Review Article

The development and current status of Intensive Care Unit management of prospective organ donors

Margaret Kathleen Menzel Ellis, Mitchell Brett Sally[1], Darren Malinoski[1]

Department of Anesthesiology, Sections of Anesthesiology and Surgical Critical Care, Portland VA Medical Center, Oregon Health and Science University, [1]Division of Trauma, Critical Care, and Acute Care Surgery, Section of Surgical Critical Care, Portland VA Medical Center, Oregon Health and Science University, Portland, OR, USA

ABSTRACT

Introduction: Despite continuous advances in transplant medicine, there is a persistent worldwide shortage of organs available for donation. There is a growing body of research that supports that optimal management of deceased organ donors in Intensive Care Unit can substantially increase the availability of organs for transplant and improve outcomes in transplant recipients.

Methods: A systematic literature review was performed, comprising a comprehensive search of the PubMed database for relevant terms, as well as individual assessment of references included in large original investigations, and comprehensive society guidelines.

Results: In addition to overall adherence to catastrophic brain injury guidelines, optimization of physiologic state in accordance with established donor management goals (DMGs), and establishment of system-wide processes for ensuring early referral to organ procurement organizations (OPOs), several specific critical care management strategies have been associated with improved rates and outcomes of renal transplantation from deceased donors. These include vasoactive medication selection, maintenance of euvolemia, avoidance of hydroxyethyl starch, glycemic control, targeted temperature management, and blood transfusions if indicated.

Conclusions: Management of deceased organ donors should focus first on maintaining adequate perfusion to all organ systems through adherence to standard critical care guidelines, early referral to OPOs, and family support. Furthermore, several specific DMGs and strategies have been recently shown to improve both the rates and outcomes of organ transplantation.

Key words: Critical care, donor management, kidney transplant, renal transplant

INTRODUCTION

Despite continuous advances in transplant medicine, there is a persistent worldwide shortage of organs available for donation. In the United States alone, over 121,000 people were on the United Network for Organ Sharing (UNOS) waiting list in 2015; however, only 25,767 organs were transplanted that year and an average of 22 patients die each day waiting for an organ (United States Organ Procurement and Transplantation Network data, 2015). While a paucity of level 1 evidence exists to guide deceased donor management, there is a growing body of research that supports the use of both facility/system-wide processes as well as patient/donor-level interventions. This review will focus on the critical care management of deceased subjects who are potential kidney donors.

Currently, there are two distinct categories of deceased organ donors: Those who are donors after neurologic determination of death (DNDD) and those who proceed

For correspondence: Dr. Margaret Kathleen Menzel Ellis, Portland VA Medical Center, 3710 SW US Veterans Hospital Road, Mail Code P3-Anes, Portland, 97239 OR, USA.
E-mail: menzel@ohsu.edu

Access this article online	
Quick Response Code:	Website: www.indianjurol.com
	DOI: 10.4103/0970-1591.185103

How to cite this article: Ellis MK, Sally MB, Malinoski D. The development and current status of Intensive Care Unit management of prospective organ donors. Indian J Urol 2016;32:178-85.

with donation after a circulatory determination of death (DCDD). While renal transplantation outcomes tend to be better with kidneys procured from DNDDs,[1-5] the use of organs from DCDDs is necessary to address the shortage of organs. This review will focus on the management of DNDDs, who are potential kidney donors, as there is a much greater opportunity for critical care interventions after neurologic determination of death in this population.

Since the earliest days of transplantation, the development of organ donation and transplantation systems has been evolving in countries and regions across the world. Each system must take into consideration the nuanced characteristics, cultural and religious landscape, and legal and ethical complexities of the society within which it functions. Authors in northern India have described challenges with distrust of the medical system and fear of bodily mutilation as barriers to authorization for organ donation in DNDDs.[6] Lack of government infrastructural support, lack of approval by Islamic scholars, and lack of public awareness and education have been cited as barriers to transplantation in Islamic countries.[7] In Japan, public opinion surrounding organ transplantation has been strained since the first heart transplant performed there, in 1968, after which questions arose regarding whether or not the donor was truly deceased. Following this controversy, organ procurement from deceased donors was outlawed, only becoming legal again in 1997.[8] German experts have described changing approaches to end-of-life care and the limitation of deceased donors to standard criteria DNDDs (rather than including DCDDs or expanded criteria DNDDs) as contributing factors to the shortage of organs available for donation in their country.[9]

