PAPER

A 100% 2-Year Graft Survival Can Be Attained in High-Risk 15-kg or Smaller Infant Recipients of Kidney Allografts

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Background: Infants make up the most high-risk, difficult to care for subgroup undergoing kidney transplantation, with the lowest 1- and 2-year graft survival rates of any other age group. The principal causes of graft loss have been graft thrombosis, primary nonfunction, technical error, and irreversible acute rejection.

Hypothesis: Infants undergoing kidney transplantation can achieve near 100% graft survival at 2 years following surgery, despite their very high-risk status.

Design: Analysis of 45 consecutive kidney transplants performed in patients weighing less than or equal to 15 kg during an 8-year period beginning August 1991. Patients included complex referrals from throughout the United States and all received transplants and were cared for by the same pediatric kidney transplantation team.

Results: Mean weight at transplantation was 11.2 kg. Renal failure was due to congenital or urologic causes in the majority (53%) of cases. Size-discrepant adult-sized kidney grafts were transplanted in 80% of patients; 64% received live-donor grafts; 78% were receiving dialysis prior to transplantation; and 27% had extremely small bladders ($<20\ cm^3$) requiring modification of the ureteral implantation. Excluding 1 transplant-unrelated death, graft and patient survival at 2 years was 100%. Eight-year patient and graft survival rates (for our combined live and cadaver donor series) were 89.6% and 84.6%, respectively. This compares favorably with much lower graft survival in low-risk adult recipients. Delayed graft function occurred in only 1 patient (2%). Rate of incidence of rejection was 9.3% within 2 years of transplantation and the overall rejection rate was 15.5%. No graft was lost to vascular thrombosis, primary nonfunction, technical error, or acute rejection. The mean creatinine level was 53.04 µmol/L (0.6 mg/dL) and 61.9 µmol/L (0.7 mg/dL) at 1 and 2 years, respectively, and 88.4 µmol/L (1.0 mg/dL) at 3, 4, and 5 years after transplantation.

Conclusion: One hundred percent 2-year and excellent 8-year graft survival rates can be achieved in what has historically been the highest-risk and most difficult to care for patient subgroup undergoing kidney transplantation.

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COMPARED WITH adults and larger pediatric patients, infants with end-stage renal disease are the most challenging subgroup of patients undergoing renal transplantation. They are at the highest risk for early graft loss, and have been reported to consistently have a higher mortality rate.[1] With dialysis and without transplantation, however, these patients have an even higher mortality rate (14% at 1 year and 25% at 2 years) because of accompanying comorbid factors and difficulty maintaining long-term dialysis access.[2,3]

Nationally, principal causes of renal allograft loss in infants have been vascular thrombosis, primary nonfunction, technical error, and irreversible acute rejection. The United Network for Organ Sharing Registry, with mandatory reporting by all US centers, reveals that 33.4% of live-donor grafts lost in recipients younger than 2 years are for these reasons, with graft thrombosis accounting for 23.8%.[4] Recipients aged 2 to 5 years also have a high graft thrombosis rate, accounting for 16.3% of grafts lost. These technical causes of early graft loss in live-donor transplantation underscore the difficulties with infant recipients, especially since live-donor transplantation provides the highest expectation of success. The incidence of graft loss from irreversible acute rejection is also greatest in patients younger than 6 years.[1] Acute rejection has been found to be the most important risk factor for chronic rejection, and the leading cause of graft loss after the first year after transplantation.[5,6] The reported rate of delayed graft function (DGF) in pediatric transplants is

