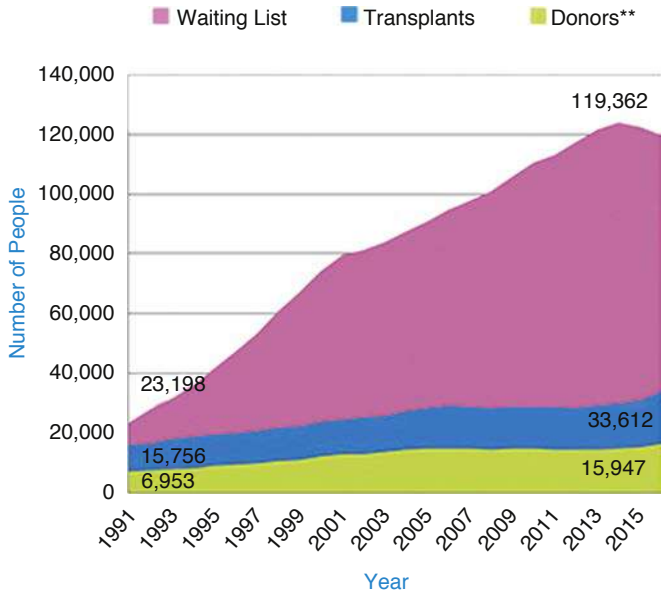

Fig. 61.1 The gap in the United States between the number of donors, patients transplanted, and patients on the waitlist by year, 1991 to 2015. The gap has declined since 2013. **Donors can be deceased and living. http://www.organdonor.gov/statistics-stories/statistics.html.

TABLE 61.1 Pathophysiologic Changes Associated With Neurologic Death

Signs and Symptoms	Pathophysiologic Changes	Incidence (%)
Hypertension	Catecholamine storm	80-90
Hypotension	Vasoplegia, hypovolemia, reduced coronary blood flow, myocardial dysfunction	80-90
Bradycardia and other arrhythmias	Catecholamine storm, myocardial damage, reduced coronary blood flow	25-30
Pulmonary edema	Acute blood volume diversion, capillary damage	10-20
Diabetes insipidus	Posterior pituitary damage	45-80
Disseminated intravascular coagulation	Tissue factor release, coagulopathy	30-55
Hypothermia	Hypothalamic damage, reduced metabolic rate, vasodilation, and heat loss	Varied
Hyperglycemia	Decreased insulin concentration, increased insulin resistance	Common

living-related and living-unrelated donors is widespread in countries with moral or legal objections to neurologic death and is an important worldwide donor source. Many policies have been proposed to promote the best practices in organ donation.[3,4] There are several areas that have the potential to expand the donor pool, which include deaths that are not referred to the organ sharing agencies and organs that have been procured, but unused for transplant.

Organ transplantation is a complex process that requires close coordination among many specialized teams. Procurement organizations, transplant coordinators, social workers, nurses, surgeons, internists, intensivists, and anesthesiologists are involved in the process. To maximize the number of organs transplanted and to preserve the best possible function of donated organs, anesthesiologists need to understand the pathophysiologic derangements associated with donation and ischemia-reperfusion injury. In addition, anesthesiologists must be aware of the ethical and legal issues related to the declaration of death and organ donation.

Management of Organ Donors After Declaration of Neurologic Death

DND (also called after declaration of brain death) provides the majority of donated organs in the United States.[3] Organ procurement from DND donors can only occur after the declaration of death. The concept of neurologic death emerged in the 1950s. In 1968, a Harvard Ad Hoc Committee on Irreversible Coma established a set of criteria that has been widely used for the determination of neurologic death.[5] In the United States, the Uniform Determination of Death Act was approved in 1981 by the National Conference of Commissioners on Uniform State Laws, in cooperation with the American Medical Association, the American Bar Association, and the President's Commission for the Study of Ethical Problems in Medicine and Biomedical and Behavioral Research. Although the criteria for the declaration of neurologic death were based on ethical principles established several decades ago, the criteria remain valid today.[6]

Although the concept of neurologic death has been widely accepted in Western cultures, minor variations in definition and implementation exist in different countries. Despite these differences, the clinical criteria are similar.[7] A larger difference exists among different cultures in accepting and implementing the neurologic death criteria. In fact, neurologic death has not reached a legal status in some countries, such as China.

PATHOPHYSIOLOGIC CHANGES WITH NEUROLOGIC DEATH

A variety of pathophysiologic changes are associated with neurologic death. The pathophysiologic mechanisms of neurologic death have profound effects at the molecular, cellular, and tissue levels. The clinical presentations associated with neurologic death may be complex and vary from patient to patient. They can be further complicated by prior pathologic abnormalities, disease, and therapy. The typical pathophysiologic changes associated with neurologic death are further described in Table 61.1.

CARDIOVASCULAR RESPONSES TO NEUROLOGIC DEATH

The cardiovascular system is closely regulated by the central neural system. Cardiovascular responses to neurologic death usually consist of two phases. The first phase is characterized by sympathetic discharge (catecholamine

storm), which causes intense vasoconstriction or elevated systemic vascular resistance (hypertensive crisis), tachycardia, and a redistribution of blood volume with visceral ischemia. Acute myocardial injury can occur in neurologic-dead donors without a history of coronary artery disease.[8] Echocardiographic evidence of myocardial dysfunction is observed in 40% of neurologic-dead donors under consideration for heart donation.[9] At times, parasympathetic activation can result in bradycardia. After the sympathetic discharge of the first phase, the loss of sympathetic tone, decreased cardiac output, blunted hemostatic responses, and severe peripheral vasodilatation (vasoplegia) characterize the second phase. In addition to neurohormonal disturbances, other contributing factors include blood loss, intravascular depletion attributable to capillary leakage, osmotic therapy for rising intracranial pressure (ICP), and diabetes insipidus.

The first phase is correlated with ischemia in various parts of the brain and is attributable to an increase of ICP, and the second phase is caused by cerebral herniation and spinal cord ischemia. Although the first hypertensive phase generally represents a transient period in the progression to neurologic death, the second hypotensive phase is profound and sustained. Failure to correct these cardiovascular derangements results in poor organ perfusion and inadequate tissue oxygenation, which will threaten the viability of the donated organs.

RESPIRATORY RESPONSES TO NEUROLOGIC DEATH

An increase in systemic vascular resistance after neurologic death results in blood shifting from the systemic circulation to the more compliant pulmonary circulation. The resulting increase in hydrostatic pressure in the pulmonary circulation causes pulmonary capillary leakage and pulmonary edema. Sympathetic activity triggers a sterile systemic inflammatory response, initiating infiltration of neutrophils and increasing pulmonary endothelial permeability, which further contributes to lung injury. Proinflammatory cytokines are released at the alveoli and are associated with early graft failure and mortality after lung transplantation. The inflammatory response in neurologic-dead donors is associated with the deterioration in cardiac function and a shift to anaerobic metabolism. Hormonal instability can reduce alveolar fluid clearance, resulting in significant accumulation of extravascular lung water. If ventilation is not supported, then respiratory arrhythmia progresses to apnea and cardiac arrest.[10,11]