Many countries, including the United States, Germany, Greece, the majority of the United Kingdom, India, and Japan, take an "opt-in" approach to organ donation, in which citizens or their surrogate decision makers must actively decide to donate organs in the event of neurologic or cardiac determination of death. In these countries, media campaigns, a focus on the altruistic gift of organ donation, and "mandated choice" approaches, in which an organ donation preference must be indicated when registering for a driver's license or during another governmental process, have been employed to increase the number of registered organ donors. In several other countries, including Wales, Austria, Spain, and Singapore, an opt-out approach to organ donor status, in which everyone is assumed to be an organ donor after death unless they specifically state otherwise, has increased the availability of organs available for donation. However, this approach has led to ethical debate regarding autonomy and authorization in an opt-out system. Israel employs a unique system colloquially known as "do not give, do not get," in which registered organ donors are given preference as organ recipients. Iran has taken the approach of legalizing the organ trade, allowing financial reimbursement of living kidney donors. While this approach has effectively eliminated the kidney shortage in Iran, ethical concerns have been raised regarding financial coercion of vulnerable donors.

In the United States, the donor management process consists of a multifaceted effort, involving several key stakeholders. In the initial phase of management, critical care physicians stabilize patients and work with support staff to identify potential donors. Once a potential donor is identified, an independent organ procurement organization (OPO) is notified and begins the process of evaluating the potential donor, discussing the option of donation with the patient's family and requesting authorization for donation and transplantation. Centers in which a large number of potential donors may be managed, such as level 1 trauma centers, often have an OPO transplant coordinator in-house at all times; this practice has been associated with increased conversion rates of potential to actual donors in observational studies.[10-14] Once a donor has been identified and authorized, OPO coordinators initiate critical care practices to optimize the function of all potentially transplantable organs, and transplant physicians evaluate the specific characteristics of the available organs and determine their suitability for transplantation into specific recipients.

When it comes to studying the effectiveness of interventions in potential deceased kidney donors, two specific outcomes are commonly reported: The number of organs transplanted per donor (OTPD, maximum of eight) and the rate of delayed graft function (DGF) in the recipient, defined by UNOS as the requirement for dialysis within 7 days of renal transplantation. These outcomes are both clinically relevant and clearly defined, making them appropriate targets for interventions to improve the success of donor management.

In this systematic literature review, we report upon the current state of the literature and recommendations guiding the management of DNDDs, focusing on management strategies that are associated with improved outcomes in terms of increased overall OTPD as well as decreased renal recipient DGF. We describe organizational strategies to identify and authorize potential organ donors, guidelines for medical management of patients with nonsurvivable brain injuries before declaration of death according to neurologic criteria, and important aspects of medical management for authorized donors before organ procurement. This review will not address interventions that occur after organ recovery, such as pulsatile machine perfusion or the administration of tissue plasminogen activator.

METHODS

A comprehensive search of the PubMed database was performed using the main term "donor management" in conjunction with one of the following terms: "Kidney

transplant," "renal transplant," "DMG," "OTPD," "DGF," or "transplant outcome." Studies were included if they were written in English and if the full text was available for review through PubMed or an institutional subscription. Large original investigations and comprehensive society guidelines were prioritized, and the reference sections of these articles were also reviewed. Relevant references that were not included in the original search were individually assessed and considered for inclusion in this systematic literature review.

IDENTIFYING AND AUTHORIZING POTENTIAL DONORS

Clinical triggers and timely referrals

It is critically important to identify potential organ donors and to notify an OPO to begin the process of evaluating them as early as possible. Early identification, defined by the Center for Medicare Services as notification of an OPO within 1 h of a patient meeting a clinical trigger, facilitates timely medical evaluation of a potential donor, may minimize time pressure when discussing the possibility of donation with a patient's family, and has been associated with an increased likelihood of organ donation.[15] In patients with a neurologic injury that requires mechanical ventilation, specific clinical triggers for notification of an OPO include (1) a Glasgow coma score of 5 or less, (2) loss of a brainstem reflex, and (3) if a family discussion is being planned that may result in withdrawal of life-sustaining therapy. While it is not recommended that physicians directly address organ donation decisions during end-of-life discussions due to ethical concerns about conflict of interest, there is evidence that the majority of families choose to authorize donation when approached in a timely manner by a trained, designated requestor (United States Organ Procurement and Transplantation Network data, January 2008 to June 2010).

Criteria for determination of death in a potential donor

The majority of transplanted organs are procured from DNDD.[16] Death according to neurologic criteria occurs when all brain functions, including those of the brainstem, cease irreversibly; neurologic criteria for determination of death, including recommendations for ancillary testing when clinical methods of determination (complete neurologic examination and apnea testing) are not possible or must be aborted, have been defined by the American Academy of Neurology.[17,18]

