Renal Donation after Cardiac Death

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Renal transplantation is the treatment of choice for most patients with ESRD because transplantation dramatically improves both the length and the quality of life for dialysis patients. More than 80,000 patients in the United States are on the deceased-donor waiting list, with average wait times now exceeding 5 years. Yearly mortality on the deceased-donor list exceeds 6% per year and 10% per year in high-risk groups such as patients with diabetes. More patients are now thought to die while waiting for a deceased donor transplant than actually receive one.

The burgeoning use of kidneys from extended-criteria donors (ECDs) and donation after cardiac death (DCD) has positively affected the shortage of kidneys. ECD kidneys now account for 18% of all renal transplantations performed in the United States. Unfortunately, this seems to be because the resource may have reached its ceiling for the maximum number of potential organs available to procure."1 The survival benefits of ECD kidneys have been validated in high-risk dialysis populations (age >40 years and history of diabetes, among others), in whom concerns regarding the ECD kidney, such as 70% decreased survival compared with standard-criteria donors (SCDs), are outweighed by the increased mortality and morbidity of remaining on dialysis.2

DCD kidneys have excellent short- (1 year) and long-term (10 to 15 years) survival with outcomes similar to SCD kidneys.3 In a 1997 editorial in Clinical Transplantation, Terasaki et al.4 predicted that full use of DCD kidneys could resolve the shortfall of the kidney supply. Although DCD kidneys now account for 10% of all deceased donors in the United States, they remain underused still.

There is a reluctance to use DCD kidneys in general and by select transplant centers in particular because of an expected higher rate of delayed graft function (DGF) and primary graft nonfunction. DGF rates are reported, center “report cards” may affect contracts with commercial payers, and new transplant referrals to the transplant center can be adversely affected by an increase in DGF. In addition, DGF leads to extended hospital stays, resulting in increased costs that lower the prof-

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See related article, “Reactive Oxygen Species Promote Caspase-12 Expression and Tubular Apoptosis in Diabetic Nephropathy,” on pages 943–954.


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itability of using DCD kidneys. Interestingly, several groups reported that DGF does not increase the risk for acute rejection and does not result in diminished long-term outcomes as experienced with SCD kidneys.5–7 In addition, time on dialysis is a major risk factor for decreased allograft and patient survival. As short as 6 to 12 months of pretransplantation dialysis associates with a 37% increase in long-term graft loss compared with preemptive transplantation.8 A recent study observed that 50% of patients who were older than 60 years died before receiving a transplant.9 An effective DCD program would markedly decrease waiting times, which may improve the survival and quality of life for many who are currently on deceased-donor waiting lists.7

Despite the aforementioned issues, the study by Snoeijis et al.10 in this issue of JASN provides strong support for the use of DCD kidneys. This large observational cohort study includes all patients registered on the Dutch waiting list for their first renal transplant during a defined 5-year period. The authors convincingly show the use of DCD kidneys reduces overall mortality rates by 56%, which translates into 2.4 months of increased life expectancy during the first 4 years after transplantation. The authors carefully accounted for potential confounders and bias in their analysis and conclude that a greater allograft longevity advantage would be realized with longer follow-up. The use of a sequential stratification analysis, which rigorously compares transplant recipients only with those still active on the waiting list, prevents a common selection bias that would have overestimated allograft survival. Recent reports suggested that approximately 33% of patients on the deceased-donor waiting list are inactive because of undercurrent illness but are still incorporated in statistical analyses.11

The results of the study by Snoeijis et al.10 are more robust when one considers the lack of selectivity demonstrated for donor organs and recipients. Age and comorbidities are effect modifier of gender disparities,12 and the DCD recipients here are statistically older (4.8 years) and higher percentages are male than in the SCD population. Older age and male gender are known to reduce allograft outcomes, as does donor age as it relates to aortic stiffness in recipients.13 The authors also used a high percentage (12%) of DCD organs obtained during an uncontrolled cardiac death. Organs procured in this manner are expected to experience greater warm ischemia times and higher rates of primary nonfunction than controlled cardiac death kidneys. The large University of Wisconsin experience previously supported controlled donation to minimize the incidence of primary nonfunction and graft loss within the first 30 days by reducing warm ischemia time to <30 minutes.5