ENDOCRINE, METABOLIC, AND STRESS RESPONSES TO NEUROLOGIC DEATH

Neurologic death is frequently associated with pituitary failure and disturbances of cortisol, thyroid hormones, antidiuretic hormone, and insulin. Posterior pituitary function in neurologic-dead donors is frequently lost. The development of central diabetes insipidus results in severe fluid and electrolyte derangements and can be observed in up to 90% of neurologic-dead donors.[10] Anterior pituitary function in neurologic death can also be affected, resulting in a deficiency in triiodothyronine (T_3) and thyroxine (T_4), adrenocorticotropic hormone, thyroid-stimulating hormone, and human growth hormone. Thyroid hormonal deficiency may be similar to the euthyroid sick syndrome commonly observed in the non-neurologic injured patient with multisystem organ failure. Hyperglycemia is commonly encountered in neurologic-dead donors because of decreased insulin concentrations and increased insulin resistance. Hypothalamic function and control of body temperature are lost. Although hyperpyrexia may initially occur, hypothermia follows, which is caused by a reduction in metabolic rate and muscle activity, in combination with peripheral vasodilation. Disseminated intravascular coagulation is present in up to one-third of isolated patients with head injuries and is believed to be caused by the release of tissue thromboplastin from brain tissue.[11]

Donation After Circulatory (Cardiac) Death

Before the acceptance of neurologic death, all organs procured were from donors who suffered a cardiac demise (DCD, previously known as donation from a non–heart-beating donor). After the establishment of the Harvard criteria for neurologic death, DND quickly became the principal source of organ donation. However, an interest in the use of DCD organs has been renewed in recent years, driven by the persistent shortage of DND donors and the lack of acceptance of neurologic death in some countries. Policies and protocols developed by healthcare organizations now encourage DCD organs, and their use is increasing in the United States and other countries. In the United States, the number of DCD donors continues to increase, and accounted for over 17% of donors in 2016 (Fig. 61.2).[3] During the same period, the number of living donors dropped slightly from 7000 to 6600. Kidney grafts accounted for over 95% of the organs transplanted from living donors during this period. The American Society of Anesthesiologists established a Sample Policy for Organ Donation after Circulatory Death, with the recommendation that its members actively participate in the development of institutional DCD protocols.

DCD donors are divided into five categories: I, patients who are dead on arrival at the hospital; II, unsuccessfully resuscitated patients; III, patients in whom cardiac arrest is imminent; IV, cardiac arrest in neurologic-dead donors; V, unexpected arrest in the intensive care unit (ICU). Categories III and IV are considered as controlled DCDs, whereas the remaining categories are considered uncontrolled DCDs. Controlled DCD implies that life-support withdrawal can be planned and the transplant team is awaiting the cardiac arrest and is ready for rapid organ recovery. In contrast, uncontrolled DCD implies the patient has experienced an unanticipated cardiac arrest, and organ donation is considered only after an unsuccessful resuscitation. Warm ischemia time is significantly longer in uncontrolled DCDs. Currently, most DCD donors for organ transplantation are controlled DCD donors. Successful use of the uncontrolled DCD grafts has been reported in several studies.[12]

DCD donors usually suffer from irreversible brain or spinal injury but do not meet the neurologic death criteria. The prognosis for a meaningful quality of life is poor. Withdrawal of therapy must be based on a clinical decision of

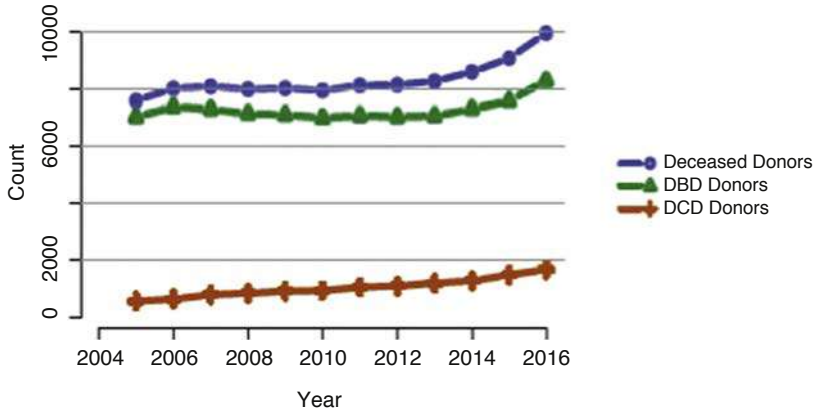

Fig. 61.2 Total number of organ donors in the United States by year, 2005 to 2016. *DBD*, Donation after brain death; *DCD*, donation after cardiac death. (Redrawn from Israni AK, Zaun D, Rosendale JD, et al. OPTN / SRTR 2016 Annual Data Report: Deceased organ donation. *Am J Transplant.* 2018;18:434–463.)

futility and conform to the wishes of the patient and family. The consideration of the withdrawal of life-sustaining therapies must be independent from any discussion related to transplantation. The transplantation team cannot be involved in this decision. Drugs can be used to relieve pain and anxiety and to provide comfort for the patient during withdrawal. Therapies designed to improve graft quality, but without benefit to the patient, are controversial; however, therapies with minimal impact on the patient that improve organ survival are allowed in some protocols.

Declaration of circulatory death should follow procedures proposed by national organizations and policies adopted by the local institution.[13,14] After a decision has been made to withdraw support, the trachea is extubated and life support is stopped. A physician who is not involved with organ transplantation declares cessation of cardiac function. Declaration of circulatory death is not different from clinical practice, which requires a clinical examination to confirm pulselessness or the absence of an arterial waveform. The duration between cessation of cardiovascular activities and the declaration of circulatory death is usually 2 to 5 minutes to ensure irreversibility. Organ procurement starts after death is declared.

Although organs procured from DCD donors are not exposed to the physiologic derangements of neurologic death, they are at greater risk for ischemia-reperfusion injury than organs from DND donors. This results from hypoxemia and ischemia in a warm environment, which is unique during DCD procurement. The time elapsed from extubation to circulatory death is an important factor for determining the suitability of organ donation. If spontaneous breathing and/or heart function continues for a prolonged period after life support withdrawal, then the organs may not be suitable for transplantation, particularly in donors with comorbidities. To assist physicians in predicting how long a patient will sustain life after the withdrawal of life support, a 6-variable score was developed by the University of Wisconsin (UW) (Table 61.2). A low score (8-12) means that breathing and/or cardiac function will continue for some time. A high score (19-24) means that apnea and cardiac arrest are imminent.[15]

The two separate definitions and procedures used for DND and DCD have led to a new debate about the definition and determination of death. A uniform concept of death, which combines all previous criteria for death, is emerging.

TABLE 61.2 University of Wisconsin Criteria for Donation After Circulatory Death: An Evaluation Tool

Variables	Points
SPONTANEOUS RESPIRATION AFTER 10 MIN	
Respiratory rate > 12 breaths/min	1
Respiratory rate < 12 breaths/min	3
Tidal volume > 200 mL	1
Tidal volume < 200 mL	3
Negative inspiratory force > 20 cm H_2O	1
Negative inspiratory force < 20 cm H_2O	3
No spontaneous respiration	9
BODY MASS INDEX (KG/M^2)	
<25	1
25-29	2
≥30	3
VASOPRESSORS	
None	1
1 pressor	2
≥2 pressors	3
PATIENT AGE (YEARS)	
0-30	1
31-50	2
>50	3
INTUBATION	
Endotracheal tube	3
Tracheostomy	1
OXYGENATION AFTER 10 MIN	
O_2 saturation > 90%	1
O_2 saturation 80%-90%	2
O_2 saturation < 80%	3

University of Wisconsin score: 8-12, high probability; 13-18, moderate probability; and 19-24, low probability for continuing to breathe after extubation. (From Lewis J, Peltier J, Nelson H, et al. Development of the University of Wisconsin Donation After Circulatory Death Evaluation Tool. *Prog Transplant.* 2003;13:265–273.)

