CHAPTER 132

Renal Protection in the Organ Donor

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OBJECTIVES

This chapter will:

1. Provide an overview of deceased kidney donation and discuss donor medical suitability.
2. Describe the physiologic sequelae of brain death, the effect on organ function, and protective strategies that may prevent damage to transplantable organs.
3. Provide an overview of the clinical management of the brain-dead potential organ donor that will facilitate successful organ procurement, minimize organ damage, and optimize outcome for the kidney transplant recipient.
4. Discuss donation after circulatory death.

Kidney transplantation for the treatment of chronic renal failure results in improved health and longevity.[1] Rates of living and deceased (cadaveric) donation vary considerably internationally.[2] In the United States,[3] Europe,[4] the United Kingdom,[5] and Australia[6] the majority of transplanted kidneys are from deceased donors.

Deceased donation is of two types: (1) donation from persons declared deceased using neurologic criteria—that is, donation after brain death (DBD); and (2) donation after irreversible cessation of the circulation, otherwise known as donation after circulatory death (DCD) or "non–heart-beating organ donation." Because of the universal shortage of organs for transplantation, there has been renewed interest in DCD, with increasing numbers of kidney donations through this pathway in the last decade, notably in the United Kingdom,[7] Netherlands,[8] and Australia.[6] Despite a higher incidence of delayed graft function (usually defined as a need for dialysis in the first week posttransplantation) in kidneys from DCD donors, recipients who receive kidneys from DCD and DBD donors have similar outcome in terms of long-term allograft and patient survival.[9–11]

MEDICAL SUITABILITY

Because of the shortage of donated organs and advances in transplantation medicine, the criteria for donor suitability are constantly broadening. As with other therapies, a decision about whether to accept an organ for transplantation must be individualized based on risk and benefit analysis in the particular recipient.

Absolute contraindications to kidney donation are few but include metastatic or incurable malignant disease (or a history of malignancy that poses a high risk for subsequent transmission) and transmissible spongiform encephalopathy such as Creutzfeldt-Jacob disease (CJD). Although HIV generally is considered an absolute contraindication, there has been some recent experience with kidney donation from HIV-infected deceased donors to HIV-infected recipients with favorable outcomes.[12] Patients with a history of malignancy and a long cancer-free interval represent a small risk of transmission and should be considered as potential donors.[13,14] Treated bacterial infection, including bacterial meningitis,[15] also should not be considered a contraindication. Organs from potential donors infected with (or with evidence of past infection with) hepatitis B virus (HBV) may be transplanted into recipients infected with the same virus, or indeed HBV-immune recipients with careful consideration of posttransplantation passive immunoprophylaxis and antiviral therapy.[16] Although hepatitis C–infected donors have been considered for donation only generally to hepatitis C–infected kidney recipients, the recent availability of direct-acting antivirals may alter this.[17] Patients with negative testing for HIV and hepatitis C but with a history of intravenous drug use or other risk factors for contracting these blood-borne viruses should be referred to the donor agency for careful exploration of the risk to potential recipients.

Medical comorbidities in the donor that potentially affect recipient graft function, including hypertension, acute kidney injury, and vascular disease, as well as age, previously were incorporated into an expanded criteria donor (ECD) stratification in the United States for offer to preconsented potential recipients.[18] More recently, a new kidney allocation system has been developed, using 10 donor factors (those listed above in addition to diabetes mellitus, proposed DCD pathway, and others) to calculate a Kidney Donor Risk Index (KDRI), which is a prediction of graft function on a continuous scale.[19] As well as providing improved survival matching of donor graft and recipient, an outcome of this system and others such as the Eurotransplant Senior Program initiative is to maximize access to transplantation through use of organs that otherwise may not be able to be matched to a recipient.[20] Whatever local system is in place, neither donor age nor any of these comorbidities universally precludes kidney donation, and a survival benefit for ECD kidney transplantation has been demonstrated when compared with "standard therapy" of waiting for a non-ECD kidney.[21]

BRAIN DEATH AND PHYSIOLOGIC SEQUELAE

Brain death is associated with progressive physiologic instability that ultimately can affect kidney graft function after transplantation (Fig. 132.1). Timely confirmation of brain death, referral to the organ donor agency, and procurement of organs minimize the loss of donors and maximize the number of organs suitable for transplantation. Reported loss of potential donors through failed physiologic support ranges from 5% to 25%.[22,23] Those who medically manage the potential donor and oversee the logistics of organ donation should work to minimize this loss through ensuring timely procurement and provision of excellent supportive treatment.