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PATIENTS AND METHODS

Forty-five consecutive kidney transplantations were performed in patients weighing less than or equal to 15 kg from August 1991 to December 1999 and represent 28% (45/161) of our total pediatric experience during this period. These patients were operated on and cared for by the same pediatric renal transplant team. All transplantations, except for 1 case with in utero thrombosis of the vena cava, were performed transperitoneally. The renal artery was anastomosed to the recipient aorta, and the renal vein was anastomosed to the recipient inferior vena cava. Reperitonealization of the allograft was accomplished at the end of the procedure to ensure stabilization of the kidney and to facilitate renal biopsy in the future, if necessary. The ureter was preferentially implanted through a submucosal tunnel using a modified transvesical Politano-Leadbetter technique. In recipients with small defunctionalized bladders where a submucosal tunnel could not be created, the ureter was implanted directly using an extravesical approach before December 1997, and thereafter, the transvesical "trough" technique was developed and used in subsequent patients.[8] Aggressive intravenous hydration was used intraoperatively and in the postoperative period, while nasogastric or gastrostomy tube feeding was maintained for 6 to 12 months following our report of hemodynamic studies in infants.[9] Aggressive fluid and sodium administration was maintained to support blood pressures to greater than the 95th percentile for age.

Standard immunosuppression consisted of administering intraoperative methylprednisolone with or without antibody preparation. A calcineurin inhibitor, via the intravenous route, was initiated in the operating room after revascularization and continued until oral administration was possible to achieve early target trough blood levels of 350 ng/mL to 400 ng/mL for cyclosporine (flourescence polarized immunoassay; Abbott Labs, Abbott Park, Ill) and 15 ng/mL to 20 ng/mL for tacrolimus (INCSTAR enzyme-linked immunosorbent assay; INCSTAR Inc, Stillwater, Minn). Doses were gradually tapered to achieve trough levels of 200 ng/mL for cyclosporine and 5 ng/mL for tacrolimus at 6 months. Tight immunosuppressive management was maintained with frequent blood drug-level monitoring, especially during the first 6 months after transplantation. Based on risk stratification, viral prophylaxis was administered beginning in 1993.

Graft survival for the series includes live- and cadaver-donor grafts combined, and was calculated by actuarial methods. Otherwise, data are presented as means ± SDs.

12%.[7] Grafts with DGF have a significantly lower rate of 2-year graft survival. For example, in living-related transplants, those without DGF experienced an 89.6% graft survival rate compared with those with DGF, who experienced a 41.6% graft survival rate.[7] In addition to these risks, infants frequently display various inherited and sporadic syndromes with multiorgan involvement. Infants with renal failure have a high incidence of obstructive uropathy and other anomalies of the genitourinary system that pose challenging anatomical and functional problems and require special approaches in preparation for transplantation.

We report our results on 45 consecutive kidney transplantations, without exclusions, in infants weighing less than or equal to 15 kg, and examine factors that may optimize early and long-term graft survival rates and functioning in these patients.

Table 1. Patient Characteristics (N = 45)

Mean ± SD age at transplantation, mo	24.4 ± 14.2
Mean ± SD weight, kg	11.2 ± 2.6
Patients receiving dialysis prior to transplantation, %	78
Mean ± SD time on dialysis prior to transplantation, mo	13.4 ± 11
Mode of dialysis, No. (%) of patients	
None	10 (22)
Peritoneal dialysis alone	19 (42)
Hemodialysis alone	7 (16)
Peritoneal dialysis and hemodialysis	9 (20)

RESULTS

PATIENT AND TRANSPLANT CHARACTERISTICS

The majority (53%) of the infants in the study had a congenital urologic abnormality as the cause of their renal failure, including obstructive uropathy (n=14), autosomal recessive polycystic kidney disease (n=5), renal dysplasia/agenesis (n=4), and congenital renal vein thrombosis (n=1). Nephrosis from congenital nephrotic syndrome (n=4), diffuse mesangiosclerosis (n=1), and focal segmental glomerulosclerosis (n=1) accounted for 13% of cases. Acquired conditions such as hemolytic uremic syndrome (n=4), ischemic cortical necrosis (n=3), and twin-to-twin transfusion (n=1) were responsible for renal failure in 18% of patients. Seven patients (16%) with hyperoxaluria type I underwent a combined kidney and liver transplantation.