Absolute and relative contraindications to organ donation

Once authorization for donation has been obtained from a potential donor's legal surrogate or advanced directive, the transplant physician's responsibilities include assessing the suitability of the donor organs for transplantation. There are surprisingly few donor characteristics that present absolute contraindications to renal transplantation. While a history of malignancy is not in itself a contraindication to organ donation, and while donor tumor transmission is uncommon, any active malignancy or any history of melanoma in the donor are both absolute contraindications for organ donation. Unexplained intracranial hemorrhage should prompt a high level of suspicion for active malignancy since hemorrhage may be the presenting sign of brain metastasis. Furthermore, UNOS cautions against transplanting organs from donors with a history of lymphoma or carcinomas of breast, lung, kidney, or colon. In general, the low but present risk of donor tumor transmission should be weighed against the risk of not undergoing transplantation.[19]

Bacteremia does not preclude suitability for organ donation;[20,21] in fact, no differences in graft function or mortality were identified between cohorts of recipients whose donors did or did not have positive blood cultures as long as a course of appropriate antibiotics was administered to the recipients either before donation (if donor blood cultures were known to be positive) or immediately upon discovery of positive donor blood cultures.[22] Regarding viral infections, there is evidence that seropositivity for human immunodeficiency virus (HIV) may not be a contraindication for kidney donation if the recipient is already infected with HIV.[23] Similarly, donors with hepatitis C virus (HCV) seropositivity may be considered as possible donors for recipients who are also seropositive for HCV. While positive hepatitis B virus (HBV) core antibody (reflecting hepatitis B natural immunity or resolved infection) is not considered an absolute contraindication for organ donation, a positive HBV surface antigen reflects an active infection and is an absolute contraindication to organ donation. Potential donors with a history of high-risk behaviors associated with HIV, HBV, and HCV exposure (as defined by the United States Public Health Service)[24] should undergo nucleic acid amplification testing, which can detect HIV RNA in up to half of potential donors in a high-risk category.[25,26] Finally, while patients with meningitis may be considered as potential donors, those with febrile illness, paralysis, or encephalitis of unclear origin are not considered acceptable donors due to the risk for transmission of difficult-to-diagnose pathogens.[27,28]

Patient characteristics, including relative contraindications to organ donation, must be considered on an individual basis within the context of the risks and benefits to the recipient of transplantation versus continued waiting. The kidney donor risk index, which is based upon donor characteristics, can be used by transplant surgeons to counsel patients on the relative risk of graft failure when a kidney is transplanted from a donor who does not meet standard criteria.[29] The utilization of organs from expanded criteria donors (ECDs) has increased the pool of potential organ donors and is an area of ongoing investigation. Since potential donors who do not meet standard criteria for donation or who have relative contraindications to donation may still be able to donate organs, it is crucial that Intensive Care Unit (ICU) nurses and physicians broadly refer patients under their

care who meet clinical triggers for potential organ donation to an OPO for further evaluation and not try to determine suitability themselves.

Patients who have experienced a catastrophic brain injury but who do not meet criteria for neurologic determination of death should continue to receive standard neurocritical care as current evidence from North America and the Netherlands supports that neurologic prognosis following a catastrophic brain injury should not be defined until 72 h have passed.[30,31] During this time, all efforts should be made to perfuse the brain, and clinical protocols, also known as catastrophic brain injury guidelines (CBIGs), exist to guide the management of such patients.[31-33] As a consequence of maintaining favorable hemodynamics for adequate brain perfusion, perfusion of other organ systems is also promoted. Thus, if the patient's neurologic status improves, adherence to CBIGs increases the likelihood of a successful outcome due to protection of other organ systems. If the patient does not experience neurologic recovery or regresses to death by neurologic determination, adherence to CBIGs also preserves the option for the patient's family to proceed with organ donation as a secondary benefit.[31,34]

DONOR MANAGEMENT GOAL BUNDLES

Death by neurologic criteria leads to massive physiologic changes as the normal neurologic regulation of the body is lost. To balance the competing needs of various potentially transplantable organs within the context of this instability, many expert groups and OPOs have established checklists of critical care endpoints[16,35-39] to guide physicians in maintaining optimal stability in a potential donor. When checklists or "bundles" of these endpoints, also known as donor management goals (DMGs), have been compiled and followed, it has consistently been shown that the mean number of OTPD is increased in both standard and ECDs.[39-41] Furthermore, when DMG bundle criteria are met during donor hospital ICU management immediately before authorization for donation and transitioning care to bedside OPO staff, DGF in kidney recipients is less likely.[42] An example of the DMG bundle used in several UNOS regions is shown in Table 1.