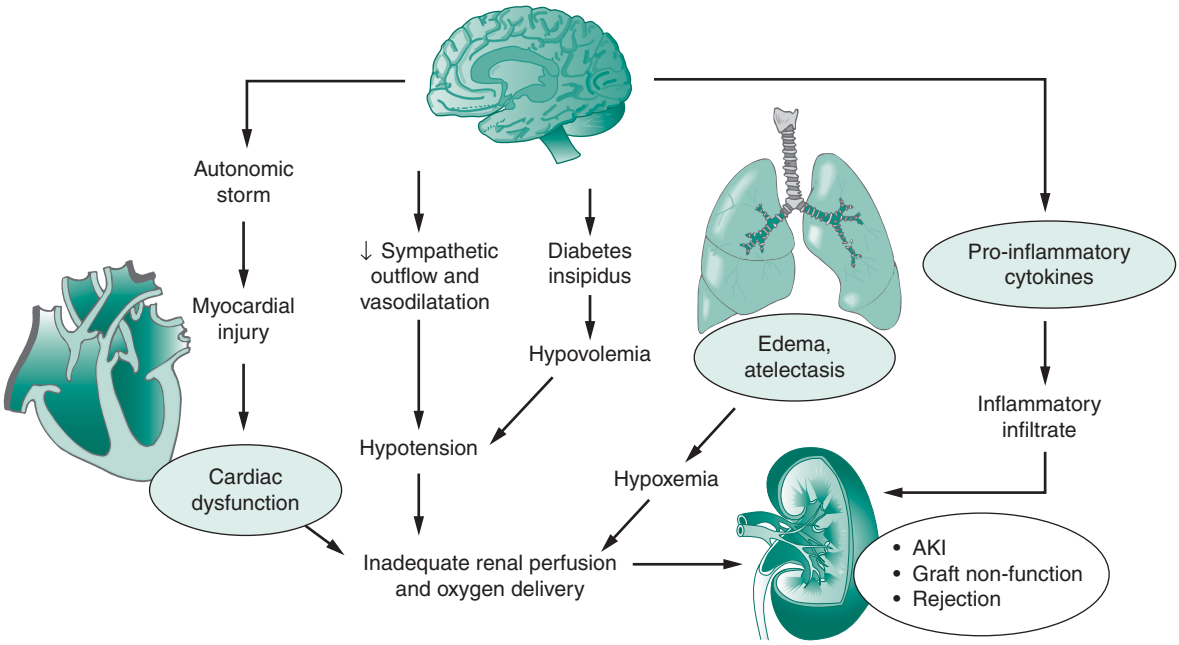

FIGURE 132.1 Brain death and effect on kidney function. *AKI,* Acute kidney injury.

Brain death may develop as a result of progressive brain swelling in the hours or days after a severe brain injury (e.g., trauma, cerebral hemorrhage, cerebral infarction, anoxic injury). Because the brain is contained within a rigid skull that limits its expansion, progressive edema and/or hemorrhage results in rising intracranial pressure and inadequate cerebral perfusion pressure. A cycle of cerebral infarction, edema, and further increase in intracranial pressure occurs with eventual loss of blood flow to the entire brain, including the brainstem. Brain death has implications on maintaining homeostasis with potential effects on kidney graft function as described below. Moreover, acute neurologic injury and acute kidney injury may coexist not only because of shared risk factors but also through kidney-brain crosstalk (e.g., mediated by cytokine secretion, inflammation, or oxidative damage[24]).

Cardiovascular

This process of brainstem ischemia may result in an intense sympathetic surge with marked hypertension, tachycardia (or reflex bradycardia [Cushing's reflex]), and/or arrhythmias, known as the "autonomic storm." This is usually short-lived but may result in cardiac ischemia and myocyte necrosis, electrocardiographic changes, and cardiac dysfunction, and pharmacologically blunting this process mitigates against myocardial injury.[25,26] Any drugs administered for this purpose should have a very short duration of action, because longer-acting agents will exacerbate the hypotension that usually follows this period.

