Transplantation and the Primary Care Physician

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Increasing appreciation of the survival benefits of kidney transplantation, compared with chronic dialysis, has resulted in more patients with kidney disease being referred and receiving organs. The evolving disparity between a rapidly increasing pool of candidates and a smaller pool of available donors has created new issues for the physicians who care for kidney patients and their potential living donors. This article outlines current efforts to address the growing number of patients who await transplantation, including relaxation of traditional donation criteria, maximization of living donation, and donation schemas that permit incompatible donor–recipient pairs to participate through paired donation and transplantation chains. New ethical issues faced by donors and recipients are discussed. Surgical advances that reduce the morbidity of donors are also described, as is the role of the primary physician in medical issues of both donors and recipients.

Key Words: Kidney transplantation, Organ donation, Living donors, Kidney paired donation

Kidney transplantation offers patients with severe kidney failure both improved quality of life and increased survival. Advances in immunosuppressive regimens have increased the success of transplantation operations, and long-term survival of an initially successful graft averages 10 to 11 years for a cadaver kidney and 18 to 19 years for a living donor organ.[1] Transplantation is also cost-effective; maintaining a functioning transplant patient over the course of a year can be achieved for 30% to 40% of the cost of maintenance hemodialysis. Increasing numbers of patients are living with successful kidney transplants, and may interact with the health care system in various ways, not always through nephrologists or transplantation centers. Kidney transplant recipients have increased susceptibilities to accelerated atherosclerosis, malignancy, and infections. Over the past 20 years, kidney recipients have received more intensive perioperative immune conditioning regimens, and cyclosporine and azathioprine have been largely supplanted by tacrolimus and mycophenolate.[1] A multitude of new approaches to chronic antirejection therapy are being developed, and active areas include the need for chronic corticosteroids, and whether exposure to calcineurin inhibitors (cyclosporine and tacrolimus) can be reduced without incurring increased rejection. These approaches are well documented elsewhere, and are primarily of interest to nephrologists.

The Role of the Primary Care Physician

Nephrologists, however, see only a fraction of the patients with CKD. Many patients who could benefit from astute preparation for kidney transplantation are cared for by primary care physicians, who can promote the chances of expedited transplant candidacy by meticulous care of cardiovascular and infectious comorbidities, early patient education, and appropriately timed referral to transplantation resources. Early preparation becomes increasingly important with the recognition of the survival advantages accruing to patients who receive kidney transplants without having been subjected to dialysis therapies. Donation of kidneys has not kept pace with the number of people awaiting transplant and has decreased over the past 5 years, despite increased willingness of transplant teams to use older and less stringently selected organs. The initiatives of organ procurement agencies have not overcome obstacles to consent that arise from public misinformation and fear. Even in countries where deceased donation consent is presumed, kidney transplantation is not available without waiting; the increase in deceased donor kidneys in these countries is partially offset by decreased living donation. In the United States, where consent for donation must be explicitly obtained from patients or family members, decisions regarding donation may be heavily affected by regional and ethnic considerations. The decision for donation may therefore occur at difficult and stressful times, and the support and guidance of a knowledgeable and trusted primary physician is likely to be both comforting and productive. The primary care physician may represent the potential kidney transplant recipient, and is certainly the impartial advocate for the interests of a living kidney donor or a potential kidney donor. This discussion therefore will focus on the medical issues surrounding living donors and kidney recipients.

The Organ Shortage: Magnitude of the Problem

Approximately one-third of a million Americans live with kidney disease and dialysis. According to the Organ Procurement and Transplantation Network, almost 88,000 patients currently wait for kidney transplants in the United States. The waiting list increases continually,

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as the 14,000 to 16,000 kidney transplants performed each year are more than replenished by entry of new patients on the list. Depending on blood type, geographical region, and immunological sensitization, a patient on the waiting list may wait between 2 to 7 years for a cadaver organ to become available. Many patients die, still awaiting transplantation. Studies suggest that survival is greater among patients who receive kidney transplants than among matched patients who remain on the waiting list,[2] suggesting that some of these deaths might be attributable to long waiting times.