A growing consensus is that all criteria used to diagnose human death rely on the demonstration of the irreversible loss of the capacity to breath, combined with the irreversible loss of the capacity for consciousness. The irreversible loss of these two functions equates to human death.[16]

Category III (impending cardiac arrest) DCD is the ideal source for organ transplant. Kidneys from DCD donors are frequently used. Several studies have shown that, despite a

higher incidence of delayed graft function (DGF), kidneys from DCD donors have comparable short- and long-term graft survival.[12] Livers from DCD donors have a higher likelihood of postoperative biliary complications such as diffuse ischemic cholangiopathy with intrahepatic biliary stricture and may also have a higher incidence of primary graft nonfunction and DGF compared to grafts from DND donors.[17] Ischemic cholangiopathy occurs more frequently if the donor is older, is overweight, and has a prolonged ischemic period. Heart and lungs are susceptible to ischemia and only a few cases of the successful use of such grafts from DCD donors have been reported.[15]

Extended Criteria Donor

Traditionally, DND organ donors are young and otherwise healthy until stricken by an isolated cerebral event or head injury (SCDs). As the numbers of patients waiting for transplant increase, many centers have extended donor criteria to minimize waiting-list mortality. Many terms, including suboptimal donor, marginal donor, inferior donor, nonstandard donor, and high-risk donor, have been used.[18] The criteria that make up the ECD group are more elusive and evolving. Donor characteristics of ECDs vary from organ to organ but generally include advanced age, prolonged cold ischemia time, inferior organ function, and other comorbidities.[18,19] However, donor risk is a relative term and should be described as a continuum, not a dichotomy of SCD and ECD. Therefore, donor risk index (DRI) has been developed for donors.

The kidney DRI has been developed using 10 donor characteristics (Box 61.1).[20] The kidney DRI can be converted into the kidney donor profile index (scale 1%-100%). A higher kidney donor profile index indicates a higher graft failure rate. The DRI has been defined for liver grafts. DRI is a quantitative assessment of the risk of graft failure associated with the donor. Liver DRI is calculated from eight donor characteristics (Box 61.2).[21] Despite an increased risk of graft failure, moderate-to-high acuity transplant candidates who receive a high DRI graft have a survival benefit compared with those remaining on the wait list.[22] Calculation of the DRI can help physicians make a decision to accept or reject a donor offer; however, the calculation requires a projected cold ischemia time.

The use of ECD or high-risk DRI grafts has implications on intraoperative management. In a study of liver transplantation, several donor characteristics are associated with a high incidence of intraoperative hyperkalemia in adults: DCD grafts, prolonged ischemia time, and prolonged donor hospital stay before procurements.[23] ECD liver grafts are also associated with postreperfusion syndrome, intraoperative bleeding, and postoperative reoperation.[24]

Management of Organ Donors Before Procurement

As previously discussed, various physiologic derangements are common in DND donors. If not treated, these derangements can lead to graft deterioration, resulting in organs unsuitable for transplantation. A discussion of treatment strategies follows.

BOX 61.1 Kidney Donor Profile Index

The following donor characteristics are used to calculate the kidney donor profile index
Age
Height
Weight
Ethnicity
History of hypertension
History of diabetes
Cause of death
Serum creatinine
Hepatitis C Virus status
Donation after circulatory death status

From https://optn.transplant.hrsa.gov/resources/allocation-calculators/kdpi-calculator.

BOX 61.2 Liver Donor Risk Index

Age (four categories): >40, >50, >60, >70 years
Cause of death (two categories): cerebrovascular accident (lower risk) versus other
Race: African American (higher risk) versus other
Donation after circulatory death: yes or no
Partial or split graft: yes or no
Height: increasing risk as height decreases below 170 cm
Regional or national share: yes or no
Cold ischemia time

CARDIOVASCULAR MANAGEMENT

Although both hypertension and hypotension are associated with neurologic death and can result in poor perfusion to the organs, hypotension is more profound and difficult to treat. Maintaining adequate intravascular volume is probably the most effective therapy for vasoplegia. No evidence demonstrates that a specific crystalloid solution is superior to another. Adequate resuscitation, as evidenced by a mean arterial pressure of 60 to 100 mm Hg, may decrease cytokine levels and increase the number of organs available for transplantation.[25] Large doses of starch-based colloids should be avoided because they may be associated with DGF.[26]

When hemodynamic stabilization is not achieved with fluid resuscitation, vasoactive drugs should be considered. Dopamine is most commonly used in this setting. If a large dose of dopamine is required, then a second vasoactive agent can be added. Dopamine and other catecholamines have beneficial antiinflammatory and immunomodulatory effects. Vasopressin is recommended as the initial therapy of choice for potential heart donors by the American College of Cardiology.[27] Vasopressin reduces catecholamine requirements and is an effective treatment for diabetes insipidus.

For a potential heart donor, cardiac function should be assessed, with early interventions to improve the donor procurement rate. Echocardiography is useful since it can identify both functional and structural abnormalities. Functional abnormalities identified in the early stage can be managed before heart transplantation, whereas structural abnormalities may preclude transplantation. Coronary angiography is useful in older donors with suspected or

known coronary artery disease. Myocardial damage caused by catecholamine storm may be prevented or attenuated by controlling cardiovascular responses, which may increase the number of heart transplants.[11] However, large doses of norepinephrine are associated with increased cardiac graft dysfunction and increased recipient mortality.[28]

Excessive intravascular fluid therapy may have detrimental effects and should be avoided in lung donors. Fluid restriction increases the number of lung grafts available for transplantation.[10] Because this practice creates a conflict of interest on the basis of which organs will be procured, particularly between the lungs and kidneys, fluid management should be balanced to optimize overall donation potential.[10] The goal is to maintain a euvolemic state and to maintain arterial blood pressure and cardiac output with the least amount of vasoactive support possible. Invasive hemodynamic monitoring may be used to guide intravascular fluid therapy.

PULMONARY MANAGEMENT

The lungs are vulnerable to injury and, consequently, are one of the most difficult organs to preserve. Only 15% to 25% of donated lungs are used in transplantation. Current pulmonary management for potential lung donors favors small tidal volume ventilation. The focus of pulmonary management is to recruit and retain lung units while limiting tidal volume and inspiratory pressure. This strategy is extrapolated from studies in acute respiratory distress syndrome. Specific approaches to ventilator management for the donor are variable, but a common approach is a low tidal volume (6-8 mL/kg), low fraction of inspired oxygen concentration (FiO_2), and relatively high positive end-expiratory pressure (PEEP).[29] Pulmonary recruitment maneuvers, using pressure-controlled ventilation and high PEEP (15 cm water), followed by a return to conventional volume-controlled ventilation with a lower PEEP, are recommended by others. The administration of aerosolized terbutaline increases alveolar fluid clearance via β-adrenergic stimulation.[30] As previously discussed, a large amount of intravascular fluid and/or large-dose vasopressors are associated with impaired graft function in potential lung donors.[10]

Adequate gas exchange and good oxygenation are the most important indicators of the functional quality of the lung. However, an initial PaO_2/FiO_2 ratio less than 300 mm Hg should not be used as grounds for exclusion. Reversible processes such as secretions, pulmonary edema, and atelectasis can affect the PaO_2/FiO_2 ratio. Bronchoscopy is generally performed to remove mucous plugs that are present.