Table 1: United Network for Organ Sharing (UNOS) Donor Management Goals (DMGs)

Donor management goal	Parameter
Mean arterial pressure (mmHg)	60-110
Central venous pressure (mmHg)	4-12
Left ventricular ejection fraction (%)	>50
Low-dose vasopressors*, number of agents	≤1
Arterial blood gas pH	7.3-7.5
PaO_2:FiO_2 ratio	>300
Serum sodium (mEq/L)	<155
Urine output (mL/kg/h over 4 h)	>0.5
Glucose (mg/dL)	<180

*Less than or equal one vasopressor used and at a low dose (dopamine <10 mcg/kg/min; phenylephrine <1 mcg/kg/min; norepinephrine <0.2 mcg/kg/min), with any dose of epinephrine resulting in the element not being met. mmHg=Millimeters of mercury, PaO_2=Arterial partial pressure of oxygen, FiO_2=Fraction of inspired oxygen

SPECIAL TOPICS IN INTENSIVE CARE UNIT MANAGEMENT OF KIDNEY DONORS

Aside from adherence to CBIGs and DMG bundles, which have been clearly associated with improved outcomes and increased OTPD across the deceased organ donor population, several specific critical care interventions in DNDDs have been studied with regard to the development of DGF and mortality in renal transplant recipients. The Society of Critical Care Medicine (SCCM), the American College of Chest Physicians (ACCP), and the Association of Organ Procurement Organizations (AOPO) have recently published a consensus statement to guide the management of the potential organ donor in ICU.[16] Similar guidelines have been published by the Canadian Council for Donation and Transplantation[43] and the European Renal Best Practice Transplantation Guideline Development Group.[44] This section both summarizes the SCCM/ACCP/AOPO recommendations as they apply to kidney donors and describes new areas of research in kidney donor management.

General considerations

During intensive care management of potential kidney donors, consideration should be given to medications and interventions that could lead to nephrotoxicity. While there is no reported association of intravenous contrast administration with DGF or graft failure,[16] any plan for imaging or interventional studies requiring the administration of intravenous contrast should prompt discussion of the necessity of the study and alternatives to contrast use given the potential for the development of contrast nephropathy. If intravenous contrast is absolutely necessary, additional intravenous fluids should be administered for renal protection.

There is no requirement for additional diagnostic maneuvers to assess a potential donor kidney. Imaging studies may be useful in donors with a family history of polycystic kidney disease or a personal history of kidney stones or urologic anomalies. Regarding kidney biopsy before transplant, it is generally unnecessary unless recommended by the OPO, which may be the case for some ECDs.[16]

Cardiovascular

Meeting hemodynamic DMGs can be challenging in the face of the often severe hemodynamic instability associated with a neurologic determination of death. Vasopressors and inotropes are frequently necessary to

support the cardiovascular system, to prevent intractable arrhythmias or cardiovascular collapse, and to maintain perfusion to crucial organs. While evidence is limited, the use of low-dose vasopressors and inotropes to support hemodynamics is supported.[16,40,42] With regard to individual medication choice, catecholamine use in the donor has been associated with improved graft survival in recipients in at least one German study;[45] however, epinephrine has also been associated with higher levels of donor serum creatinine in a study done in France.[46] Low-dose dopamine (<5 mcg/kg/min) infusion has been associated with a reduction in DGF.[47] Finally, arginine vasopressin, which is commonly administered as part of hormonal replacement therapy, has been associated with increased OTPD, including a significant increase in the number of kidneys recovered from DNDDs.[48]

Endocrine

Although glucose control in the critically ill has been an ongoing topic of controversy for many years, current recommendations from the SCCM advocate for the avoidance of hyperglycemia above 180 mg/dL.[49] However, it has been unclear how these guidelines apply to deceased donors. Poor glucose control in DNDDs has been associated with elevated terminal serum creatinine in kidney donors before organ recovery,[50] which has been independently associated with higher rates of DGF in recipients.[51,52] Recently, a study of prospectively collected characteristics of over 1600 DNDDs was performed using multivariate analysis to determine the effect of hyperglycemia on OTPD and renal graft function. Three separate blood glucose target levels (150 mg/dL or less, 180 mg/dL or less, and 200 mg/dL or less) were evaluated. While target glucose levels of both 180 mg/dL and 200 mg/dL were associated with increased OTPD, only the 180 mg/dL level was an independent predictor of 4 or more OTPD. All three levels were associated with higher kidney graft survival when compared with patients who did not achieve any of the three glucose targets.[53] This evidence suggests that the generally accepted critical care guideline for glucose control of <180 md/dL is also appropriate for DNDDs.

