

Variables during care of adult donors that can influence outcomes of kidney transplantation

Publications that relate characteristics of donors to renal function of recipients are reviewed. Most publications report retrospective observations that relate outcomes to donor variables that cannot be altered during donor care. Factors that can be altered in adult donors in an effort to improve recipients' outcomes include urine output and creatinine level. Increasing urine output to more than 100 mL/h, at least during the hour before explantation, and returning the creatinine level to match its serum concentration when the patient was admitted can improve outcomes. Ways of accomplishing those goals during donor care are discussed, with emphasis on support of renal blood flow. (*Progress in Transplantation*. 2005;15:219-225)

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Notice to CE enrollees:

A closed-book, multiple-choice examination following this article tests your ability to accomplish the following objectives:

1. Identify factors that can be altered in adult donors to improve recipients' outcomes of kidney transplantation
2. Discuss interventions used to maintain cardiac output and renal blood flow that are critical to kidney function during donor care
3. Describe clinical interventions that should be avoided during donor care

Kidneys tolerate some variables during transplantation, such as longer ischemia and transport times, better than other organs. This tolerance extends to other donor characteristics noted below and permits wider organ allocation.^{1,2} This discussion, however, emphasizes characteristics that can be modified by procurement coordinators during care of adult donors.

Methods

Publications from 1976 to 2004 that described studies in which characteristics of human adult kidney donors were related to some outcome measure(s) of graft function or status of the recipient after transplantation were obtained from the Pub Med database. Other articles were added from the bibliographies of those publications and the author's files. The statistical analyses used in the studies were recorded, and associations

were specifically sought between outcome measures and characteristics of donors that could be modified during donor care.

Results

The publications reviewed and their results are summarized in the Table. Many were analyses of large databases compiled by the United Network for Organ Sharing, the Organ Procurement and Transplantation Network, the South-Eastern Organ Procurement Foundation, and historically related or similar consortia. Those organizations selected donor criteria and outcome measures for inclusion in their databases, and thus those variables are the only ones available for analysis. Authors select available criteria of interest from those databases. Thus donor information is filtered twice before publication. In addition, data entry may be incomplete for some characteristics, thereby eliminating other donors and/or relevant information. The design of these studies is usually an observational retrospective statistical comparison between selected donor variables and outcome measures to determine whether an association occurs more often than "by chance."²³ Two general statistical testing methods, univariate and multivariate analyses, are often used. Univariate calculations are used to evaluate the association of a single variable or factor with the outcome measure(s). Multivariate analysis incorporates the possible effect of more than 1 factor and mathematically "controls" for the effect of each factor by isolating its inde-

Donor variables and associations with adverse outcomes after kidney transplantation

| Donor variable | Reference number and statistical analysis used | |
|---|---|------------------------------------|
| | Studies confirming adverse effect | Studies not finding adverse effect |
| African American race | 3u,m; 4m; 5m; 6u,m; 7m | 8u; 9m; 10m; 11 other |
| History of hypertension | 3u; 4m; 5m; 12m; 13 other | 3m |
| Cold ischemia time | 3u; 4m; 6u,m; 7m; 9u,m; 14 other | 3m; 8u |
| History of diabetes | 4m; 6u,m; 12m; 13 other; 15 other | 3u,m; 5m |
| Cause of death | 3u; 5m (CVA); 9u,m (CVA); 16m (CVA) | 3m; 7m; 8m; 12m |
| Age | 3u (>51 y old); 4m; 5m (>50 y old); 6u,m (>55 y old); 7m (>35 y old); 8u,m (>55 y old); 9u; 17m (>54 y old); 10m (>50 y old); 14 other (>45 y old, >60 y old); 16m; 13 other (>55 y old); 18 other (>50 y old); 19m (>50 y old) | 20 ns |
| Body mass index or weight | 3u; 4m; 8u; 9u | 3m; 8m |
| Sex | 3u; 4m; 5m; 6m; 7m; 16u | 3m; 8u; 9m; 10m; 12m; 16m; 20ns |
| Creatinine clearance or final serum level of creatinine | 3u; 5m; 8u,m; 13 other; 18 other | 3m; 7m; 12m; 20ns |
| Administration of pressors | | 8u |
| Occurrence of cardiac arrest | | 8u |
| Hypotension or use of vasoactive drugs | 13 other; 18 other; 20ns | 8u; 9m |
| Blood type | 18 other | |
| Length of stay in intensive care unit | 8u; 18 other | 8m |
| Urine output | 18 other | 20ns |
| Proteinuria | 18 other | |
| Central venous pressure | | 20ns |
| Urinary tract infection or bacteremia | | 21ns; 22ns |