Transplantation was performed early, at a mean age of 24.4 months after the stabilization of medical issues, optimization of nutrition, and reaching of the desired weight of at least 7.5 kg, but preferably 10 kg. Most patients received dialysis for less than 1 year. Because the majority of these patients were too small for safe hemodialysis, most (62%) had either peritoneal dialysis alone or in combination with hemodialysis. Preemptive transplantation was carried out in 22% of cases (**Table 1**).

Because rejection and acute tubular necrosis (ATN) are poorly tolerated by infants, living-related transplantation was our preferred therapy for this group. In addition to better immunologic matching, this approach provides the most reliable mode of minimizing DGF. In 64% of infants, live-donor grafts were used with an overall 1-haplotype mismatch. As a consequence of this and our preference for adult-sized cadaver kidneys for those without living donors, the majority of grafts (80%) im-

Table 2. Characteristics of Transplants*

Donor	
Living	29 (64)
Cadaver	16 (36)
Size of graft	
Pediatric	9 (20)
Adult-sized	36 (80)
Transplant No.	
Primary transplantation	42 (93)
Second transplantation†	3 (7)
Combined transplants	
Kidney-liver	7‡
HLA mismatch, mean ± SD	
Overall	2.9 ± 1.4
Living-related/unrelated	2.3 ± 1.1
Cadaver	4.0 ± 1.0

*All values are expressed as number (percentage) of patients unless otherwise indicated.

†Three patients received retransplantation as infants after referral from outside institutions for failed primary grafts. Causes of previous graft loss included renal infarct after attempted intraluminal angioplasty of renal artery stenosis, late acute tubular necrosis and recurrent oxalate deposition after complications of liver transplantation, and renal vein thrombosis.

‡One patient underwent a kidney transplantation after undergoing liver transplantation.

planted into the infants in our study were size-discrepant adult-sized kidneys (**Table 2**).

The length of hospital stay was 20.8 ± 9.4 days and 7% of the recipients had surgical complications requiring reoperation during the initial transplantation hospitalization. Reoperation was for spontaneous small-bowel perforation, wound dehiscence, and bladder rupture secondary to suprapubic catheter malfunction. The incidence rate of documented cytomegalovirus infection was 6.7%, and that of serologic conversion was 17.7%. Epstein-Barr virus occurred in 7% of patients, including 2 cases of posttransplantation lymphoproliferative disease. These patients were treated with reduction of immunosuppression and antiviral therapy. There was 1 death due to sepsis complicating posttransplantation lymphoproliferative disease.

GRAFT AND PATIENT SURVIVAL

There were only 4 of 45 grafts lost for the entire series, for an overall actual graft survival rate of 91%. Mean time of follow-up was 48.1 months (range, 3.3-102.2 months). No grafts were lost to vascular thrombosis, primary nonfunction, technical error, or acute rejection. The only graft loss occuring within the first 2 years after transplantation was due to potassium overdose at 1 day after transplantation in an infant with a serum creatinine level of 35.36 µmol/L (0.4 mg/dL). Excluding this transplant-unrelated death, graft and patient survival at 2 years is 100%. After 2 years, graft loss was due to patient death from sepsis (n=2) at 34 and 41 months, respectively. Both of these patients had good renal function at death. The fourth graft loss was at 53 months after transplantation, secondary to chronic rejection following late ATN due to hypotension during orthopedic surgery. Of all the infants in this series, this patient represented the only one

