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High-Risk Donors: Expanding Donor Criteria

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IN THE CURRENT era of transplantation, the limitation of the cadaveric donor pool has necessitated a re-evaluation of donor criteria to include organs that were previously considered high risk. The number of patients on the waiting list for all organs has since increased by 22% per year so that by the end of 1995, a total of 44,000 patients were registered (13,000 extrarenal and 31,000 renal).[1] Concurrently, deaths on the waiting list have increased by 18% per year while the total number of transplantations has only increased by 8% per year. In 1996, 13,000 kidney transplants were performed in the United States and 934 in Canada. Simultaneously, the number of cadaveric organ donors has remained relatively static, with only a 4% increase per year from 1988 to 1994. Most of this incrementally small increase has been through the use of "expanded" donors, reflected by the fact that the use of donors older than 50 years old increased by 24% per year from 1988 to 1994, while those younger than 50 years increased by only 1.5% per year. In 1996, there were a total of 4,500 cadaveric donors in the United States and 450 in Canada, representing a donor rate of approximately 15 per million population, which has been static since 1987[2,3] despite estimates of potential organ donor rates of up to 50 per million population. A large study of the characterization of the potential renal organ donor pool in Pennsylvania concluded that the current ratio of organ donation could be increased by at least a factor of 2.[4] To increase the potential donor supply, the implementation of presumed consent and financial incentives for donation have been proposed. In the United States, public attitude towards organ donation is such that presumed consent would probably not be acceptable. There has been resistance to financial incentives to the donor family because of the perceived danger of this escalating to the selling of organs as currently takes place in Southeast Asia and India. Efforts to expand the donor pool in this country are therefore limited to expanding the criteria for the use of "suboptimal" organs. This group would include kidneys from young (younger than 5 years old) pediatric donors, older donors, donors testing positive for hepatitis C antibody (HCV+), diabetic and hypertensive donors, and nonheartbeating donors (NHBD).

THE PEDIATRIC DONOR

In a report from the UCLA Transplant Registry, kidneys from donors younger than 10 years old accounted for less than 10% of first cadaver donor kidneys between 1984 and 1989.[5] There has been no significant increase in this utilization rate during the last 10 years. Overall, kidneys from donors aged 1 to 5 years had the lowest graft survival rate (68% at 1 year) followed by donors aged 6 to 10 years (70%) compared to the best survival rate (81%) using kidneys from donors aged 16 to 18 years.[5] As recently as 1990, very poor survival rates of kidneys from donors younger than 3 years have been reported, with only a 40% 1-year graft survival from donor kidneys aged 13 months to 3 years and an extremely poor 19% 1-year graft survival using donors younger than 1 year.[6] Other studies have recommended that even older pediatric donors (younger than 10 years) should not be used.[7] Despite these apparently dismal results with young pediatric donors, several institutions, including our own, have used these kidneys with success rates approaching those of adult donor kidneys. Pediatric donor kidneys may be used as single units or transplanted en bloc. We have used the en bloc approach to transplant pediatric kidneys from cadaveric donors younger than the age of 5 years.[8,9] In our most recent published experience,[10] recipients of pediatric en bloc kidneys, when compared with recipients of adult cadaveric kidneys, have comparable 1- and 3-year patient survival rates (94% and 94% versus 95% and 91%, respectively) and comparable 1- and 3-year graft survival rates (84% and 84% versus 89% and 79%, respectively). Renal function was better in recipients of en bloc kidneys, with a mean serum creatinine (SCR) level of 1.4 ± 1.8 mg/dL versus 2.0 ± 1.5 mg/dL (P = .01). Overall, growth and development of pediatric en bloc kidneys is excellent. A doubling of renal size is usually found within the first 3 months after transplantation on radiologic examination with significant improvement in

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calculated glomerular filtration rates (GFR).[10,11] Some investigators have preferred to transplant kidneys from very young pediatric donors as single units. Lippman et al used single kidneys from donors aged 11 to 48 months in 50 cases.[12] One-year graft survival was reported at 71% compared with 76% in recipients of adult donor kidneys at the same institution. Other investigators who have used single pediatric kidneys have reported 1-year graft survival rates of 84%.[13] Regardless of the method of transplanting these small kidneys, it has become clear that excellent graft survival rates may be achieved. These organs are an underused resource that could have a significant impact on increasing the donor pool.