Abbreviations: CVA, cerebrovascular accident (stroke); statistical analyses: "m," multivariate; "ns," not specified; "u," univariate.

pendent effect. Various types of multivariate analyses may be used depending on the study question, the variables chosen, and the outcome measures to be compared. In general, a multivariate technique is considered superior to univariate methods in defining if an outcome is most likely a consequence of the selected variable, that is, if a causal relationship is present.²⁴

The table also specifies the statistical method(s) used in the publications. Variables associated from a univariate analysis are labeled "u"; "m" indicates an association from multivariate analysis; "other" indicates that other statistical methods were used; and "ns" means that the statistical tests used were not specified in the publication. An association found by univariate methods may not be substantiated when included in multivariate analysis.

Unfortunately for the purposes of this discussion, most of the donor characteristics chosen, although important for allocation decisions, are not amenable to change during donor care (see Table). However, those few variables that might be altered plus other issues related to donor care are discussed here.

Urine Output

In a 5-year prospective analysis from the South-Eastern Organ Procurement Foundation¹⁸ and a retrospective study from Greece,²⁰ the relationship between the donor's urine output before nephrectomy and the recipient's outcome was assessed. Grekas et al²⁰ found no association between delayed graft function and the donor's final 24-hour urine output.

When the donor's final 1-hour urine output was greater than 100 mL, however, Lucas et al¹⁸ reported that a higher percentage of the implanted kidneys had better immediate function and 1-year graft survival than when the donor's output was lower. Urine output in the last hour before transplantation appeared to be more important than maximum or minimum hourly urine output throughout earlier donor care. Unfortunately, no information is provided about the percentage of donors who required fluid administration, diuretics, vasopressor support, or, conversely, antidiuretic hormone, to achieve that benchmark urine flow. Extreme urine output (>300 mL/h) did not show the same benefit. The authors emphasize the obvious rela-

relationship between supporting components of cardiac output and ensuring renal perfusion.^{18,25}

Serum Level of Creatinine

Serum level of creatinine reflects the filtration rate of blood through the renal glomeruli and is a measure of the kidneys' ability to remove creatinine, one of the many metabolic compounds produced in the body and excreted through the urinary system. Creatinine level is also considered a measure of the quantity of remaining nephrons in the kidney, that is, the "renal reserve" available to the recipient.^{7,8} Nephrons may be lost over time as a result of hypertension, atherosclerotic vascular disease, or diabetes, thus elevating the serum level of creatinine. Additional nephrons are usually lost after transplantation because of rejection and other factors. A low serum level of creatinine in the donor indicates that the renal reserve may be sufficient for the recipient to tolerate the anticipated loss of nephrons after transplantation and still have adequate renal function. The maximum level, final level, and change in level of serum creatinine were examined by Lucas et al.¹⁸ An improving serum level of creatinine, as long as the maximum level was less than 2 mg/dL (176.8 μ mol/L) appeared to have a favorable effect on graft function in recipients. Port et al.,⁵ however, found that a serum level of creatinine that exceeded 1.5 mg/dL (132.6 μ mol/L) just before explantation shortened the time to graft failure. In a retrospective study, Kouli et al.⁸ found that an elevated serum level of creatinine (not specified) in donors was associated with worse renal function in recipients 2 and 3 years after transplantation.

Creatinine clearance represents the dynamic process executed by the kidney to remove creatinine from the blood. Some consider creatinine clearance to be a better assessment of renal status than is serum level of creatinine alone. Creatinine clearance is reported as the volume of blood from which creatinine would be removed per minute; normal creatinine clearance is about 125 mL/min.

Most commonly, creatinine clearance is calculated from a measured 24-hour urine collection, but estimates from shorter collection times may be used. Creatinine clearance can also be estimated from single blood measurements of the serum level of creatinine by using the Cockcroft-Gault equation:

$$(140 - \text{age in years}) \times \text{lean body wt (kg)} \\ \text{Serum level of creatinine (mg/dL)} \times 72$$

This equation is intended for calculation of creatinine clearance in men; values for women are calculated with the same equation but the result is multiplied by 0.85 to yield the final estimated creatinine clearance.