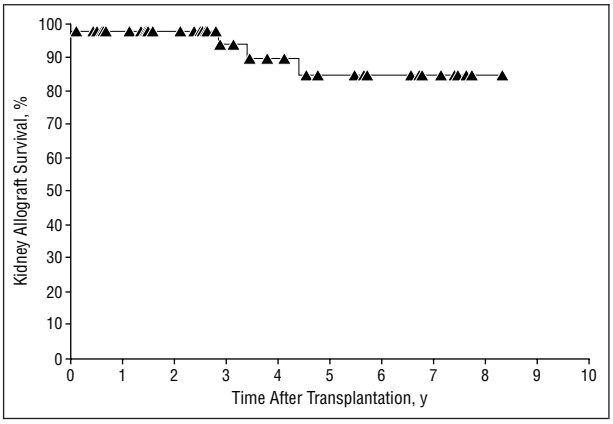

Figure 1. *Kidney allograft survival.*

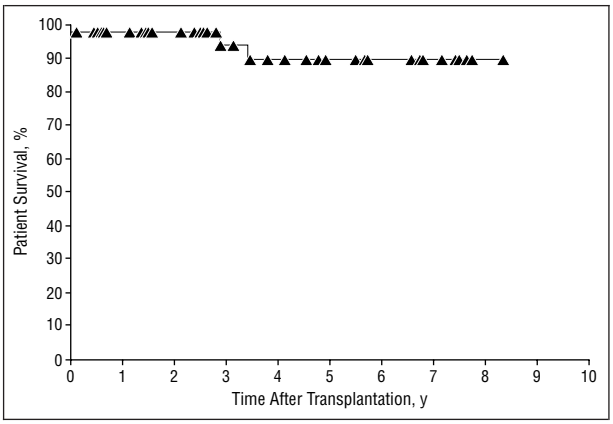

Figure 2. *Patient survival.*

who required retransplantation, so that 42 (93%) of 45 patients are currently alive with well-functioning grafts.

Actuarial graft and patient survival rates in this series are depicted in **Figure 1** and **Figure 2**. At 8 years, the long-term actuarial graft survival rate was 85%, and the patient survival rate was 90%.

RENAL ALLOGRAFT FUNCTION

The mean serum creatinine level was 53.04 µmol/L (0.6 mg/dL) and 61.9 µmol/L (0.7 mg/dL) at 1 and 2 years, respectively. From 3 to 5 years, the serum creatinine level plateaued at 88.4 µmol/L (1.0 mg/dL). The initial rise in creatinine after the first 2 years may represent growth and increased muscle mass in these patients, as well as the infant to adult-sized kidney adaptation with the obligatory loss of kidney volume that we have previously described.[9] Low-grade nephrotoxicity from calcineurin inhibitors is another consideration, as 15% of these patients had some evidence of these findings in biopsy results.

Only 1 patient (2%) required dialysis for DGF. The allograft in this case was from a less than ideal 37-year-old donor with a 10-year history of hypertension, 15-year smoking history, profound hypotension during organ procurement, and multiple thrombi involving the contralateral renal artery and a branch artery of the transplanted kidney. This transplant represented a desperate

Table 3. Modes of Ureteral Implantation

Technique	No. of Patients (N = 45)	Percentage
Politano-Leadbetter	29	64
Extravesical	9	20
"Trough" technique	6	13
Ileal conduit	1	2

measure in a highly sensitized child (panel reactive antibodies, 98%) with no dialysis access due to multiple previous abdominal operations and multiple-line thromboses. This donor provided the first instance of a negative cross-match on a current serum for this patient. There was full recovery in this case with a creatinine level of 61.9 µmol/L (0.7 mg/dL) at the latest follow-up (8 months).

IMMUNOSUPPRESSION AND REJECTION

Antibody induction therapy was used in 36 (80%) of the 45 patients. Since June 1998, we have been routinely using a humanized monoclonal antibody (dacluzimab) that is directed specifically to the interleukin 2 receptor. This preparation avoids cytokine release and other nonspecific effects of other antibody preparations. One highly sensitized patient, described above, had both OKT3 (Ortho Pharmaceutical Group, Raritan, NJ) and dacluzimab induction therapy. With the exception of the latter patient, intravenous administration of a calcineurin inhibitor (80% cyclosporine, 20% tacrolimus) was initiated in all other patients at the time of graft implantation, as described in the "Patients and Methods" section.