Due to the irreversible loss of hypothalamic function and subsequent cessation of antidiuretic hormone (ADH) production, DNDDs are at risk for severe central diabetes insipidus (DI). Without ADH to stimulate reabsorption of water in the kidney, the DNDD with DI will produce large volumes of dilute urine (specific gravity <1.005 and/or urine osmolality <200 mOsm/kg H_2O). This results in hypovolemia, hyperosmolality, and hypernatremia.[54] DI should be managed with a combination of volume resuscitation with hypotonic saline (0.25% or 0.5%) and hormonal replacement with the ADH analogs desmopressin and/or vasopressin.[16] Due to its stimulation of Von Willebrand Factor release, desmopressin may be particularly useful in patients who are also coagulopathic, while vasopressin serves a dual role as a vasopressor and has been shown to improve transplant outcomes as described above. The goals of DI management are the restoration and maintenance of euvolemic fluid balance, a decrease of urine output to no >4 mL/kg/h, and maintenance of sodium levels <155 mEq/L.[16]

Fluid resuscitation

While the maintenance of euvolemia is an agreed-upon goal in the DNDD,[16] controversy exists regarding the most beneficial choice of intravenous fluid for resuscitation. Crystalloid solutions are generally employed during volume resuscitation; however, concern for deleterious effects of large-volume crystalloid resuscitation (interstitial and cardiogenic pulmonary edema) has prompted the use of colloid solutions, including synthetic colloids such as hydroxyethyl starch (HES). While a Finnish study demonstrated that the use of HES can indeed reduce the total volume of intravenous fluid required for resuscitation[55] in DNDDs, multiple studies have suggested either no difference or an increased risk in DGF in patients who received kidneys from DNDDs treated with HES. Recently, in the largest study of HES use in DNDDs to date, HES use in the donor was strongly associated with a significant increase in DGF in renal transplant recipients.[56] Given the lack of demonstrable benefit and the compelling evidence for harm associated with HES use, it cannot be recommended as a safe strategy for volume resuscitation in potential kidney donors. Lower molecular weight HES or colloids other than HES, such as albumin, may provide a safer alternative as shown in data from studies conducted in France, but evidence is inconclusive and ongoing study in this area is needed.[57-59]

Hematologic

Due to their immunosuppressive effects, blood transfusions were often historically administered to recipients before renal transplantation as part of a strategy to reduce acute rejection and improve graft function.[60-62] However, this practice fell out of favor with the advent of modern immunosuppressive therapy, the potential for recipients to develop donor-specific antibodies, as well as a growing appreciation for the many deleterious effects of blood transfusions, in general. On the other hand, the effect of blood transfusions in deceased donors upon DGF in renal transplant recipients has only recently been evaluated. In a propensity analysis, any blood transfusion in the donor was associated with a significant reduction in the development of DGF in the recipient and the effect was seen most strongly in donors who received large-volume blood transfusions.[63] A potential explanation for this protective effect is down-regulation of the dysfunctional inflammatory processes that are associated with a neurologic determination of death and predispose transplanted kidneys to reperfusion injury and diminished function. At this time, OPO guidelines vary regarding target serum hematocrit (ranging from 21% to 30%); further, prospective randomized studies are needed to inform evidence-based practices in this area.

Temperature regulation

Wide swings in temperature often occur in the setting of death by neurologic determination as the hypothalamic regulation of body temperature is lost, and active rewarming is frequently necessary to maintain normothermia in potential organ donors. Mounting evidence for an association between mild hypothermia and renal protection in models of cardiac arrest prompted further investigation for the role of temperature management in the DNDD. A recent multicenter trial of targeted temperature management in 394 DNDDs compared rates of DGF in recipients of kidneys from donors randomized to either mild hypothermia (34–35°C) or normothermia (36.5–37.5°C). Donors in the mild hypothermia group had a significantly lower rate of DGF (28% vs. 39%, OR = 0.62 [CI 0.43–0.92]); this effect was so compelling that the study was stopped early for overwhelming efficacy.[64] The protective effect of mild hypothermia was most powerful in ECDs and donors within other higher-risk subgroups.

SUMMARY AND RECOMMENDATIONS

Management of potential organ donors should be focused on maintaining adequate perfusion to all organ systems through adherence to standard critical care guidelines, early referral to OPOs, and family support.[16,31] There is good evidence that by achieving specific DMGs, critical care providers can optimize both the number of OTPD and to reduce the incidence of DGF in transplanted kidneys. Several specific critical care management strategies, including careful consideration of vasopressor and inotrope selection, maintenance of euvolemia, avoidance of hydroxyethyl starches as volume expanders, glycemic control (with a target blood glucose of <180), blood transfusion if indicated, and targeted temperature management with a goal of mild hypothermia, have all been associated with improved outcomes in transplanted kidneys. As the emerging field of donor management research continues to grow, these recommendations will continue to evolve. Ultimately, the persistent shortage of organs available for transplantation may be diminished through optimizing the care of potential organ donors.