Clinical Considerations

These publications present limited data in support of ensuring that the donor's urine output remains at

approximately 100 to 300 mL/h. In the general population of patients, the serum level of creatinine usually reflects renal performance over a longer period than a single hospitalization. However, among patients who become donors, many factors during neurosurgical/neurological and subsequent donor care may jeopardize normal renal function and reversibly increase the serum level of creatinine. Those factors include intentional dehydration leading to serum hyperosmolarity; unintentional hypovolemia while attempting dehydration; administration of mannitol, which can directly injure renal tubular cells; and hypotension or relative hypovolemia after vascular dilatation during the evolution of brain death. The kidneys, therefore, are at high risk for injury before and during donor care. The challenge for procurement coordinators is to reverse all renal injuries that might have been temporary. An important indicator of achievable renal reserve is the serum level of creatinine when the patient was admitted. The organ procurement coordinator should strive to at least return the serum level of creatinine to its level at admission.

Improvement and/or maintenance of renal blood flow is the most important goal for kidney support. Renal blood flow depends on the factors that determine cardiac output; namely, preload, heart rate, afterload, and contractility. These factors are discussed elsewhere²⁵⁻²⁷ and are not reviewed further here. Other treatments, noted below, may be important to ensure urine output or an optimal serum level of creatinine and to avoid potential harm.

Diuretics

Diuretics primarily produce an effect by disrupting a normal physiological process, either by causing an unnatural osmotic burden (mannitol) or by interfering with normal reabsorption of fluids and electrolytes in the renal tubules (furosemide and others). No publications examined treatment with diuretics to maintain urine output during donor care. However, administration of diuretics should not be the first response to decreasing urine output. Cautious administration of fluids with an appropriate colloid, crystalloid, or blood product and appropriate hemodynamic monitoring should initiate therapy. Further treatment may include diuretics if the preload is adequate, but the dosage of diuretics should be titrated on the basis of cardiovascular parameters and the resulting urine output.

Diabetes Insipidus

Medications intended to decrease polyuria caused by diabetes insipidus should be given carefully so as to avoid an excessive reduction in urine output.²⁸ Lucas et al.¹⁸ showed that maintaining donors' urine output above 100 to 300 mL during the final hour of care did not

increase the percentage of functioning kidneys 1 year after transplantation. Polyuria is, therefore, not beneficial. Careful titration of fluid balance by using aqueous vasopressin or desmopressin and appropriate replacement of fluids lost as urine may ensure that urine flow is adequate while avoiding drug-induced oliguria.²⁸⁻³⁰

Dopamine

Low-dose dopamine has been advocated to stimulate intrarenal dopaminergic receptors so as to improve kidney function and increase urine output.^{31,32} Other authors³³⁻³⁵ have not agreed, and although the donor population has not been selectively studied, it appears that the use of low-dose dopamine to increase urine output cannot be supported.

Hetastarch

One prospective study³⁶ has indicated that the administration of hetastarch to donors is associated with early failure of renal grafts, earlier need for hemodialysis among recipients, and worse function of the transplanted kidney 1 and 5 years after transplantation.³⁷ Similar findings in intensive care patients reflect abnormal renal function and coagulation after various forms of hetastarch are given.³⁸⁻⁴⁰ Other authors⁴¹⁻⁴³ disagree. Therefore, whether hetastarch (eg, Hespan, Hextend) should be used as a resuscitation fluid should be specified in the protocol of each organ procurement organization.