Expansion of the Cadaver Donation Criteria

Recognition of waiting time as a risk factor for mortality has driven a number of strategies to expand the pool of transplantable organs. Survival data from the Organ Procurement and Transplantation Network and the Scientific Registry of Transplant Recipients were examined to evaluate the impact of deceased donor criteria on the risk for graft failure. Using a Cox proportional hazards model, criteria were determined to define a relative risk of 1.7 for graft failure. Donor age >60 years was sufficient as a single criterion, or the presence of 2 of the following in a donor aged 50 to 59 years: renal insufficiency (defined as a terminal serum creatinine level of >1.5 mg/dL), hypertension, or death due to cerebrovascular accident.[3] Kidneys from donors who meet these criteria are known as "expanded criteria donor (ECD)" kidneys.[4] Use of ECD kidneys, previously not considered as transplantable because of increased risk of primary nonfunction, is now considered acceptable for a selected population of potential recipients.[5] The decision of whether to accept a possible ECD kidney is made as part of the initial waiting list registration; patients remain listed for standard criteria kidneys, but are more likely to receive an ECD kidney because the pool of potential recipients competing for each ECD kidney does not include the recipients who do not accept ECD organs. The decision for ECD transplantation requires meaningful recipient informed consent, which in turn requires superb communication between the kidney recipient and the transplantation team. Currently, ECD kidneys represent 18% of cadaver organs.[6] Acceptance of an ECD kidney predictably reduces both 1-year graft survival (from 90% to 82%) and patient survival (from 95% to 91%), but long-term survival may be up to 17% higher than patients who remain on the waiting list, in certain groups.[5,7] An individual recipient's decision to consider receiving an ECD allograft must be guided by an honest assessment of his/her potential to survive additional time on the waiting list, the amount of anticipated waiting time, and the potential for less successful engraftment. An algorithm to estimate risks and benefits of accepting an ECD kidney was introduced in 2005.[5] Patients with factors associated with lower survival, such as diabetes, hypertensive nephropathy, and advanced age, may benefit from accepting an ECD kidney. Patients who may anticipate spending more than 44 months on the waiting list, based on the performance of their regional organ procurement organization, and the disparity among races in organ donation, may also benefit from consideration of an ECD kidney.[3,5]

CLINICAL SUMMARY

- Kidney transplantation has proven benefits compared to dialysis, but wait-list time is increasing due to a critical shortage of available organs.
- Advocacy of physicians for living and deceased kidney donation may improve the availability of organs.
- Expanded strategies for recruitment of living and deceased donors, including paired-donor programs, can increase transplantation.
- The reduced morbidity of laparoscopic donation surgery may encourage more kidney donation.
- Kidney recipients present complicated issues that require deftly coordinated care from their front-line physicians, nephrologists, and transplant clinics.

Organ Trafficking and Transplantation Tourism

The ethical justification for ECD transplantation cannot be extrapolated to the procurement of kidneys from vulnerable groups of donors, who are often motivated by economic despair or other types of coercion. "Transplant tourism," in which well-funded patients from developed nations seek readily available organs among impoverished citizens of other countries, is an unethical practice that persists despite worldwide condemnation in the Declaration of Istanbul on Organ Trafficking and Transplant Tourism.[8] Patients seeking information from their physicians regarding the advisability of this practice also need to be aware that the outcomes of such transplants are compromised due to high rates of acute rejection and severe infectious complications. Transplantation operations occurring in these profit-motivated settings were rarely accompanied by induction immunosuppression therapy or appropriate prophylactic therapy for pneumocystis or cytomegalovirus (CMV). Patients not infrequently returned to their native countries in medical crisis, with insufficient documentation to guide physicians following their care. The rate of infections among returning transplant tourists exceeded 50%, and included life-threatening sepsis. One-year graft and patient survival rates were significantly lower than a matched population transplanted under standard conditions.[9]

Strategies to Expand the Living Donor Pool

Even with expanded criteria, cadaver organ allocation is inadequate to meet the needs of waitlisted patients;