In addition to the previously discussed technical issues regarding DCD donation, ethical concerns historically have remained a barrier and limit use of DCD kidneys. A consensus conference with broad representation elucidated areas of controversy, including recommendations of death determination that is in concert with the Society of Critical Care Medicine. The Joint Commission now also requires hospitals to have a specific protocol in place regarding organ donation after cardiac death to prevent, for example, conflicts of interest between independent organ procurement and critical care teams. Hospitals still have the option to forgo DCD donation if the providers, nurses, or families find it unacceptable; however, the donor family should be provided education regarding common misconceptions to allay fears. There should be reassurance that strict determinations of death are in place to ensure patients are not alive when procurement occurs.14

The discrepancy in our nation’s renal transplant supply versus demand is expected to grow as the population ages, as the prevalence of diabetes increases, and with the increased need for a growing number of patients whose previous allografts fail to undergo retransplantation. The study by Snoeijis et al.10 adds to a considerable body of evidence that long-term outcomes with DCD kidneys are equivalent to SCD kidneys, and it is one of the first studies to demonstrate improved patient survival versus remaining on the deceased-donor wait list. Regulatory organizations can reduce disincentives that limit DCD use by placing less emphasis on delayed graft function rates in this setting. With increasing experience, guidelines and validated selection criteria will emerge to assist transplant centers in accepting DCD organs that are likely to be successful. Viability testing, the use of automated chest compression devices, and extracorporeal membrane oxygenation promise to lower warm ischemia times and result in less short-term complications.15

In short, the preponderance of evidence supports the placement of DCD organs. Although barriers to success exist, many of the concerns are more perceptual than actual and may dissipate with further knowledge and experience. Transplant centers should maximally use DCD kidneys to optimize the quality of life and minimize mortality of their patients on the waiting list.

DISCLOSURES

None.

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DISCLOSURES

None.

The clinical importance of nephron mass is a widely recognized determinant of renal fate and function. Those who are born with adequate numbers of nephrons get through life with less risk for cardiovascular and chronic kidney disease. Size also matters when it comes to selecting a donor for renal allograft transplantation. In their interesting and provocative article in this issue of JASN, Giral et al describe a new clinical marker of allograft success: The ratio of the weight of the renal allograft before implantation to the recipient weight, or Kw/Rw.

Recipients of a kidney with a Kw/Rw of <2.3 g/kg had worse long-term graft survival, worse long-term graft function as measured by the GFR, more proteinuria, more hypertension, and more glomerulosclerosis than recipients of a kidney with a Kw/Rw of >2.3 g/kg. These investigators describe this risk for deterioration in graft function as occurring late, beyond 7 years after transplantation. They based their observations on an analysis of more than 1000 adult patients, virtually all deceased-donor kidney recipients. Not surprising, more female donors and male recipients were associated with lower ratios. The occurrence of acute rejection also had a more detrimental effect in patients with a low Kw/Rw.

These observations represent a new and elegant way of quantifying the potentially negative effect of nephron underdosing and make the additional point that this effect takes a longer time to appear after transplantation than we once thought. Most studies of outcomes after kidney transplantation suffer from the problem of insufficient follow-up, and, in fact, the authors’ previous publication on this subject showed no impact of Kw/Rw on 3-year outcomes.

There are some caveats to consider. Because living donors made up <1% of the case material, it is not clear that these observations hold true in anyone other than recipients of deceased-donor kidneys. Kidneys from very young pediatric donors might also be associated with different outcomes, particularly when transplanted en bloc. No data in this article address these issues.

One may also speculate whether the current observation would hold true for recipients who were not receiving long-term calcineurin inhibitors. If calcineurin inhibitor–sparking or other avoidance regimes are used in an increasing percentage of patients, it will be interesting to see whether these observations on weight ratios remain relevant. Finally, it will be important to replicate these provocative observations of Giral et al in other large cohorts of patients with sufficiently long follow-up. In the meantime, the authors are to be congratulated for describing a novel measure that may have important implications for long-term outcomes in renal allograft recipients.

Size Matters in Renal Allograft Survival
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The clinical importance of nephron mass is a widely recognized determinant of renal fate and function. Those who are born with adequate numbers of nephrons get through life with less risk for