Blood Transfusion

Blood transfusion may be needed to support oxygen delivery to all organs but also provides intravascular fluid to support preload and potentially renal blood flow and urine output. A variety of harmful effects following transfusion, possibly germane to donor care, have been identified:

- Acute lung injury up to 4 hours after transfusion; suggested to be due to antibodies and lipids from small amounts of plasma within packed red cell transfusions⁴⁴
- Allergic hemolytic and febrile responses, sensitization to platelet and white blood cell antigens, and rare transmission of viral infections (eg, HIV, hepatitis, cytomegalovirus)^{45,46}
- Unspecified effects on the immune system leading to increased nosocomial infections⁴⁵; although this complication clearly influences care of patients in the intensive care unit, it is not clear if donors would be affected if transfusions were given after brain death
- Possibly reduced oxygen delivery to donor organs; red blood cells stored in blood banks for more than 15 days may not carry oxygen effectively and may contain more circulating cytokines⁴⁷⁻⁴⁹

The relationship between nosocomial infection and blood transfusion appears to depend on the white blood cells remaining in the transfusion red cell pack. Spe-

cially centrifuged (“leukocyte-depleted” or “leukocyte-poor”) red cell preparations significantly reduce the risk of nosocomial infection.⁴⁵ These preparations, however, are more costly than other red cell preparations and have not been evaluated among donors.

These several issues have supported lowering the “transfusion threshold” for critically ill patients^{50,51} to a hematocrit of 0.23 unless cardiovascular compromise is significant.⁴⁷ The consequences of minimizing the hemoglobin concentration or hematocrit among donors have not been studied.

It is, therefore, important for each organ procurement organization to establish the lowest acceptable hemoglobin concentration or hematocrit beyond which blood transfusion is needed. Similarly, each organ procurement organization should consider possible benefits of leukocyte-depleted packed red cells. It is unlikely that blood substitutes are presently suitable for administration to donors, but ongoing clinical trials may soon indicate specific advantages.^{52,53}

Administration of Catecholamines

The table does not show any association of hypotension among donors or use of vasoactive medications by donors with adverse outcomes after renal transplantation. However, data support a beneficial effect from administration of some catecholamines (dopamine and norepinephrine,⁵⁴⁻⁵⁶ but not epinephrine⁵¹) independent of a blood pressure effect. Possibly related to the down-regulating effects of proinflammatory mediators on intravascular receptors, administration of catecholamines has been associated with improved longer-term survival of renal allografts.⁵⁵ It must be noted, however, that use of catecholamines was also associated with worse outcome for liver and heart transplantation.⁵⁴ Any possible benefit for the kidneys, therefore, might be justified only if other organs had been declined. No other corroborating studies could be found. Therefore, administration of catecholamines, except for blood pressure support, is difficult to support on the basis of current published data.

Infection

In 2 studies,^{21,22} kidneys from donors with bacteremia, urinary tract infections, or both could still be transplanted. Battaglia et al²¹ recommend that the presence of *Pseudomonas aeruginosa* or *Candida albicans* in urine or blood, however, should exclude kidneys from procurement. Appropriate treatment of known pathogens at any site in the donor is expected to continue in the recipient.

Summary

Interventions to maintain cardiac output and hence renal blood flow and urine output are critical to kidney function during donor care. Ensuring effective

cardiac preload and contractility while controlling afterload best maintains urine output and the potential to reduce serum level of creatinine to the lowest concentration possible, thus maximizing renal reserves. Minimizing cold ischemia time remains important, but the cold ischemia time is most often a function of final allocation decisions. Use of low-dose dopamine, diuretics, and hetastarch should probably be avoided. Blood transfusions should be used in accord with the protocol at each organ procurement organization to maintain a minimally acceptable hemoglobin concentration or hematocrit.

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Learning objectives: 1. Identify factors that can be altered in adult donors to improve recipients' outcomes of kidney transplantation
 2. Discuss interventions used to maintain cardiac output and renal blood flow that are critical to kidney function during donor care
 3. Describe clinical interventions that should be avoided during donor care

1. Which of the following donor variables has had the most studies associated with adverse advents?

- a. Hypertension
- b. Age
- c. Body mass index
- d. Diabetes

2. Which of the following parameters of urine output appear to be more important throughout earlier donor care?

- a. Maximum hourly urine output
- b. Minimum hourly urine output
- c. Urine output in the last hour before transplantation
- d. Urine output in the first hour after transplantation

3. What level of serum creatinine has been associated with favorable effects on graft function in transplant recipients?

- a. <2 mg/dL
- b. 2.0-2.5 mg/dL
- c. 2.5-3.5 mg/dL
- d. >3.5 mg/dL

4. What is the normal creatinine clearance?

- a. 50 mL/min
- b. 100 mL/min
- c. 125 mL/min
- d. 200 mL/min

5. What level of serum creatinine has been demonstrated to be an important indicator of achievable renal reserve?

- a. The level before transplantation
- b. The level upon hospital admission for transplantation
- c. The level 1 day after transplantation
- d. The level 1 month after transplantation