TEMPERATURE

Since hypothalamic function and regulation of body temperature are lost, DND donors usually have initial hyperpyrexia followed by hypothermia. Donor hypothermia is also contributed by reduced metabolic rate and peripheral vasodilatation. Normothermia has been traditionally recommended before and during procurement by using active warming devices. A recent report from a prospective trial challenges this traditional temperature management before procurement. In this trial, organ donors were randomized into two targeted temperature groups: mild hypothermia (34°C-35°C) or normothermia (36.5°C-37.5°C). The hypothermia group is associated with a significantly lower rate of DGF after kidney transplantation.[31] In a retrospective study, mild hypothermia is confirmed to reduce DGF, but not graft survival in kidney transplantation.[32]

HORMONES, STEROIDS, ELECTROLYTES, AND GLYCEMIC CONTROL

Hormonal deficiency is common in neurologic-dead donors and hormonal replacement is beneficial.[8,10] Exogenous replacement of antidiuretic hormone in neurologic-dead donors improves graft function in kidney, liver, and cardiac recipients.[10] Thyroid hormone replacement improves the number of organs transplanted per donor and cardiac recipient survival.[25,33] However, most studies showing advantages to hormone supplement are retrospective; adequately powered randomized trials are lacking.

The systemic inflammatory response associated with neurologic death leads to pulmonary infiltration of neutrophils and the elevation of interleukins. The systemic inflammatory response of the donor is associated with graft failure and recipient mortality. Methylprednisolone administration can moderate the inflammatory response and may improve oxygenation, reduce lung water, and increase lung yield. Methylprednisolone administration can also decrease inflammation in the liver, heart, and kidney.

Intravascular volume replacement is essential in the donor management. An isotonic crystalloid (lactated Ringer solution or 0.9% saline) is the preferred choice. However, 0.9% saline may not be the best choice due to the development of hyperchloremic metabolic acidosis. Colloid solutions are appropriate for rapid intravascular volume expansion. Routine use of hydroxyethyl starch is not recommended since it is associated with potential acute kidney injury, and coagulopathy. After administering initial fluid to correct hypovolemia, hypernatremia should be treated by giving a hypotonic solution.[10] Studies have demonstrated that donor hypernatremia (>155 mmol/L) is associated with poor post–liver transplant outcomes.[34] Analysis of heart donors in Europe showed increased recipient mortality when donor sodium was less than 130 or greater than 170 mmol/L.[35] Correction of severe hypernatremia before organ procurement appears to attenuate post–transplant liver dysfunction.[10] Hyperglycemia in the donor is common and exacerbated by steroid therapy. Poor glucose control adversely affects donor renal function.[36] Insulin management should target a glucose level between 120 and 180 mg/dL. Routine use of IV fluid containing dextrose is not recommended.[33]

DONOR MANAGEMENT GOALS

Current recommendations stress the use of standardized donor management with specific preprocurement goals. The objective of donor management goals (DMGs) is to maintain cardiovascular, pulmonary, renal, and endocrine homeostasis. The primary hemodynamic goal is to maximize perfusion for organ preservation by ensuring adequate intravascular volume and cardiac output.[33] Table 61.3 summarizes common goals reported by various

TABLE 61.3 Donor Management Goals, as Reported by Various Authors

Preset Clinical End Points	Six DMGs*	Eight DMGs†	Ten DMGs‡
Mean arterial pressure (mm Hg)	≥60	60–120	60–100
Central venous pressure (mm Hg)	≤10 (or serum osmolality 285-295 mmol/L)	4–12	4–10
Final sodium (mmol/L)	≤155	≤155	135–160
Pressors	≤1 (1 plus vasopressin to treat DI is acceptable)	≤1 or low dose	≤1 and low dose
PaO_2 (mm Hg) or PaO_2/FiO_2 ratio	$PaO_2 \geq 300$ while on 100% oxygen (or $PaCO_2/FiO_2$ ratio > 3)	Final $PaO_2 > 100$	PaO_2/FiO_2 ratio: >300 on PEEP = 5 cm H_2O
Arterial blood gas: pH	7.25–7.50	7.30–7.50	7.30–7.45
Glucose (mg/dL)		≤150	<150
Urine output (mL/kg/h) in 4 h before procurement		0.5–3.0	1–3
Ejection fraction of left ventricle			>50%
Hemoglobin (mg/dL)			>10

DI, Diabetes insipidus; *FiO_2,* fraction of inspired oxygen concentration; *$PaCO_2$,* partial arterial pressure of carbon dioxide; *PaO_2,* partial arterial pressure of oxygen; *PEEP,* positive end-expiratory pressure.

*Hagan ME, McClean D, Falcone CA, et al. Attaining specific donor management goals increases number of organs transplanted per donor: a quality improvement project. *Prog Transplant*. 2009;19(3):227–231.

†Franklin GA, Santos AP, Smith JW, et al. Optimization of donor management goals yields increased organ use. *Am Surg*. 2010;76(6):587–594.

‡Malinoski DJ, Daly MC, Patel MS, et al. Achieving donor management goals before deceased donor procurement is associated with more organs transplanted per donor. *J Trauma*. 2011;71(4):990–995, discussion: 996.

studies and recommended by some committees. Studies have shown that compliance with predetermined goals significantly improves the number of organs procured and transplanted.[25,37] Early achievement of DMGs is important. Donors with four or more organs transplanted per donor have significantly more individual DMGs met at the time of consent. Efforts should focus on early management in patients with catastrophic neurologic injury until the intent to donate is known.[38] One study showed that only 15% of donors met DMGs at the time of consent, although the rate was higher immediately before organ procurement.

Management of Donors After Circulatory Death

The majority of DCD donors are patients awaiting cardiac arrest in the ICU (category III). To minimize warm ischemia time, life support is usually withdrawn in the surgical unit. However, the family's desire to be present has led some institutions to withdraw life support in other nearby locations. The procurement team should not take part in patient management before a determination of irreversible death, which includes the period during which withdrawal of support and declaration of death occur. The administration of pharmacologic drugs for the purpose of maximizing donation potential, particularly therapies capable of hastening death, is controversial. However, narcotics and benzodiazepines are commonly continued and can be titrated to blunt sympathetic responses. Premortem administration of heparin can facilitate organ procurement but, because of the bleeding risk, is omitted in some institutional policies. Most protocols require specific consent for premortem donor therapy.

Invasive premortem techniques for reducing warm ischemia time have been described. These include cannulation of the femoral artery and vein before the withdrawal of life support, which allows rapid infusion of cold preservation solution after the declaration of death. These cannulas can also be used for extracorporeal membrane oxygenation (ECMO) after death. However, the postmortem use of ECMO to restore the blood flow to vital organs generates vigorous debate, which highlights the ongoing ethical questions in donor management—the need to protect the best interest of the dying patient, while facilitating his or her wish to donate.[39]

Management of Organ Donor During Procurement Surgery

Anesthesia care for organ procurement is required only in the case of neurologic-dead donors. The majority of organ procurement occurs at community hospitals, not tertiary medical centers. As a result, the logistics of organ procurement, the social circumstances, and the unusual sequence of intraoperative events may seem intimidating to the anesthesiologist.

Surgical techniques may vary, depending on whether single or multiple organs are procured. Generally, wide exposure of the surgical field is established via a midline laparotomy extended by sternotomy. A cannula is placed in the aorta to flush the organs with the cold preservation solution. Ice is applied to the surgical field to further protect the organs. The organs are removed with their vascular structures after isolation in an order according to their susceptibility to ischemia, with the heart first and the kidney last.