THE OLDER DONOR

Reluctance to use kidneys from older donors is based on the structural changes in the aging kidney including loss of glomeruli, reduction of glomerular surface area, overall reduction of functional renal mass, as well as obliteration of cortical vessels and spiraling of medullary arterioles with resulting functional changes in renal blood flow, GFR, and concentrating capacity.[14] These structural changes are not universal and may not occur in all donors. Therefore, at our center we no longer place a strict upper age limit for cadaveric renal donors. We evaluate each donor individually on the basis of the available medical history and renal function, including SCR and 4-hour creatinine clearance during the period immediately preceeding organ recovery. Open renal biopsy with frozen section examination are performed for donors older than 50 years or with a history of significant hypertension. The kidney is generally used if there are fewer than 20% sclerotic glomeruli and if the degree of interstitial fibrosis is mild or less. In an earlier study from our institution, Vivas et al[15] found that in 31 cadaver kidneys from donors older than 60 years of age, 1-year graft survival was 65%; however, those kidneys that had a cold ischemia time (CIT) of more than 48 hours had a much inferior graft survival of 38% compared to those kidneys with CIT less than 48 hours, which had a very acceptable 76% 1-year graft survival. In our most recent experience[10] with donors older than 60 years of age, compared with donors younger than 60 years of age, we observed worse 1- and 3-year patient survival rates (88% and 80% versus 96% and 94%, respectively, $P < .03$) and poorer 1- and 3-year graft survival rates (74% and 62% versus 91% and 83%, respectively; $P < .0001$). Renal function was also decreased in the older group, with an SCR level of 2.7 ± 1.2 mg/dL versus 1.9 ± 1.5 mg/dL ($P = .01$). The functional reserve of such older donor kidneys may be limited and hence any increased insult including prolonged CIT, nephrotoxic drug injury, or rejection may limit the eventual outcome. We have also recently begun using "expanded" pancreas donors (older than 45 years and/or vasopressor support) with acceptable results.[16] It has recently been proposed that older donor kidneys that would otherwise be discarded can be used as double organs,[17] but long-term outcome is still unknown.

THE HYPERTENSIVE AND DIABETIC DONOR

Madden reported 88 patients who received cadaveric kidneys from donors with a history of either diabetes or hypertension ("non-ideal") were compared to 440 recipients of "ideal" organs.[18] Although the overall graft survival of the non-ideal organs was somewhat less (69% versus 74%), these differences were not significant. Again, these kidneys should be evaluated on an individual basis by biopsy and donor history.

FEMALE DONORS

Female donors have been associated with inferior graft survival after renal transplantation. In our experience,[10] female donor kidneys, compared with male donors, are associated with comparable 1- and 3-year patient survival rates (96% and 93% versus 95% and 92%, respectively) and comparable 1- and 3-year graft survival rates (90% and 80% versus 88% and 81%, respectively). Renal function was also similar.

THE DONOR WITH HEPATITIS C

The use of the hepatitis C (HCV)+ donor organ is controversial and is a subject of ongoing current debate. Prevalence of HCV positivity in organ donors has been reported to be between 2% and 6% with contradictory data with respect to the risk of transmission of HCV from positive organ donors. Some of this confusion may have arisen from the methods of detection of HCV positivity, which in many early studies relied on a first generation assay with a significant false-positive rate. Pereira et al[19] showed that 75% of seropositive donors transmitted HCV to the transplant recipient. In contrast, Vincenti et al,[20] found that six of seven transplant recipients who were seronegative before transplantation did not show any evidence of detectable HCV infection after transplantation with HCV+ organs. In HCV+ recipients of HCV+ kidneys, the Mendez group reported a low (16%) incidence of liver dysfunction which was reversible in half of the patients with no adverse impact on patient or grafts survival.[21] However, seroconversion was observed in 59% of HCV- recipients of HCV+ organs. A similar transmission rate of 56% was noted by Tesi in 43 patients.[22] Because of conflicting data, no uniform policy regarding the use of the HCV+ kidney can currently be recommended. At our own institution, current policy is to use HCV + organs in HCV+ recipients if the donor liver biopsy is normal. To date, no patient transplanted at our institution under these guidelines has developed chronic liver disease; however, the follow-up is currently too short to draw any final conclusions.

THE "ANATOMICALLY CHALLENGED" KIDNEY

Techniques of reconstructing kidneys with multiple or transected vessels due to organ recovery injury have been

well described.[23] We have recently successfully transplanted a kidney that had undergone a one-third surgical amputation (upper pole) and another kidney that had been previously transplanted 5 years earlier (reuse of the transplant kidney). Although these examples represent extreme situations, they show additional means for expanding the donor pool.

NHBD

The use of NHBD has been increasing in the United States in recent years, and is commonplace in Japan, which has no legal brain death laws. NHBD kidneys, in both the controlled and uncontrolled donor result in delayed graft function in 60% to 80% of cases, but are generally associated with acceptable graft survival rates.[24]

SUMMARY

Advances in the surgical techniques, preservation solutions, and methods for predicting eventual long-term renal function from expanded donors will be critical in allowing precise selection criteria for kidneys for transplantation, resulting in the optimum use of a scarce and precious resource. Until other options such as xenotransplantation or tissue engineering become realistic, the challenge for the millennium will be to identify which donor organs previously considered suboptimal can be safely used to expand the organ donor pool.

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