6. Which of the following clinical parameters is the most important goal for kidney support?

- a. Maintenance of baseline creatinine
- b. Maintenance of adequate urine output
- c. Maintenance of renal blood flow
- d. Maintenance of adequate blood pressure

7. Which of the following interventions cannot be supported for renal blood flow?

- a. Diuretics
- b. Hetastarch
- c. Blood transfusion
- d. Dopamine

8. For how many days have red blood cells that may not carry oxygen effectively and may contain more circulating cytokines been stored in blood banks?

- a. 5 days
- b. 5 to 10 days
- c. More than 15 days
- d. More than 30 days

9. Which of the following types of transfusions can significantly reduce the risk of nosocomial infections?

- a. Whole blood transfusion
- b. Packed red blood cell transfusion
- c. Leukocyte-rich transfusion
- d. Leukocyte-depleted transfusion

10. What level of hematocrit is considered the "transfusion threshold" for critically ill patients?

- a. 0.23
- b. 0.25
- c. 0.28
- d. 0.30

11. Which of the following donor variables is not associated with confirmed adverse effects after kidney transplantation?

- a. Hypertension
- b. Age
- c. Body mass index
- d. Urinary tract infection

12. Which of the following donor variables has had the most univariate studies conducted on outcomes after kidney transplantation?

- a. Blood type
- b. Age
- c. Body mass index
- d. Sex

13. Which of the following donor variables has had the most multivariate studies conducted on outcomes after kidney transplantation?

- a. Hypertension
- b. Age
- c. Body mass index
- d. Creatinine level

Test answers: Mark only one box for your answer to each question. You may photocopy this form.

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| <input type="checkbox"/> c | <input type="checkbox"/> c | <input type="checkbox"/> c | <input type="checkbox"/> c | <input type="checkbox"/> c | <input type="checkbox"/> c | <input type="checkbox"/> c | <input type="checkbox"/> c | <input type="checkbox"/> c | <input type="checkbox"/> c | <input type="checkbox"/> c | <input type="checkbox"/> c | <input type="checkbox"/> c |
| <input type="checkbox"/> d | <input type="checkbox"/> d | <input type="checkbox"/> d | <input type="checkbox"/> d | <input type="checkbox"/> d | <input type="checkbox"/> d | <input type="checkbox"/> d | <input type="checkbox"/> d | <input type="checkbox"/> d | <input type="checkbox"/> d | <input type="checkbox"/> d | <input type="checkbox"/> d | <input type="checkbox"/> d |

Test ID: 4000-J41 Form expires: September 1, 2007 Contact hours: 1.5 Fee: \$11 Passing score: 10 correct (77%) AACN category: A ABTC category: I
 Test writer: Ruth Kleinpell-Nowell, RN, PhD, CS, CCNS

AMERICAN
ASSOCIATION
of CRITICAL-CARE
NURSES

Mail this entire page to:

AACN
101 Columbia
Aliso Viejo, CA 92656
(800) 899-2226

Program evaluation

| | Yes | No |
|--|--------------------------|--------------------------|
| Objective 1 was met | <input type="checkbox"/> | <input type="checkbox"/> |
| Objective 2 was met | <input type="checkbox"/> | <input type="checkbox"/> |
| Objective 3 was met | <input type="checkbox"/> | <input type="checkbox"/> |
| Content was relevant to my nursing practice | <input type="checkbox"/> | <input type="checkbox"/> |
| My expectations were met | <input type="checkbox"/> | <input type="checkbox"/> |
| This method of CE is effective for this content | <input type="checkbox"/> | <input type="checkbox"/> |
| The level of difficulty of this test was: | | |
| <input type="checkbox"/> easy <input type="checkbox"/> medium <input type="checkbox"/> difficult | | |
| To complete this program, it took me _____ hours/minutes. | | |

Name _____
 Address _____
 City _____ State _____ ZIP _____
 Social Security No. _____ Phone () _____
 If applicable: State(s) of licensure _____
 License number(s) _____
 ABTC certification number _____
 CPTC, expiration _____
 CCTC, expiration _____
 I would like to receive my certificate via e-mail.
 E-mail address: _____