Acknowledgments

We would like to acknowledge John M. Barry, MD, for his guidance in the preparation and review of this manuscript.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

REFERENCES

1. Alonso A, Fernández-Rivera C, Villaverde P, Oliver J, Cillero S, Lorenzo D, *et al.* Renal transplantation from non-heart-beating donors: A single-center 10-year experience. Transplant Proc 2005;37:3658-60.
2. Gok MA, Buckley PE, Shenton BK, Balupuri S, El-Sheikh MA, Robertson H, *et al.* Long-term renal function in kidneys from non-heart-beating donors: A single-center experience. Transplantation 2002;74:664-9.
3. Matsuno N, Tashiro J, Uchiyama M, Iwamoto H, Hama K, Nakamura Y, *et al.* Early graft function in kidney transplantation from non-heart-beating donors. Ann Transplant 2004;9:21-2.
4. Nicholson ML, Metcalfe MS, White SA, Waller JR, Doughman TM, Horsburgh T, *et al.* A comparison of the results of renal transplantation from non-heart-beating, conventional cadaveric, and living donors. Kidney Int 2000;58:2585-91.
5. Nishikido M, Noguchi M, Koga S, Kanetake H, Matsuya F, Hayashi M, *et al.* Kidney transplantation from non-heart-beating donors: Analysis of organ procurement and outcome. Transplant Proc 2004;36:1888-90.
6. Gupta V, Chandra A, Rahul, Singh M, Shrivastava PK, Singhai A, *et al.* Establishing a deceased donor program in north Indian region: Lessons learnt. Clin Transplant 2016;30:633-40.
7. Ghods AJ. Current status of organ transplant in Islamic countries. Exp Clin Transplant 2015;13 Suppl 1:13-7.
8. Kita Y, Aranami Y, Aranami Y, Nomura Y, Johnson K, Wakabayashi T, *et al.* Japanese organ transplant law: A historical perspective. Prog Transplant 2000;10:106-8.
9. Tacke F, Kroy DC, Barreiros AP, Neumann UP. Liver transplantation in Germany. Liver Transpl 2016. doi: 10.1002/lt. 24461. [Epub ahead of print].
10. Shafer TJ, Ehrle RN, Davis KD, Durand RE, Holtzman SM, Van Buren CT, *et al.* Increasing organ recovery from level I trauma centers: The in-house coordinator intervention. Prog Transplant 2004;14:250-63.
11. Sullivan H, Blakely D, Davis K. An in-house coordinator program to increase organ donation in public teaching hospitals. J Transpl Coord 1998;8:40-2.
12. Shafer T, Hueneke M, Wolff S, Davis K, Ehrle R, Van Buren C, *et al.* The texas Nondonor hospital project: A preliminary report on the impact of inhouse coordinators on organ donation rates in nondonor hospitals. Transplant Proc 1997;29:3261-2.
13. Shafer TJ, Davis KD, Holtzman SM, Van Buren CT, Crafts NJ, Durand R. Location of in-house organ procurement organization staff in level I trauma centers increases conversion of potential donors to actual donors. Transplantation 2003;75:1330-5.
14. Salim A, Berry C, Ley EJ, Schulman D, Desai C, Navarro S, *et al.* In-house coordinator programs improve conversion rates for organ donation. J Trauma 2011;71:733-6.
15. Dickerson J, Valadka AB, Levert T, Davis K, Kurian M, Robertson CS. Organ donation rates in a neurosurgical intensive care unit. J Neurosurg 2002;97:811-4.
16. Kotloff RM, Blosser S, Fulda GJ, Malinoski D, Ahya VN, Angel L, *et al*. Management of the potential organ donor in the ICU: Society of critical care medicine/American college of chest physicians/Association of organ procurement organizations consensus statement. Crit Care Med 2015;43:1291-325.
17. Wijdicks EF. Determining brain death in adults. Neurology 1995;45:1003-11.
18. Wijdicks EF, Varelas PN, Gronseth GS, Greer DM; American Academy of Neurology. Evidence-based guideline update: Determining brain death in adults: Report of the quality standards subcommittee of the American academy of neurology. Neurology 2010;74:1911-8.
19. Kauffman HM, Cherikh WS, McBride MA, Cheng Y, Hanto DW. Deceased