Most donors arrive in the surgical unit with an endotracheal tube in place, and supported by the intravenous administration of vasoactive drugs. During procurement surgery, patients can have movements resulting from spinal reflexes; therefore, neuromuscular blockers are desirable. Spontaneous spinal reflex or surgical stimulation can cause catecholamine release and hypertension. Hypertension can be managed by a number of drugs including vasodilators, opioids, and anesthetics; however, volatile anesthetics are commonly preferred. As previously mentioned, volatile anesthetics may provide additional benefits that include ischemic preconditioning and the reduction of ischemia-reperfusion injury.[40]

The intravascular administration of fluids and vasoactive drugs can treat blood loss and cardiovascular instability caused by surgical manipulation. Maintaining hemodynamic stability allows surgeons to procure the organs without further damage to the organs. Vasodilators such as phentolamine or alprostadil (for lung recovery) may be administered during cross-clamping with the goal of decreasing systemic vascular resistance and allowing an even distribution of the preservation solution. Clinically significant bradycardia in neurologic-dead donors does not respond to atropine; therefore, a direct-acting chronotrope such as isoproterenol should be readily available. Heparin is usually administered before cross-clamping the aorta. If recovery of the heart or lung is anticipated, then pulmonary artery catheters and/or CVP catheters need to be withdrawn before cross-clamping. If lung recovery is anticipated, then the lungs are ventilated well beyond cross-clamping. Communication between the surgical team and the anesthesiologist is crucial to ensure optimal organ quality. As soon as the organs are perfused with the cold solution, mechanical ventilation and anesthesia care can be stopped.

Management of Living Organ Donors

Living donor organ transplantation has been successfully used as an alternative to deceased donor transplantation. In the United States the number of living donor organ transplants has remained flat since 2011.[3] In some Asian countries such as Japan and Korea, living donor transplantation is a standard procedure since DND is unusual because of cultural beliefs in these countries. Living donor organ transplantation has some advantages. The procedure can be scheduled as elective surgery at the same facility, which allows donor and recipient surgeries to be coordinated and the cold ischemia time to be minimized. Additionally, the graft is not exposed to the physiologic alterations associated with DND or DCD donors. Living donors direct their donation to a specific recipient; therefore, the timing of the transplant can be optimized for the recipient, and prolonged waiting times associated with deceased donor transplantation are typically avoided. As a result, the recipient is generally in better overall condition. Although living organ transplantation has its advantages, it exposes healthy donors to medical risks. Additional concerns are potential decreased quality of life and an adverse financial impact after donation. The ethical aspect of living organ donation, particularly liver donation, continues to be vigorously scrutinized.[41,42]

Living donation should be preceded by a thorough medical, psychologic, and social evaluation that confirms the absence of contraindications and the lack of coercion. The informed consent includes full disclosure of possible complications and is facilitated by a patient advocate in many institutions with no relationship to the recipient. In the past, donors were typically related to the prospective recipient. Now, living unrelated donors make up a greater proportion of living kidney transplant in the United States.[1] Paired or chain donation allows two or more recipients with incompatible living donors to exchange donors, improving the graft match for both recipients. Similar to the expansion of deceased donor criteria, living donor criteria have been extended to include donors of advanced age and those with obesity.[43] Living multi-organ donation from a single donor, either simultaneously or sequentially, although rare, has been reported. Careful selection of such donors, disclosure of risks, and close follow-up are needed.[44]

LIVING KIDNEY DONOR

Because the kidney is a paired organ, it is a natural choice for living donation. The first successful kidney transplant was a living organ transplant performed between identical twins in 1954. Now, living donors account for approximately 29% of kidney transplants in the United States.[1,45] Living donor kidney transplantation provides the optimized timing for transplant and can avoid pretransplant dialysis, which is associated with improved survival.[46] In addition, living donor grafts provide better function and last longer than grafts from deceased donors.[47] A wide range of medical and nonmedical factors need to be considered to ensure donor safety. To ensure a sufficient reserve after donation, many transplant centers use a glomerular filtration rate (GFR) greater than 80 mL/min/1.73 m^2 as a cutoff for donation. GFR is typically estimated by the measurement of urine creatinine clearance. If the estimated GFR is marginal, then radioactive and nonradioactive tracers can provide additional information.[48] Some centers allow a lower GFR.[49]

Traditionally, living kidney donor surgery was performed via open nephrectomy via a subcostal lateral incision. Now, it is commonly performed via laparoscopy. With this approach, donors experience less postoperative pain, a faster recovery, and a shorter hospital stay.[49] Either the left or the right kidney can be used for transplant; however, the left kidney is usually preferred because of the easier surgical exposure and longer vascular supply. The right kidney has a short vein, and its artery courses posterior to the inferior vena cava.

The patient is placed in a lateral position with the table flexed and the kidney rest elevated. The surgical procedure begins with mobilization of the kidney with subsequent identification and dissection of the ureter, renal vein, and artery, and separation of the adrenal vein. When the right donor nephrectomy is performed, additional steps include duodenal mobilization and separation of the kidney from the liver. After mobilization of the kidney and clamping of the vascular structures, the kidney is retrieved through a small incision by either a hand-assisted or non–hand-assisted technique. Donor nephrectomy can be performed via a transabdominal route but is increasingly accomplished via

a retroperitoneal approach using minimally invasive techniques. The advantage of a retroperitoneal approach is less manipulation of intraabdominal viscera. Single-incision donor nephrectomy has been described using uniquely designed devices. Recently, robotic-assisted laparoscopic living donor nephrectomy has been reported.[49,50] This technique may further decrease the trauma and discomfort to the donor.

Anesthetic management of elective laparoscopic donor surgery on a healthy patient is similar to that used for elective laparoscopic nephrectomy. Standard noninvasive monitors are usually sufficient. One or two large-bore peripheral intravenous lines are usually placed. Transfusion of red blood cells is rare; however, type and screen, or type and cross for 1 to 2 units of blood, is routine practice in some centers in case of injury to major vessels. General anesthesia is required for laparoscopic nephrectomy and general anesthesia combined with epidural anesthesia is often used if open nephrectomy is planned.

Although laparoscopic nephrectomy on a healthy patient may be routine, some concerns in addition to potential blood loss exist. High intraabdominal pressure reduces venous return and has been associated with postoperative renal dysfunction. Lower insufflation pressure may prevent compression of the renal veins and parenchyma.[51] Adequate intravascular fluid administration appears to be the best strategy to preserve kidney function. Some advocate liberal fluid administration (10-20 mL/kg/h), although laparoscopic nephrectomy is typically associated with minimal blood loss. Others use urinary output as an indicator for fluid management. To ensure that the urinary output is greater than 2 mL/kg/h, fluid is usually given in excess of the physiologic need throughout the procedure. The surgeon may request the administration of furosemide and/or mannitol during the surgery for the purpose of increasing urine output. The preferred type of fluid for intravascular volume expansion during donor nephrectomy is not known. In the absence of evidence, most centers use an isotonic crystalloid solution. Nitrous oxide is best avoided because of a concern over bowel distention and poor surgical exposure. Intravenous heparin (3000-5000 international units [IU]) is often administered immediately before the renal vessels are clamped. Protocols may vary among institutions, and close communication with the transplant surgeon is essential. If hypotension occurs after adequate fluid replacement, then dopamine and ephedrine are preferable to direct-acting vasopressors to minimize vasoconstriction in the graft. After the kidney is retrieved, anesthesiologists should be prepared for a quick closure and ensure that neuromuscular blockade is reversed.