The incidence of acute rejection episodes was 9.3% within 2 years of transplantation, with an overall rate of 15.5% for the entire series. The 4 patients with early rejections experienced them within 2 months of transplantation. Three of these 4 received cadaver grafts, and the fourth was a retransplantation. All patients recovered after treatment for their rejection episodes, with serum creatinine levels between 53 µmol/L (0.6 mg/dL) and 79.5 µmol/L (0.9 mg/dL) at 1 month after rejection, and 61.9 µmol/L (0.7 mg/dL) to 79.5 µmol/L (0.9 mg/dL) at 1 year after rejection.

With regard to donor-organ size, there were no rejection episodes in patients who received adult-sized kidneys who did not have any episodes of early or late ATN, nor was there rejection in those patients receiving combined kidney-liver transplants. Seven rejection episodes occurred in 3 patients who received pediatric donor kidneys despite lack of ATN, and rejection occurred in 4 with adult-sized kidney grafts preceded by an ATN episode. Of these ATN cases, only 1 represented DGF. The other episodes of ATN were remote from time of transplantation and were secondary to episodes of prolonged hypovolemia. A dramatic example of this was seen in 1 patient who had a severe bout of ATN following hypotension during orthopedic surgery, with subsequent acute and chronic rejection leading to graft loss at 53 months.

VASCULAR CONSIDERATIONS

There were no cases of arterial or venous thrombosis. There were 2 cases of renal artery stenosis for an overall rate of 4%. Both patients had poorly controlled hypertension and both were managed successfully with balloon angioplasty. In 1 case, the stenosis was nonanastomotic and occurred as a longitudinal lesion on the main renal artery. The other was the only anastomotic stenosis in the series and occurred in the aforementioned highly sensitized patient with the high-risk organ.

UROLOGIC CONSIDERATIONS

Sixteen (36%) of 45 patients had major urologic surgery prior to transplantation. Abdominal operations for nonurologic indications were also performed in many of these patients. Simultaneous native nephrectomies were performed in 67% of patients at the time of transplantation. Indications for nephrectomy included congenital obstructive uropathy and space considerations in fitting an adult-sized kidney into an infant. Twenty-nine percent had other reconstructive urological procedures besides nephrectomy performed at the time of kidney transplantation.

The complexity of the patients in this series is underscored by a 27% incidence of small, defunctionalized urinary bladders with capacities of less than 20 cm^3, which did not allow the performance of a conventional submucosal ureteral implantation. Prior to 1997, ureters were implanted into these small bladders with an extravesical technique that did not permit a formal antireflux tunnel. Since then, we have used our recently described "trough" technique,[8] which allows for the formation of an effective antireflux neosubmucosal tunnel. Modes of ureteral implantation are listed in **Table 3**.

Ureter revision rate was 9% for stenosis (n=1), grade IV reflux (n=2), and ureteropelvic junction obstruction (n=1). The first case was caused by ureteral kinking 2 cm superior to the ureterovesical junction from upward migration of the ureteral implantation, as the initially small contracted bladder enlarged. The last case with de novo ureteropelvic junction obstruction followed a severe rejection episode accompanied by severe urothelial inflammation and thickening in the renal pelvis and upper ureter. As opposed to the standard technique, the first 3 cases were originally implanted via an extravesical technique and were revised with a modified Polatino-Leadbetter approach. Because of severe scarring at the ureteropelvic junction, the fourth case was repaired with a Boari flap neoureter attached to the lower renal calyx. No patients demonstrated evidence of reflux or obstruction after revision.