donors with a past history of malignancy: An organ procurement and transplantation network/united network for organ sharing update. Transplantation 2007;84:272-4.
20. Cohen J, Michowiz R, Ashkenazi T, Pitlik S, Singer P. Successful organ transplantation from donors with Acinetobacter baumannii septic shock. Transplantation 2006;81:853-5.
21. Freeman RB, Giatras I, Falagas ME, Supran S, O'Connor K, Bradley J, *et al.* Outcome of transplantation of organs procured from bacteremic donors. Transplantation 1999;68:1107-11.
22. Zibari GB, Lipka J, Zizzi H, Abreo KD, Jacobbi L, McDonald JC. The use of contaminated donor organs in transplantation. Clin Transplant 2000;14(4 Pt 2):397-400.
23. Muller E, Barday Z, Mendelson M, Kahn D. HIV-positive-to-HIV-positive kidney transplantation – Results at 3 to 5 years. N Engl J Med 2015;372:613-20.
24. Seem DL, Lee I, Umscheid CA, Kuehnert MJ; United States Public Health Service. PHS guideline for reducing human immunodeficiency virus, hepatitis B virus, and hepatitis C virus transmission through organ transplantation. Public Health Rep 2013;128:247-343.
25. Kucirka LM, Sarathy H, Govindan P, Wolf JH, Ellison TA, Hart LJ, *et al.* Risk of window period HIV infection in high infectious risk donors: Systematic review and meta-analysis. Am J Transplant 2011;11:1176-87.
26. Theodoropoulos N, Jaramillo A, Ladner DP, Ison MG. Deceased organ donor screening for HIV, hepatitis B, and hepatitis C viruses: A survey of organ procurement organization practices. Am J Transplant 2013;13:2186-90.
27. Srinivasan A, Burton EC, Kuehnert MJ, Rupprecht C, Sutker WL, Ksiazek TG, *et al.* Transmission of rabies virus from an organ donor to four transplant recipients. N Engl J Med 2005;352:1103-11.
28. Fischer SA, Graham MB, Kuehnert MJ, Kotton CN, Srinivasan A, Marty FM, *et al.* Transmission of lymphocytic choriomeningitis virus by organ transplantation. N Engl J Med 2006;354:2235-49.
29. Rao PS, Schaubel DE, Guidinger MK, Andreoni KA, Wolfe RA, Merion RM, *et al.* A comprehensive risk quantification score for deceased donor kidneys: The kidney donor risk index. Transplantation 2009;88:231-6.
30. Cronberg T, Horn J, Kulper MA, Friberg H, Nielsen N. A structured approach to neurologic prognostication in clinical cardiac arrest trials. Scand J Trauma Resus Emerg Med 2013;21:1-6.
31. Souter MJ, Blissitt PA, Blosser S, Bonomo J, Greer D, Jichici D, *et al.* Recommendations for the critical care management of devastating brain injury: Prognostication, psychosocial, and ethical management: A position statement for healthcare professionals from the neurocritical care society. Neurocrit Care 2015;23:4-13.
32. Quinn L, McTague W, Orlowski JP. Impact of catastrophic brain injury guidelines on donor management goals at a level I trauma center. Transplant Proc 2012;44:2190-2.
33. Bloom MB, Raza S, Bhakta A, Ewing T, Patel M, Ley EJ, *et al.* Impact of deceased organ donor demographics and critical care end points on liver transplantation and graft survival rates. J Am Coll Surg 2015;220:38-47.
34. Malinoski DJ, Patel MS, Lush S, Willis ML, Navarro S, Schulman D, *et al.* Impact of compliance with the American college of surgeons trauma center verification requirements on organ donation-related outcomes. J Am Coll Surg 2012;215:186-92.
35. Wood KE, Becker BN, McCartney JG, D'Alessandro AM, Coursin DB. Care of the potential organ donor. N Engl J Med 2004;351:2730-9.
36. Hagan ME, McClean D, Falcone CA, Arrington J, Matthews D, Summe C. Attaining specific donor management goals increases number of organs transplanted per donor: A quality improvement project. Prog Transplant 2009;19:227-31.
37. Billeter AT, Sklare S, Franklin GA, Wright J, Morgan G, O'Flynn PE, *et al.* Sequential improvements in organ procurement increase the organ donation rate. Injury 2012;43:1805-10.
38. Franklin GA. Addressing the national organ shortage with targeted donor management. Crit Care Med 2012;40:2902-3.
39. Malinoski DJ, Daly MC, Patel MS, Oley-Graybill C, Foster CE 3rd, Salim A. Achieving donor management goals before deceased donor procurement is associated with more organs transplanted per donor. J Trauma 2011;71:990-5.
40. Patel MS, Zatarain J, De La Cruz S, Sally MB, Ewing T, Crutchfield M, *et al*. The impact of meeting donor management goals on the number of organs transplanted per donor: A prospective study from the UNOS region 5 donor management goals workgroup. JAMA Surg 2014;149:969-75.
41. Franklin GA, Santos AP, Smith JW, Galbraith S, Harbrecht BG, Garrison RN. Optimization of donor management goals yields increased organ use. Am Surg 2010;76:587-94.
42. Malinoski DJ, Patel MS, Ahmed O, Daly MC, Mooney S, Graybill CO, *et al.* The impact of meeting donor management goals on the development of delayed graft function in kidney transplant recipients. Am J Transplant 2013;13:993-1000.
43. Shemie SD, Ross H, Pagliarello J, Baker AJ, Greig PD, Brand T, *et al.* Organ donor management in Canada: Recommendations of the forum on Medical Management to Optimize Donor Organ Potential. CMAJ 2006;174:S13-32.
44. Abramowicz D, Cochat P, Claas F, Dudley C, Harden P, Heeman U, *et al*. ERBP guideline on the management and evaluation of kidney donor and recipient. Nephrol Dial Transplant 2013;28 Suppl 2:ii1-71.
45. Schnuelle P, Berger S, de Boer J, Persijn G, van der Woude FJ. Effects of catecholamine application to brain-dead donors on graft survival in solid organ transplantation. Transplantation 2001;72:455-63.
46. Blasco V, Leone M, Bouvenot J, Geissler A, Albanèse J, Martin C. Impact of intensive care on renal function before graft harvest: Results of a monocentric study. Crit Care 2007;11:R103.
47. Schnuelle P, Gottmann U, Hoeger S, Boesebeck D, Lauchart W, Weiss C, *et al.* Effects of donor pretreatment with dopamine on graft function after kidney transplantation: A randomized controlled trial. JAMA 2009;302:1067-75.
48. Plurad DS, Bricker S, Neville A, Bongard F, Putnam B. Arginine vasopressin significantly increases the rate of successful organ procurement in potential donors. Am J Surg 2012;204:856-60.
49. Jacobi J, Bircher N, Krinsley J, Agus M, Braithwaite SS, Deutschman C, *et al.* Guidelines for the use of an insulin infusion for the management of hyperglycemia in critically ill patients. Crit Care Med 2012;40:3251-76.
50. Blasi-Ibanez A, Hirose R, Feiner J, Freise C, Stock PG, Roberts JP, *et al.* Predictors associated with terminal renal function in deceased organ donors in the intensive care unit. Anesthesiology 2009;110:333-41.
51. Heilman RL, Smith ML, Kurian SM, Huskey J, Batra RK, Chakkera HA, *et al.* Transplanting kidneys from deceased donors with severe acute kidney injury. Am J Transplant 2015;15:2143-51.
52. Farney AC, Rogers J, Orlando G, al-Geizawi S, Buckley M, Farooq U, *et al.* Evolving experience using kidneys from deceased donors with terminal acute kidney injury. J Am Coll Surg 2013;216:645-55.
53. Sally MB, Ewing T, Crutchfield M, Patel MS, Raza S, De La Cruz S, *et al.* Determining optimal threshold for glucose control in organ donors after neurologic determination of death: A United network for organ Sharing Region 5 Donor Management Goals Workgroup prospective analysis. J Trauma Acute Care Surg 2014;76:62-8.
54. Smith M. Physiologic changes during brain stem death – Lessons for management of the organ donor. J Heart Lung Transplant 2004;23 9 Suppl: S217-22.
55. Randell T, Orko R, Höckerstedt K. Peroperative fluid management of the brain-dead multiorgan donor. Acta Anaesthesiol Scand 1990;34:592-5.
56. Patel MS, Niemann CU, Sally MB, De La Cruz S, Zatarain J, Ewing T, *et al.* The Impact of hydroxyethyl starch use in deceased organ donors on the