Subsequent to the autonomic storm, there is usually loss of sympathetic outflow, resulting in vasodilation and hypotension. The hypotension may be exacerbated by preexisting hypovolemia, polyuria from diabetes insipidus (DI), and cardiac dysfunction. Adequate support of blood pressure and cardiac output is necessary to optimize organ perfusion and therefore the outcome of kidney transplantation. Vasopressor agents and/or inotropic drugs often are required for persistent hemodynamic disturbance after correction of volume depletion.

Diabetes Insipidus

DI occurs in approximately 80% to 90% of brain-dead potential donors and is caused by the loss of posterior pituitary function, which results in deficiency of antidiuretic hormone (ADH).[27] This results in polyuria, hypernatremia, and hypovolemia. Prior treatments for raised intracranial pressure, such as hypertonic saline and mannitol, also may contribute to hypernatremia and hypovolemia. Polyuria can be marked if untreated, often exceeding 1 L of urine output per hour, which can contribute to hemodynamic instability and hypoperfusion. Attempts to correct the free water loss through the administration of large volumes of fluid may result in further derangements, such as hyperglycemia and hypothermia. Hypernatremia in the donor has been associated with inferior graft function at 2 and 3 years after renal transplantation.[28]

Hypothermia

Hypothermia is common after brain death because of the loss of hypothalamic thermoregulation, inability to shiver, and loss of vasoconstriction. Hypothermia may be exacerbated by the administration of large volumes of relatively cool fluids in the treatment of DI. Severe hypothermia has many adverse effects include cardiac dysfunction, arrhythmias, coagulopathy, and a leftward shift of the oxyhemoglobin dissociation curve with reduced oxygen delivery to tissues. Moreover, temperatures lower than 35°C preclude or delay the declaration of death via clinical brain death testing. As an intervention in the donor after declaration of brain death, however, the induction and maintenance of mild hypothermia (34°C to 35°C) compared with targeted normothermia was associated with a significant reduction in delayed graft function in kidney recipients.[29]

Hyperglycemia

Administration of large volumes of dextrose-containing fluids in the treatment of DI may cause hyperglycemia. Hyperglycemia also may be caused by preexisting diabetes mellitus or by increases in the levels of counter-regulatory hormones and peripheral resistance to insulin.[30] It may result in an osmotic diuresis and electrolyte abnormalities.

Anterior Pituitary Dysfunction

Animal models demonstrate that a deficiency of thyroid hormone, cortisol, and adrenocorticotropic hormone (ACTH) occurs with brain death[31] and that exogenous hormone administration may improve hemodynamics and myocardial contractility.[32,33] On the other hand, it is unclear whether clinically significant thyroid hormone or cortisol deficiency occurs in humans after brain death. There is conflicting evidence regarding the presence of adrenal insufficiency in brain-dead donors with evidence of decreased,[32] unchanged,[33], and increased[34] cortisol levels. Brain-dead patients appear to have decreased circulating T3 levels in the setting of normal or increased levels of thyroid stimulating hormone (TSH) consistent with the sick euthyroid syndrome.[34–36] In the referenced studies no correlation was found between low levels of cortisol or thyroid hormone and blood pressure or vasopressor requirement. In a further study of 32 patients, serial measurements up to 80 hours after brain death failed to show a progressive decline in the level of free triiodothyronine (T_3) or cortisol.[37]

Inflammatory and Immunologic Changes

Significant changes in the cytokine profiles, including elevation of proinflammatory cytokines such as interleukin 6 (IL-6) and IL-8, are observed in the circulation after brain death,[38] as well as being present in increased concentration in kidney grafts from brain-dead donors.[39] Grafts from these donors exhibit T cell and macrophage infiltration and significant release of inflammatory mediators on reperfusion in recipients.[40] These proinflammatory factors are thought to be mediators in posttransplant immune reaction, reperfusion injury, and graft dysfunction.[41]

Respiratory Changes

Hypoxia from atelectasis and pulmonary edema may contribute to deterioration in cardiopulmonary status, increasing the risk of cardiac arrest before organ procurement.