Mild or moderate pain after laparoscopic nephrectomy originates from the port insertion, the abdominal incision, pelvic organ manipulation, diaphragmatic irritation, and/or ureteral colic. Postoperative pain can be easily managed in most patients with supplemental intravenous opioids in the early postoperative period and later with oral opioids and acetaminophen. Nonsteroidal antiinflammatory drugs should be used with caution because of their potential prostaglandin-mediated adverse renal effects. Pain after open nephrectomy with subcostal lateral incision is severe and can last several days, which can limit the patient's efforts to breathe, cough, and move, leading to atelectasis and postoperative infection. Postoperative epidural analgesia should be considered for pain relief in these patients.

Post-donation complications reported to the Organ Procurement and Transplantation Network within 6 weeks of surgery include the need for blood transfusion (0.4%), readmission (2.1%), interventional procedures (0.9%), and reoperation (0.5%).[45] A study of more than 80,000 living kidney donors showed a 90-day mortality of 3.1 per 10,000 donors (0.03%) and remains unchanged in the last 15 years.[52] Pulmonary embolism occurred in 0.1% of donors and is the main cause of mortality.[45] Kidney donors are at moderate risk for developing venous thromboembolism; therefore, intermittent pneumatic compression devices and prophylactic heparinization are recommended until ambulation. A decrease of approximately 30% in GFR can be expected after donation, and most donors will maintain a GFR greater than 60 mL/minute at 3 months.[49] Donor nephrectomy does not appear to increase long-term mortality or end-stage renal disease. Within the donor population, the likelihood of postdonation chronic kidney disease, hypertension, and diabetes is relatively higher among certain subgroups, such as African-American and obese donors, but the impact of unilateral nephrectomy on the lifetime risks of adverse events in these subgroups is unknown because the risks without nephrectomy have not been defined.[45] It should be noted that all studies on postdonation complications are retrospective without long-term follow-ups and matched controls.

LIVING LIVER DONOR

Living donor liver transplantation (LDLT) was first introduced in 1988 for pediatric recipients[53] and later expanded to adult recipients. Although LDLT is commonly performed in some Asian countries, it only consists of a small portion (<5%) of overall liver transplants performed in the United States.[3] The primary concern, that of harm to a healthy, altruistic donor, is greater in LDLT, compared with kidney donation.

The liver's remarkable reserve, coupled with its unique capacity to regenerate, forms the basis for LDLT. After resection of as much as two-thirds of the liver, the donor's liver regains its original size in 2 to 3 weeks.[54] A portion of the adult liver (typically the left lobe or left lateral segment) transplanted to a pediatric recipient will grow with the recipient. Most LDLTs are electively performed in patients with chronic liver disease. Emergent LDLT is uncommon but is occasionally performed for acute liver failure. LDLT performed in patients with very advanced disease generates considerable debate.

The determination of donor liver volume and anticipated graft size is unique to LDLT. Formulas using demographics, including body weight, height, age, and sex, have been developed. Methods using radiologic or ultrasonic measurements also have been proposed.[55] Accurate estimation of donor liver volume and intended liver graft volume is critical to avoid small-for-size syndrome in the recipient and to preserve adequate remnant liver volume in the donor.[56] For pediatric LDLTs, the left lateral segment (segments II and III) or a total left hepatic lobectomy (segments II, III, and IV) is generally enough to provide sufficient liver mass (Fig. 61.3). From a surgical point of view,

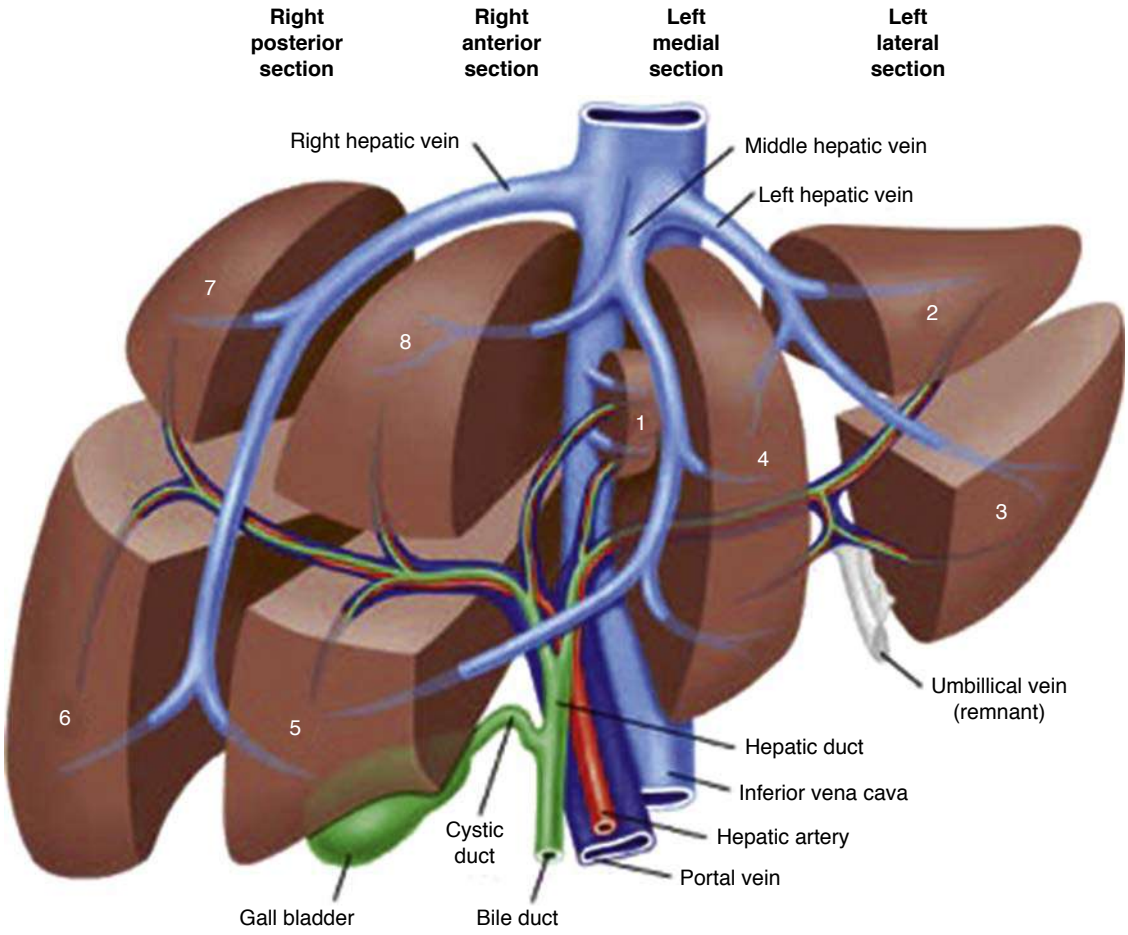

Fig. 61.3 Segmental liver anatomy illustrates the segments resected during various partial hepatectomies. (Redrawn from Steadman RH, Braunfeld M, Park H. Liver and gastrointestinal physiology. In: Hemmings HC, Egan T, eds. *Pharmacology and Physiology in Anesthesia: Foundations and Clinical Applications*. Philadelphia: Saunders; 2013:475–486.)

a left hepatectomy is less complex, and the duration of surgery is shorter. Since the first report in 2002, more living donor left lobectomies are performed using laparoscopy.[57] For adult-to-adult LDLT, right hepatic lobectomy is usually required. The surgical technique for right hepatectomy involves separation of the right hepatic lobes (segments V, VI, VII, and VIII) from the left. Compared with left hepatectomy, right hepatectomy is technically more challenging and associated with more perioperative risk. Right hepatectomy results in a graft weighing 500 to 1000 g, which leaves the donor with approximately one-third of the original liver mass. If one donor cannot provide sufficient liver mass, then a technique using two donors to one recipient has been reported.[58] For a small recipient, the left lobe of a large donor organ may suffice.