COMMENT

Infants have the worst outcomes during the first year after kidney transplantation, with a high rate of early graft loss due to technical reasons, especially graft thrombosis. Graft survival curves in older children and adults demonstrate a gradual downward trend over time following

transplantation. This contrasts sharply with the immediate and steep decline in graft survival reported in national registries of infants undergoing transplantation, where 15% of live-donor grafts and 35% of cadaver grafts are lost in the early posttransplantation period.[1,4] By minimizing adverse technical factors, one could potentially achieve more favorable early graft survival rates comparable to those seen in lower-risk adult recipients. In fact, in our combined infant series of both live-donor and cadaver grafts, we have demonstrated near 100% 1- and 2-year graft survival rates and a long-term survival rate of 85% as long as 8 years from transplantation. This compares favorably with the best United Network for Organ Sharing Registry results for infants: a 71% of seven-year graft survival rate for live-donor recipients.[4] Even in the low-risk 19-to 45-year age group receiving favorable living-related donor transplants, survival at these later times is only 68% (oral and written communication, P. Daily, PhD, United Network for Organ Sharing, January 4, 2000).

We attribute the absence of graft thrombosis, primary nonfunction, and a low postoperative ATN rate in our series to strict adherence to precise-fit vascular anastomoses and the assurance of continued optimal renal blood flow throughout the perioperative period. One of the most important considerations in performing anastomoses is to ensure that there is a perfect lie of both the donor renal artery and vein. Redundancy of any of these vessels can result in kinking, which would predispose the patient to graft thrombosis. Because the adult-sized kidney will occupy a good part of the right abdomen, there is little space for the renal vessels between the graft and the infant's aorta and vena cava, except for the short, straight, direct passage.[10] With this in mind, and also the consideration that closure of the abdominal wound would further juxtapose the adult-sized kidney against the infant's aorta and vena cava, the transplanted renal artery and vein should be amputated to prevent even the slightest redundancy after wound closure. Intermittent surface recooling of the graft also allows more time for the performance of a meticulous and precise anastomosis, without additional risk of ATN.[10] These are critical points that cannot be overly emphasized when dealing with the small, fragile infant blood vessels, so as to guarantee perfect anastomoses, perfect positioning of the donor kidney blood vessels, and protection against ATN and technical problems.

Strict avoidance of DGF and ATN imparts a significant long-term survival advantage. Aside from 3 deaths unrelated to renal allograft function, there was only 1 graft lost at 53 months after transplantation and this was a consequence of events following prolonged hypotension during an orthopedic procedure. This patient and 3 others in the series who had experienced early or late ATN all had ensuing rejection episodes. Thus, avoidance of ATN prevents immunologic as well as nonimmunologic injury to the transplanted kidney.[11]

Paramount to minimizing the incidence of ATN as well as graft thrombosis and primary nonfunction is the realization that an adult-sized kidney transplanted into an infant cannot, even with maximum intravascular volume, achieve more than two thirds of the blood flow present in this kidney prior to its removal from the donor.[9] Even with the maintenance of optimum intravascular volume during the first 6 months following transplantation, there is a 26% reduction in renal mass, which we believe is due primarily to chronic suboptimal perfusion of the allograft, compared with the higher in situ blood flow of the donor prior to the kidney's removal. The reduction in renal volume could conceivably be greater if optimum intravascular volume is not maintained. We have already reported significant differences in renal function on this basis.[12] Following our hemodynamic studies in infant recipients of adult-sized kidneys, we became more aggressive in optimizing infant intravascular volume through nasogastric or gastrostomic tube feeding of at least 2500 to 3000 mL/m^2 per day. We analyzed Schwartz glomerular filtration rates in 33 infant recipients of adult-sized kidneys before and after institution of this protocol. We found that 6- and 12-month glomerular filtration rates were significantly better in the group managed with aggressive tube feedings for up to 12 months after transplantation. The protocol infants had glomerular filtration rates of 109 cm^3 and 102 cm^3 at 6 and 12 months, respectively, whereas the nonprotocol infants had glomerular filtration rates of 70 cm^3 and 66 cm^3 at the same time points (P=.004).