Hematologic Changes

Anemia may be dilutional, resulting from bleeding resulting from trauma and exacerbated by coagulopathy. Coagulopathy may occur as an effect of substances released from the necrotic brain that induce fibrinolysis (especially in traumatic brain injury), or as a result of dilution from bleeding and fluid administration; it may be worsened by hypothermia.[4] Disseminated intravascular coagulation (DIC) in the donor may not affect short-term graft function.[42]

MANAGEMENT OF THE BRAIN-DEAD POTENTIAL ORGAN DONOR

Intensivist-led management of brain-dead organ donors has been shown to be associated with retrieval of more organs for transplantation.[43] The approach to management for the potential organ donor after brain death is similar to that for other critically ill patients with the aim of achieving and maintaining physiologic homeostasis. Meeting predefined donor management goals is associated with a reduction in delayed graft function,[44] and consensus guidelines recommend consideration of the usual spectrum of invasive and noninvasive monitoring strategies.[45] As a minimum this will require arterial pressure (and generally central venous pressure) monitoring, although there is no evidence to guide selection of an optimum monitoring tool. Earlier protocols and guidelines advocated the use of a pulmonary artery catheter (PAC).[46,47] A more recent retrospective study of PAC use in donors at a single center showed a decline in use over time and no association with increased retrieval of kidneys for transplantation,[48] albeit an association with increased heart procurement. A protocolized fluid and vasopressor management algorithm using minimally invasive hemodynamic monitoring (pulse-pressure-variation) has been evaluated in a multicenter randomized trial with no increase in the number of organs transplanted per donor.[49]

An awareness of the specific perturbations that may occur in brain death and timely institution of appropriate supportive treatment is essential.

Autonomic Storm

Autonomic storm is usually self-limited, and no treatment is required. If antihypertensive agents are used, they should be short acting (e.g., esmolol, sodium nitroprusside).

Arrhythmias

Arrhythmias may be prevented by minimizing the time between brain death and organ procurement. During this time normal serum electrolyte concentrations, blood pressure, and volume state should be sought. Standard therapy may be administered for atrial and ventricular arrhythmias (e.g., amiodarone, cardioversion). In the event of cardiac arrest, cardiopulmonary resuscitation may result in recovery of cardiac function and successful organ transplantation.[50] Bradycardia is usually resistant to atropine, but adrenaline, isoprenaline, or pacing may be effective.[51]

Hypovolemia

The volume state should be optimized by administration of intravenous fluids. Whether crystalloids or colloids are used will depend on institutional preferences; however, hydroxyethyl starch (HES) should be avoided because its use has been associated with inferior renal indices in the donation-transplantation setting[52,53] and critically ill patients in general.[54] Competing requirements for optimization of organ function may require balancing of strategies for fluid management. Although higher rates of lung procurement are achieved with a restrictive fluid balance,[55] a more liberal fluid administration strategy in the donor is associated with decreased delayed kidney graft function.[56]

Recently, however, a management protocol in donors that included restrictive fluid management (along with specific ventilation strategy, recruitment, and hormonal therapy) was shown not to be associated with worse kidney transplantation outcomes.[57]

Hypotension and Low Cardiac Output

To maintain adequate perfusion pressure (e.g., mean arterial pressure approximately 60 to 70 mm Hg) vasopressor/inotropic agents often are required post optimization of volume state. Although an association has been demonstrated between catecholamine requirement in the donor and kidney allograft dysfunction at 1 year,[58] it is unclear whether the effect is causative. Cohort studies in Europe, in fact, have suggested a beneficial effect of catecholamines such as dopamine[59] or norepinephrine[60] on graft survival. The investigators in the former study subsequently conducted a multicenter randomized control trial of dopamine involving 264 donors, in which the addition of low-dose dopamine infusion to norepinephrine (the latter targeted to hemodynamic end points) resulted in a significant decrease in delayed graft function in recipients.[61] There was a minimal effect on blood pressure, and therefore the effect was thought to be mediated by other factors (such as endothelial protection).[62] The decision to use dopamine in the donor must be considered within the broader context of the drug's decline in use in the ICU because of concerns about arrhythmogenicity and effect on patient outcomes in broader critical care cohorts.[63]

