Outcomes and Risk Factors for Graft Loss: Lessons Learned from 1,056 Pediatric Kidney Transplants at the University of Minnesota

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BACKGROUND: Advances in immunosuppression, surgical techniques, and management of infections in children receiving kidney transplants have affected outcomes.

STUDY DESIGN: We analyzed a prospectively maintained database of pediatric kidney transplantations.

RESULTS: From June 1963 through October 2016, we performed 1,056 pediatric kidney transplantations. Of these, 129 were in children less than 2 years old. The most common indications for transplant were congenital anomalies (dysplastic kidneys), obstructive uropathy, and congenital nephrotic syndrome. Living donors constituted 721 (68%) of all donors. The graft and patient survival rates remarkably improved for both deceased and living donor recipients ($p = 0.001$). Currently, graft survival rates for deceased donor recipients are 92% at 1 year, 76% at 5 years, and 57% at 10 years post-transplant; for living donor recipients, 96% at 1 year, 85% at 5 years, and 78% at 10 years. The graft half-life was 19 years in deceased donor recipients, compared with 25 years in living donor recipients ($p \leq 0.001$). Acute rejection was the most common cause of graft loss in the first year post-transplant. The following risk factors were associated with an increased risk of graft loss: deceased donor grafts ($p = 0.0001$), retransplant ($p = 0.02$), ages 11 to 18 years ($p = 0.001$) and pre-transplant urologic issues ($p = 0.04$). Living donor grafts ($p \leq 0.0001$) and pre-emptive transplants ($p = 0.02$) were associated with decreased risks of graft loss.

CONCLUSIONS: The success rates of pediatric kidney transplants have significantly improved. Pre-emptive kidney transplantation with a living donor graft continues to be superior and should be the choice in children with end-stage renal disease. (J Am Coll Surg 2017;224:473–486.

Kidney transplantation is the treatment of choice for children with end-stage renal disease (ESRD) because it is the only therapy that offers them the long-term possibility of a near-normal life. Although a child of almost any size can be supported by dialysis, current dialysis protocols cannot maintain a normal homeostatic environment and are therefore associated with major problems, including bone disease, growth failure, anemia, serious infections, cardiovascular morbidity, access issues for hemodialysis, membrane failure for peritoneal dialysis, psychological challenges, and increased overall mortality.

The first successful pediatric kidney transplant was performed at the University of Minnesota in 1963.[1] However, early pediatric kidney transplants were complicated by technical, immunologic, and logistical problems, leading to low rates of patient and graft survival. Despite the early difficult years, the Minnesota group (John S Najarian and colleagues) built a bold, innovative, and ultimately highly successful pediatric kidney transplant program.[2] Over the past 50 years, and especially the past 15 years, a number of advances have further improved patient and graft survival rates.[3]

Other members of the MNUM Pediatric Transplant Program who contributed to this article are listed in the Appendix.

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Abbreviations and Acronyms

CsA = cyclosporin A
ESRD = end-stage renal disease
HLA = human leukocyte antigen
LD = living donor
MALG = Minnesota antilymphocyte globulin
MMF = mycophenolate mofetil
PTLD = post-transplant lymphoproliferative disorder
SCr = serum creatinine

Although immunosuppressive medications and regimens are similar in pediatric and adult recipients, subtle differences may be important in the long run. For example, the risk/benefit ratio for alternate day prednisone is different for children with growth potential vs adults in whom growth is complete. Serum creatinine (SCr) remains the major serum biomarker of graft function, but in very small children with adult grafts, its elevation may present relatively late and irritability, graft swelling and tenderness, and fever or hypertension may antedate significant SCr elevation. However, the immunologic mechanisms of kidney graft rejection are generally the same. Yet many other aspects differ, including immunologic factors, the primary kidney diseases leading to ESRD, associated urologic issues, required pre-transplant immunizations, allocation policies regarding deceased donor grafts, surgical techniques, and drug metabolism.[3] Finally, close cooperative teamwork between transplant surgeons, pediatric nephrologists, urologists, transplant coordinators, nurses, pediatric nutritionists, and social workers is even more vital for the pediatric transplant program's success given the many complexities involved in the care of these small, often very fragile, patients and their families.

In this review of more than 1,000 pediatric kidney transplants at our center, we analyzed outcomes and risk factors for graft loss, with a specific emphasis on changes in immunosuppression over the past 5 decades.

METHODS

Recipient and donor selection

Our criteria for accepting pediatric kidney transplant candidates have continuously evolved. Pre-emptive transplants (ie before initiation of dialysis) are encouraged. Younger (<1 year old) and very low weight children remain transplant candidates if surgical assessment demonstrates that the abdomen has adequate space and patent vasculature.[4]

Important relative or absolute contraindications currently include active infection, active autoimmune disease (eg active systemic lupus erythematosus, high levels of antiglomerular basement membrane antibodies, active vasculitis), active malignancy, clinically significant nephrotic syndrome, uncontrolled hypertension, and some progressive brain disorders. Children with early graft loss from recurrence of atypical hemolytic syndrome or steroid resistant nephrotic syndrome may be considered as candidates for retransplantation. Those with renal failure due to hereditary hyperoxaluria are better candidates for combined liver/kidney transplantation. Transplant candidates with extra-renal congenital abnormalities such as VATER syndrome (vertebral anomalies, anal atresia, cardiac defects, tracheoesophageal fistula and/or esophageal atresia, renal and radial anomalies) have been accepted after appropriate medical or surgical treatment.

All transplant candidates undergo evaluation by a multidisciplinary team of pediatric nephrologists, surgeons, pediatric nutritionists, psychologists, and social workers, as well as other pediatric subspecialists (cardiology, gastroenterology, etc) on an individualized basis. All routine childhood immunizations, including hepatitis B, varicella and pneumococcal vaccines, are given pre-transplantation. Transplantation is delayed 6 weeks after live virus vaccinations.

The assessment of living related ABO-compatible potential donors has been previously described.[5] Incompatibility of ABO between the recipient and the donor is not an absolute contraindication. With living donors, older age (ie 60 years or older) is not a contraindication. Living donors with well controlled hypertension on a single medication are considered for donation. We avoid donors when recipients have known higher titer donor-specific antibodies. Tissue typing and crossmatching are performed as previously described.[6] We transplant across a positive B-cell crossmatch if the channel shift is minimal.

With deceased donors, donor age younger than 55 years is preferred. We avoid deceased donors at high risk (per US Public Health Services guidelines) for hepatitis B and C, or with positive serology test results for either disease. We accept deceased donors only when the crossmatch is negative to both the recipient's past and current sera.

Surgical technique

Surgical techniques have evolved over the years. Currently, we perform unilateral or bilateral nephrectomies when indicated (eg reflux demonstrated on a voiding cystourethrogram, uncontrolled hypertension, Drash syndrome in which bilateral gonadectomy is also performed).[7] Preoperatively, all recipients < 25 kg undergo dialysis catheter placement, facilitating perioperative fluid