The overall incidence of rejection in this series (16%) is extremely low when compared with national reports. In addition to the avoidance of ATN, we also attribute this rate to the use of living-related donors and an extremely tight immunosuppressive protocol, with close monitoring of renal function and drug levels.[13,14] We have maintained higher than standard early levels of calcineurin inhibitors; biopsy specimens provided evidence of drug toxicity in a small percentage of these patients, after which drug doses were lowered. However, as long as 8 years after transplantation, we have only lost 1 graft to chronic rejection, and this was not related to drug toxicity. In the living-related donor recipient population (universally acknowledged as more favorable), the national percentage of graft loss to irreversible acute rejection is a high 28.6% for the younger than 2 years age group and 38.8% for the group aged 2 to 5 years.[4] We accept the potential risk of drug nephrotoxicity in a careful balance to assure immunological stability and the best possible long-term graft function.

In addition to the aforementioned factors, urologic issues must be given the utmost consideration, as we have experienced with our incidence of congenital obstructive uropathy, which was twice the national average. More than 35% of our infants had major urologic surgery prior to transplantation and a significant number (27%) had small, contracted bladders that posed technical challenges to ureteral implantation at the time of transplantation. To avoid any risk of reflux nephropathy or urinary infection, we strongly advocate the use of an antireflux procedure in all infants receiving kidney allografts. With the high incidence of congenital obstructive uropathy in infants, the abnormal urinary bladder will perpetuate and enhance the degree of reflux if an antireflux procedure is not performed.[15] When the standard submucosal implantation is not possible, we suggest the use of our recently described "trough" technique,[8] a relatively simple approach that

has allowed an effective antireflux procedure even in the smallest bladders.

Until the late 1980s, it was commonly thought that kidney transplantation was not the best therapeutic option for infants and small children.[16] Our experience demonstrates that superior outcomes can be obtained in these patients by avoiding the technical issues discussed, as well as controlling the incidence of acute rejection episodes. With this in mind, renal transplantation clearly provides the optimal current therapy for infants with end-stage renal disease and, in a remarkable turnabout, they can now achieve better outcomes than those of older children and adults.

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DISCUSSION

David Tapper, MD, Seattle, Wash: Just to briefly summarize, they did 45 consecutive kidney transplants in children who were basically weighing less than 15 kg. Infants comprised the highest risk and the most difficult subgroup undergoing kidney transplantation, with the worst 1- and 2-year graft survival rates. According to the National Registry, the principal causes of graft loss have been graft thrombosis, technical error, and irreversible acute rejection, and they had none of those complications.

They used an intraperitoneal approach, which is somewhat different than what we discussed, but the concept of direct vascular anastomosis without any kinking is critical to the survival of these extremely large kidneys in these relatively tiny children. In two thirds of their patients, there was a simultaneous nephrectomy at the same time of the transplant and 30% required other urologic reconstruction also at the time of transplant. As I mentioned, and they have noted in their title, there was a 100% graft and patient survival of 2 years and an 84% graft function at 7 years which is truly an enviable record.

A very important point that they make in the manuscript and that was made here is that it is critical to avoid acute tubular necrosis. Acute tubular necrosis when it occurs often is a prelude to rejection and subsequent kidney damage.

I have several questions for the authors. You mentioned that you optimized nutrition in this small infant and you showed us a cute picture of a baby with an NG in his nose. In our series, we have always placed peritoneal dialysis catheters and gastrostomy tubes at the same time. I was curious as to what is your method of nutritional supplementation for these children?

You also performed several preemptive transplants; that is, you did a transplant in children without prior dialysis. What are your indications for doing a preemptive transplant in these children? I noted that on several occasions you used pediatric kidneys and their rejection rate seemed higher. What is the youngest age that you will accept as a cadaveric donor?