Diabetes Insipidus

Urinary volume loss from DI should be replaced with intravenous 5% dextrose or, if there is resistant hyperglycemia, with sterile water administered via a central venous catheter. Antidiuretic hormones, which act on V_2 receptors in the renal collecting tubules (vasopressin and/or desmopressin), often are required to avoid the side effects of large volume infusion. Desmopressin (1-desamino-8-D-arginine vasopressin, or DDAVP) may be given intravenously, intramuscularly, subcutaneously, or intranasally at a dose between 1 and 4 mg every 2 to 6 hours, or as required if urine output exceeds a particular volume (e.g., 300 mL/hr). It is more selective for V_2 receptors and therefore the drug of choice for DI without hypotension. Vasopressin (arginine vasopressin or AVP) has a shorter half-life and is given as a continuous infusion (usually 0.4 to 2.4 IU per hour). The agents can be used in combination.

Hormonal Supplementation

Vasopressin

In addition to its antidiuretic effect, vasopressin also acts on V_1 receptors located within blood vessels (causing vasoconstriction and thereby increasing blood pressure), and V_3 receptors in the anterior pituitary to stimulate the release of ACTH. Low-dose infusion in hemodynamically unstable brain-dead patients frequently results in a reduction or discontinuation of catecholamine pressor agents.[64,65] It has been used in brain-dead patients undergoing prolonged periods of support.[66] High doses (>2.4 U/hr) cause vasoconstriction of coronary, renal, and splanchnic vasculature, which may result in regional ischemia.[67] Although it is unclear whether the addition of vasopressin is preferable to using catecholamine agents alone in terms of kidney recipient outcome, a recent analysis of the Organ Procurement and Transplantation Network (OPTN) database suggested an independent benefit of vasopressin on number of organs (including kidneys) retrieved.[68] Based on vasopressin's hemodynamic and antidiuretic effects, and a potential beneficial effect on numbers of organs retrieved, a low threshold for its use in brain-dead donors appears logical, albeit with a dose restriction of 2.4 IU/hr or less.

Desmopressin

Desmopressin has no appreciable vasoconstrictive effect. Its longer duration of action (6 to 20 hours) means it may be given intermittently, usually as an intravenous bolus. As for vasopressin, despite a clear rationale for its use, evidence of recipient graft outcome benefit is limited. Guesde et al. assessed the effects of desmopressin on early and long-term renal graft function in a randomized, controlled study.[27] Desmopressin was administered to 49 brain-dead donors and 48 controls, and there was no difference in early and long-term (median, 45 months) graft function. However, a recent retrospective cohort study has suggested an association with 2-year graft survival (but not with early graft function or decreased rejection episodes).[69]

Combination Hormonal Therapy

Given the uncertain significance of anterior pituitary dysfunction in brain-dead patients, it is perhaps not surprising that efficacy of hormonal therapy in this setting is not well established. A number of studies have demonstrated an effect on hemodynamic stability. Novitzky et al. reported that T_3, cortisol, and insulin administered to 21 brain-dead donors improved cardiovascular status.[70] Salim et al. found a reduction in vasopressor requirement after administration of levothyroxine, methylprednisolone, insulin, and dextrose in 19 hemodynamically unstable brain-dead potential organ donors.[71] Jeevanandam et al. reported that six brain-dead potential donors receiving high doses of inotropes, with elevated filling pressures and depressed left ventricular function on echocardiography, had an improvement in hemodynamics with administration of T_3.[72] In addition, observational data have been published suggesting increased utilization of organs (including kidneys) for transplantation from donors who have undergone aggressive pharmacologic management (methylprednisolone bolus plus infusions of vasopressin and either T_3 or thyroxine).[73] Similarly a large cohort of potential donors from the United Network for Organ Sharing (UNOS) database was studied retrospectively, the authors cautiously recommending combination hormonal therapy (thyroid hormone, corticosteroid, ADH, and insulin) to maximize organ retrieval for transplantation.[74] There remains a paucity of prospectively validated data, however, and the role of the individual components of hormonal therapy is also not clear.