Anesthetic management starts with a preoperative discussion with the donor patient and family that addresses the risks and concerns associated with the procedure. Most transplant programs provide extensive educational materials, discussion, and support, beginning well before the day of surgery. General anesthesia with neuromuscular blockade is required for living liver donation surgery. The patient is placed in a supine position and intraoperatively uses the reverse Trendelenburg position to facilitate the exposure of the liver. Two large-bore intravenous catheters are placed. Standard noninvasive monitors and arterial blood pressure monitoring are typically used. A nasogastric tube is placed for decompression of the stomach and surgical exposure.

An L-shaped or standard bilateral subcostal incision with a midline extension is frequently used in living donor surgery. During mobilization of the liver and its vasculature, manipulation of the liver occasionally results in decreased venous return to the heart with episodes of hypotension. The return of the liver to its orthotopic position will relieve the venous obstruction; alternatively, administering short-acting vasoactive agents and/or a fluid bolus will generally treat the problem. Most blood loss occurs during transection of the liver parenchyma. With surgical devices specifically designed for hepatectomy, blood loss during living donor hepatectomy is significantly reduced. After the vasculature of the donor lobe is clamped and divided, the graft is removed, and the vasculature and bile duct are oversewn. The abdomen is closed after hemostasis is achieved.

Blood loss during hepatectomy is a major concern and is associated with adverse outcomes. Placement of the CVP catheter and the use of low CVP (<5 cm H_2O) technique are advocated in some centers to reduce blood loss and transfusion requirements.[59] Low CVP reduces blood loss by increasing venous drainage from the hepatic sinusoids and decreasing blood backflow.[59] In addition, low CVP may reduce graft edema and improve postoperative graft function.[51] Low CVP is most often achieved by intravascular

fluid restriction and sometimes by drugs, including diuretics and vasodilators.[59] Others consider the placement of a CVP catheter and low CVP technique unnecessary during hepatic resection surgery because of the inability to demonstrate a relationship between CVP and blood loss.[60] Other factors, including steatosis, body weight, and sex, may be more important than CVP in influencing blood loss during living donor hepatectomy.[61] Potential drawbacks of the low CVP technique are the risk of CVP catheter placement and difficulty reversing hemodynamic disturbances in the event of massive bleeding. Others point out that the use of low CVP originates from early experience with hepatectomy several decades ago, when blood loss was significant. With improved surgical techniques and equipment, blood loss during hepatectomy has been dramatically reduced, making CVP placement and monitoring unnecessary.[60,61] At the authors' institution, CVP placement is rarely used. Peripheral venous pressure measurements in the arm may be measured as an alternative to conventional CVP measurements.[62]

Several other blood-saving strategies have been used in living donor hepatectomy. These include cell salvage techniques and preoperative donation of 1 to 2 units of autologous blood, which reduces the chance of allogeneic blood transfusion. Intraoperative isovolemic hemodilution with retrieval of 1 to 2 units of blood in the surgical unit can minimize the likelihood of blood transfusion.[63] The application of one or more of the blood-saving strategies previously listed is usually sufficient in the vast majority of patients.[60] After the graft is removed, excessive intravascular volume should be avoided because it may impede venous return and result in congestion of the remnant liver.[51]

Most living liver donors can be extubated at the end of the procedure in the surgical unit and transferred to the postoperative care unit. Discontinuation of mechanical ventilation reduces intrathoracic pressure, which reduces congestion in the remnant liver. Admission to the ICU is generally unnecessary but preferred in some institutions. Caution is required with the use of intravenous analgesics and opioids in the immediate postoperative period. The remnant liver is assumed to have some degree of insufficiency, although this assumption has not been thoroughly investigated.[51] Optimal perfusion of the remnant liver is achieved by the maintenance of adequate cardiac output and an avoidance of hypovolemia, anemia, and hypothermia-induced coagulopathy.[51]

The use of epidural anesthesia for postoperative pain control in living donor surgery remains controversial. Similar to other upper abdominal surgery, postoperative epidural analgesia provides excellent pain control with less sedation, compared with intravenous patient-controlled analgesia.[64] By facilitating pulmonary toilet, epidural analgesia reduces the risk of respiratory infections. Despite these advantages, preoperative placement of a thoracic epidural catheter is routinely performed in some transplant centers and is entirely avoided in others. The difference of practice originates from the development of postoperative coagulopathy in patients after donor hepatectomy. Postoperatively, thrombocytopenia occurs while the prothrombin and activated partial thrombin times are prolonged. These changes peak on postoperative day 2 to 3, followed by a steady trend toward normalization in the following days.[65] Thus, concern over the potential development of an epidural hematoma is the basis for avoiding epidural catheter placement. Several studies examining the use of the epidural catheter in this population report no adverse effects. In a study of 755 donors who received an epidural catheter for postoperative pain management, no complications associated with the epidural catheter were reported.[66] Another study including 242 living liver donors also showed that epidural analgesia seems to be a safe option when carefully used.[65] Another piece of evidence supporting epidural placement is that hypercoagulability, not hypocoagulability measured by thromboelastography, can develop in the majority of patients after hepatectomy.[67,68] Despite the low overall incidence of epidural hematoma, these studies are criticized for a lack of power to assess the risk of this rare event. If the epidural catheter is placed, then the catheter should not be removed until satisfactory coagulation parameters have been retained, which usually takes 3 to 5 days.[51] If the epidural catheter is not placed, then patient-controlled analgesia is used. The choice of pain-control strategy is influenced by the patient's expectations, surgical preferences, institutional consensus, postoperative monitoring capabilities, and nursing staff familiarity with the various techniques.

Worldwide, a number of LDLT-related donor complications, including mortality, have been reported.[69,70] A multicenter observational study of 760 adult-to-adult LDLTs with up to 12 years of follow-up revealed that 40% of donors had complications (Table 61.4).[69] A total of 19% of donors had more than one complication. Although most of the complications were not associated with residual disability, some were severe. Infection is the most common complication and biliary complications such as bile leaks or stricture can be difficult to treat and can lead to prolonged hospital stays with the possibility of further surgery. Higher preoperative creatinine levels, intraoperative hypotension, and intraoperative transfusion are associated with donor complications. Increased institutional experience is not associated with decreased complications.[69] Another recent study involving 5202 living donor hepatectomies found that 12% of donors developed at least one complication, of which 3.8% were major events, which doubled after right hepatectomy.[71]

LIVING LUNG DONOR

Living lung transplantation is an alternative to deceased lung transplantation. Typically, two donors are used for one recipient in living lung transplantation, although the use of a single living donor has been reported.[72] If two donors are involved, then careful coordination and timing of the anesthetic induction of the two donors and recipient are required. The right lower lobe of one donor and the left lower lobe of the second donor are implanted in the recipient in place of the whole right and left lungs. Donor lobectomy requires sufficient bronchial, arterial, and vein cuffs to permit successful anastomoses. A bronchial air leak can result in a prolonged need for chest tube drainage, which lengthens hospital stay.