development of delayed graft function in kidney transplant recipients: A propensity-adjusted analysis. Am J Transplant 2015;15:2152-8.
57. Blasco V, Leone M, Antonini F, Geissler A, Albanèse J, Martin C. Comparison of the novel hydroxyethylstarch 130/0.4 and hydroxyethylstarch 200/0.6 in brain-dead donor resuscitation on renal function after transplantation. Br J Anaesth 2008;100:504-8.
58. Giral M, Bertola JP, Foucher Y, Villers D, Bironneau E, Blanloeil Y, *et al.* Effect of brain-dead donor resuscitation on delayed graft function: Results of a monocentric analysis. Transplantation 2007;83:1174-81.
59. Darby JM, Stein K, Grenvik A, Stuart SA. Approach to management of the heartbeating 'brain dead' organ donor. JAMA 1989;261:2222-8.
60. Cicciarelli J. UNOS Registry data: Effect of transfusions. Clin Transpl 1990:407-16.
61. Fuller TC, Burroughs JC, Delmonico FL, Rubin NT, Cosimi AB, Russell PS. Influence of frozen blood transfusions on renal allograft survival. Transplant Proc 1982;14:293-5.
62. Cecka M, Toyotome A. The transfusion effect. Clin Transpl 1989:335-41.
63. de la Cruz JS, Sally MB, Zatarain JR, Crutchfield M, Ramsey K, Nielsen J, *et al.* The impact of blood transfusions in deceased organ donors on the outcomes of 1,884 renal grafts from United Network for Organ Sharing Region 5. J Trauma Acute Care Surg 2015;79 4 Suppl 2:S164-70.
64. Niemann CU, Feiner J, Swain S, Bunting S, Friedman M, Crutchfield M, *et al.* Therapeutic hypothermia in deceased organ donors and kidney-graft function. N Engl J Med 2015;373:405-14.