Thyroid Hormone

Although retrospective data from the UNOS cohort have suggested an independent association of T3/4 on increasing the number of organs retrieved per donor,[75] clinical trials

have not demonstrated a benefit. Randell and Hockerstedt reported a lack of effect on hemodynamics in 12 patients who received T_3 intraoperatively during organ procurement, compared with 13 control patients in a nonblinded study.[76] In another blinded randomized, placebo-controlled study, T_3 administered as a bolus to 19 subjects, compared with 18 controls, resulted in no improvement in hemodynamic or echocardiographic parameters.[77] Venkateswaran et al. also evaluated 80 potential heart donors in a randomized, double-blind trial of T_3 either alone or in combination with methylprednisolone and showed no attributable effect on hemodynamic parameters or retrieval rates.[78] A meta-analysis (which included these studies) concluded that routine use of thyroid hormone in brain-dead donors is not supported by the evidence and a larger prospective trial is needed.[79] Nonetheless, it may be considered in brain-dead donors, particularly if heart retrieval is anticipated, to improve hemodynamics. In adults a 4-μg IV bolus followed by an infusion at 3 to 4 μg/hr is typically used.

Low-Dose (Replacement) Corticosteroids

A number of studies have looked at steroids independently of other components of hormonal resuscitation (vasopressin and thyroid hormone). Zaroff et al. published a retrospective review of 16 potential donors who underwent serial echocardiography during donor management that included corticosteroids in 75% of the donors and dopamine in all but one.[80] The management strategy was associated with an improvement in ejection fraction in most of the donors. More recently, low-dose hydrocortisone was shown to enable vasopressor weaning in brain-dead patients,[81] and in another study was equally as effective as high-dose methylprednisolone.[82] A larger French multicenter cluster study (CORTICOME) confirmed the hemodynamic benefit of hydrocortisone (50-mg bolus, then 10 mg/hr until aortic cross-clamp), however, with no effect on organ retrieval.[83] The only graft outcome effect was seen in kidneys, with significantly more frequent delayed graft function, the implications of which are unclear. Although protocols differ, use of low-dose hydrocortisone using the CORTICOME regimen, or intermittent boluses (e.g., 50 mg every 6 hours) would seem reasonable in patients with high or escalating vasopressor requirements.

High-Dose Corticosteroids

Dupuis et al. recently published a systematic review of corticosteroid use in brain-dead donors.[84] The majority of studies examined used high-dose methylprednisolone and did not show benefit on kidney graft outcomes. For example, in the largest randomized controlled trial in kidney donors conducted by Kainz et al., administration of 1 g of methylprednisolone to the donor 3 hours before retrieval surgery did not result in less acute renal failure in the first 7 days after transplantation despite suppression of inflammation on genomic analysis.[85] Methylprednisolone often is administered to brain-dead donors, however, because there is some evidence of benefit on liver[86] and lung[87] outcomes.

Metabolic Derangement

Serum electrolytes (sodium and potassium) should be monitored in the potential donor every 2 to 4 hours to guide fluid replacement and electrolyte supplementation. Insulin may be given by infusion to maintain blood glucose less than 180 mg/dL consistent with large critical care studies[88] and specific evidence in brain-dead organ donors.[89]

Hypothermia

Hypothermia is easier to prevent than to reverse, and it may be avoided by using warming blankets and ensuring that inhaled gases are warmed and humidified. Fluids should be warmed if large-volume intravenous fluid replacement is required. Therapeutic hypothermia (34°C to 35°C) may be considered in kidney donors, following the results of the study by Niemann et al.,[29] but the effect of the intervention on other organ transplantation is unclear.

Nutritional Considerations

The nutritional state of the brain-dead organ donor also may influence the function of transplanted organs.[90] Provision of nutrition up until organ procurement may restore energy reserves, reduce cytokine generation, and protect against ischemia and reperfusion injury.

Respiratory Changes

Careful respiratory management, including frequent suctioning, repositioning, and turning, ventilatory techniques that reduce atelectasis (e.g., positive end-expiratory pressure, recruitment maneuvers), and appropriate management of volume state, help maintain adequate oxygenation and oxygen delivery to organs.

Anemia and Coagulopathy

Blood transfusion may be required, as may the administration of coagulation factors and/or platelets in the setting of coagulopathy. Procurement should be expedited if there is worsening coagulopathy.