After the induction of general anesthesia, a single-lumen endotracheal tube is usually placed initially to facilitate fiberoptic bronchoscopic examination before incision. Once

TABLE 61.4 Type and Frequency of Complications of Living Liver Donors of 760 Donor Procedures, ~40% (296 Donors) Suffered 557 Complications; 20 Procedures Were Aborted)

Complications	Frequency (% of 760 procedures)
Infections	13.2
Pleural effusion	11.0
Bile leak or biloma	8.1
Incisional hernia	6.6
Psychologic difficulty	5.6
Neuropraxia	3.4
Ascites	2.8
Unplanned reexploration	2.7
Pulmonary edema	2.1
Bowel obstruction	1.6
Intraabdominal abscesses	1.2
Pulmonary embolism	1.0
Pneumothorax	0.8
Deep vein thrombosis	0.8
Biliary stricture	0.7
Portal vein thrombosis	0.5
Inferior vena cava thrombosis	0.4

Modified from Abecassis MM, Fisher RA, Olthoff KM, et al. Complications of living donor hepatic lobectomy—a comprehensive report. *Am J Transplant*. 2012;12:1208–1217.

a decision is made to proceed, a left-sided double-lumen endotracheal tube later replaces the single-lumen endotracheal tube. Standard noninvasive monitors, intraarterial blood pressure monitoring, and capnography may be sufficient. After placing the donor in the lateral decubitus position and rechecking the double-lumen tube position by fiberoptic bronchoscope, a thoracotomy is performed. Intraoperative cardiorespiratory and metabolic homeostasis minimizes the risk of postoperative complications. Prostaglandin E_1 is usually intravenously administered to dilate the pulmonary vessels with titration according to systemic blood pressure (hypotension needs to be avoided). After mobilization is complete, the lung is reinflated for 5 to 10 minutes, followed by the administration of heparin and a steroid. Transection of the lung is performed after the lung is recollapsed.

Thoracic epidural analgesia is a useful adjunct for perioperative care. The epidural catheter may be placed hours before surgery.[51] Although this approach may be questionable in patients undergoing heparinization, the superiority of postoperative analgesia and the avoidance of atelectasis and infection appear to justify the risk of donor epidural catheterization.[73]

ISCHEMIA-REPERFUSION INJURY

Ischemia-reperfusion injury of transplanted grafts is unavoidable if blood supply is interrupted. An interruption of the blood supply during the ischemic period results in metabolic and pathophysiologic changes. Restoration of blood flow and reoxygenation can also cause tissue injury, as well as profound immune and inflammatory responses.[74]

Ischemia-reperfusion injury results from a wide range of pathologic processes. During ischemia, a lack of oxygen supply leads to a depletion of adenosine triphosphate (ATP) and glycogen. Without ATP, sodium-potassium (Na-K) pumps cannot maintain ion gradients across the cellular membrane. As a result, extracellular sodium ions move into cells, causing swelling. Vascular permeability is increased since intracellular cyclic adenosine monophosphate levels and adenylate cyclase activity is decreased.[74,75] The restoration of the blood supply causes a series of pathophysiologic changes that lead to tissue injury. Reperfusion-related injuries include necrosis, apoptosis (programmed death), and autophagy-associated cell death. Reperfusion also activates autoimmune responses including natural antibody recognition of neoantigens, activation of the complement system, activation of innate and adaptive immune responses, and cell migration to the affected area.

Organ Preservation and Management After Procurement

After procurement, preservation of organs in a cold (4°C) solution until reperfusion remains a mainstream management after procurement. Although static cold preservation slows the metabolic rate, energy consumption is not completely stopped. Accumulation of metabolites and intracellular calcium limit the maximum time for static cold storage.[76] Various cold-storage solutions are used worldwide with the UW solution one of the most widely used. The UW solution contains high potassium and adenosine to supply ATP during cold storage. Histidine-tryptophan-ketoglutarate (HTK) solution, originally developed for cardioplegia and subsequently applied to organ preservation in Europe, has gained popularity.[77] The potential for hyperkalemia during organ reperfusion (particularly with the liver) increases when the UW solution is used, compared with the HTK solution. However, the graft is typically flushed with colloid before reperfusion, regardless of the solution used, which decreases the likelihood of severe hyperkalemia. Recent data suggest that the HTK solution may be associated with poor graft function in abdominal organ transplantation.[78,79] Organ-specific solutions, such as Perfadex solution (manufactured by Vitrolife in Göteborg, Sweden) for the lung and Celsior solution (manufactured by Genzyme in Cambridge, MA) for the heart, are available. Although ischemia time should be kept minimal, a longer storage time allows transportation of the graft to the highest acuity patient for a long distance. Generally accepted cold ischemia times during static cold preservation are 24 hours for the kidney, 12 hours for the liver, 6 hours for the heart, and 4 hours for the lung.

In addition to static cold preservation, machine perfusion can be used to preserve procured organs. The driving force for recent renewed interest in machine perfusion is to expand the donor pool.[79] The potential advantage for machine perfusion techniques include a longer storage time, ability to assess the viability of organ, and potential therapeutic interventions during preservation. Temperature during

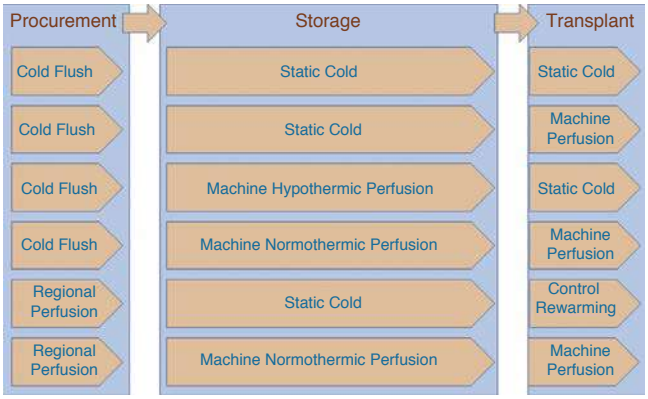

Fig. 61.4 Various techniques and combination of techniques can be used to improve donor function and recipient outcome during procurement, preservation, and transplant.

machine perfusion can be hypothermic (4°C-10°C), subnormothermic (12°C-30°C), and normothermic (35°C-37°C). Different temperatures have different advantages and disadvantages.[76] When normothermia is used, oxygen needs to be added. Combination of different techniques and temperatures may be used in different situations (Fig. 61.4).[79] Clinical trials and metaanalysis suggest machine perfusion improves short-term outcomes including a reduction in DGF and primary nonfunction. These effects are more obvious in high-risk donors.[76,80-82] Changes of biomarkers in perfusate reflect damage of preserved organs and may be used to predict posttransplant outcome. Tests using metabolomics, proteomics, and genomics approaches may provide useful information in the future.[83] Several pharmacologic and biologic agents have been tested in animal models and preclinical trials; some, including recombinant agents that block leukocyte adhesion, have shown promise.[84,85] Preconditioning with volatile anesthetics has been shown to protect tissue from ischemia-reperfusion injury in animal models.[86] In human trials, volatile anesthetics have some beneficial effects in the setting of myocardial infarction, minimizing ischemia-reperfusion injury, although the data remain inconclusive.[87]

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