Other Therapies

N-acetylcysteine has been investigated in a randomized open-label trial and not shown to be beneficial with respect to early or intermediate graft outcomes.[91] A number of other interventions are at the preclinical stage of evaluation (e.g., erythropoietin, ischemic preconditioning, statin therapy, and antiinflammatory therapies).[62]

DONATION AFTER CIRCULATORY DEATH

The use of kidneys from donation-after-circulatory-death (DCD) donors has the potential to increase the availability of organs for transplantation. Donation via this pathway can be "controlled," where death is anticipated within a short time of withdrawal of physiologic supports in ICU, or "uncontrolled," where organ procurement occurs after an unsuccessful resuscitation attempt of an individual in the community or hospital.[92]

Controlled Donation After Circulatory Death

This is the most common DCD practice in the United Kingdom, United States, and Australia (among other countries). Various local guidelines exist[96–98] but have in common the need for the careful consideration of the ethical principles underpinning the practice, including separating the decision to withdraw ICU supports from a decision to consider donation, respect for patient and family autonomy (which includes respecting the previously expressed wish of an individual to be a donor), beneficence, and nonmaleficence. In common with the brain-dead donor, support of the DCD donor before the time of withdrawal of physiologic supports is aimed at achieving and maintaining homeostasis, recognizing that there may be ethical and legal considerations in undertaking antemortem interventions that do not directly benefit the donor. After withdrawal of supports, death must occur in a limited period (generally within 60 to 120 minutes) to minimize warm ischemic damage to the kidneys. Various scoring systems and prediction models have been developed to try and predict patients who are likely to die in these timeframes after ICU supports are withdrawn,[99–102] but intensivist prediction alone may be as effective.[103] After circulation cessation, a "hands-off" period of a few minutes ensures irreversibility before death declaration and organ retrieval in the operating theater.

Uncontrolled Donation After Circulatory Death

Uncontrolled DCD is practiced in Spain, France, and the Netherlands and enables donation from patients who are unable to be resuscitated after unexpected cardiac arrest.[104] Some protocols involve recommencement of CPR and mechanical ventilation to limit warm ischemia after the "hands-off" period and declaration of death. Either regional perfusion (normothermic or hypothermic), or in situ instillation of preservation fluid then is performed through the use of femoral cannulae and a percutaneous balloon catheter inflated in the subdiaphragmatic aorta. In the Netherlands, which has experience in uncontrolled and controlled DCD, recipient outcomes have been reported to be equivalent from either process.[105]

Ex Vivo Organ Storage and Perfusion

Minimizing cold ischemic injury after organ retrieval by using machine cold perfusion as opposed to static cold storage has been found to be beneficial with grafts from brain-dead (particularly ECD),[106] but not DCD[107,108] donors. More recently, ex vivo normothermic perfusion has been evaluated as a method to condition and assess graft quality in marginal kidneys, which otherwise may not be transplanted.[109]

CONCLUSION

With attentive provision of supportive treatment, most potential organ donors should be able to be supported until the time of organ procurement. Optimal medical management is required to maximize the number of organs suitable for transplantation in each donor and to produce the best outcomes in renal transplant recipients. DCD has the potential to further increase the donor pool. The management priorities are similar, despite specific ethical and legal considerations.

Key Points

1. Brain death results in progressive physiologic instability. Timely confirmation of brain death and procurement of organs minimizes loss of donors resulting from progressive physiologic instability and maximizes the number of organs suitable for transplantation.
2. An understanding of the mechanism of brain death and the ensuing physiologic derangements is important in being able to institute appropriate supportive treatment in a timely manner.
3. The most common sequelae of brain death include hypotension, diabetes insipidus, and hypothermia. Conflicting evidence exists as to whether clinically significant anterior pituitary–adrenal/thyroid dysfunction occurs.
4. Clinical management by staff skilled in critical care practice is essential in ensuring successful support of potential donors for organ procurement and optimal posttransplantation kidney function.
5. Careful physiologic monitoring should be employed, with the aim of maintaining normal electrolyte levels and temperature, identifying and treating diabetes insipidus, and ensuring adequate organ perfusion through optimizing the volume state and use of pressor and/or inotropic agents. Respiratory care and blood product support may be required.
6. Hormonal resuscitation (vasopressin, thyroid hormone, and steroids) should be considered in the setting of hemodynamic instability.
7. The use of donation-after-cardiac death (DCD) has the potential to increase the availability of kidneys for transplantation. Controlled and uncontrolled DCD programs exist in a number of countries. Management priorities are similar before withdrawal of physiologic supports, albeit with specific ethical and legal considerations.

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