Truman M. Sasaki, MD, Washington, DC: This is an excellent result; obviously it is very difficult to surpass this. How are these patients selected from a compliance standpoint? I know that when we lose our grafts at 2 and 3 years, many of the cases are related to patient noncompliance. Obviously these children are too young to be noncompliant. How are the parents or the guardians taught to be compliant?

Michael R. Harrison, MD, San Francisco, Calif: Maria and Oscar, are you willing now to take on a baby who has no renal function? The reason I ask is that we are seeing more and more fetuses that will have predictable renal failure at birth. The ones who are severely affected, of course, don't make amniotic fluid and don't have lung development, but we can deal with that by providing amniotic fluid before birth. If we could bring a baby to term with good lung functioning, but no renal functioning, could you take them on?

Dr Salvatierra: In regards to how we manage nutrition and fluid supplementation in these infants, we do not routinely use gastrostomy tubes. If a gastrostomy tube has already been in place at the time we initially see the patient, we will continue to use it, but generally we tend to use small diameter NG tubes.

In regards to preemptive transplantation, National Registry data reveals that infants who have undergone dialysis prior to transplantation fare somewhat worse than infants who have been preemptively transplanted. The issue here is that many of these infants do not do very well with dialysis, having problems with repeated infection, dialysis access, nutrition and a relatively high mortality rate. Placing an infant on immunosuppression when he or she has not done well on dialysis places an infant at high risk for major problems following transplantation. It is thus preferable, if possible, to proceed with preemptive transplantation. In regards to timing of preemptive transplantation, this can usually be determined if the infant is not thriving, has slowed growth, and has a rising potassium level. The degree of creatinine rise in these infants will not be simi-

lar to adults, because infants have very little muscle mass. It is precisely these infants with whom we will proceed with preemptive transplantation. An important factor to consider is the better growth potential of these infants after transplantation vs dialysis and the loss of their best growth years if the transplant is deferred.

In regards to pediatric kidney donors, these donors in infant recipients provide the worst results nationally of any subgroup undergoing kidney transplantation. At Stanford, we tend to use adult-sized kidneys, preferably living donor, but also cadaver. The only instances where we will use a pediatric donor kidney is with combined kidney-liver transplantation for hyperoxaluria type I, or with preexisting thrombosis of the vena cava. If we are to use a pediatric donor kidney, our preference is for donors around the age of 5 years.

In regards to Dr Sasaki's question about compliance, this is certainly a major issue with pediatric transplantation, particularly in adolescents. Compliance in the infant age group is really not a problem, but it becomes a major issue in adolescent years. The National Registry shows that the group aged 6 to 12 years does initially well with good graft survival, but as these children get into their teenage years there is an increase in graft loss noted, most likely secondary to noncompliance. The recipient group aged 13 to 18 years does very well early following transplantation, but the graft survival curve following 1 year has the sharpest descent of all other age groups during this period of time, including both pediatric and adult. It is very important for a center that undertakes transplantation of adolescents to have a proactive program that deals with noncompliance, both pre- and posttransplantation. The program should be carefully planned and should involve pediatric social workers, psychologists, and psychiatrists. For example, at our center we enroll adolescents in such a program for 2 or more weeks prior to transplantation, and will not proceed with transplantation unless there is good evidence for future compliance. After transplantation, we continue the adolescent recipient in the program, even for a number of months after transplantation, trying to minimize the risk of noncompliance. As we look at our entire pediatric experience, even though we have a very low graft loss rate, our highest percentage of graft losses have come because of noncompliance.

In regards to Dr Harrison's question about accepting some of these infants with renal failure from the time of birth, we do accept them at Stanford. In fact, we have had some of these newborns and infants medically evacuated to us from other parts of the country; from as far as the northeastern and eastern parts of the United States. As Dr Harrison states, you can generally manage these babies' lungs, despite a degree of pulmonary hypoplasia. But what is needed is the initiation of effective dialysis and assurance of good nutrition from the start. We then follow these infants carefully and try to transplant them early, most often before their first birthday.

To conclude, I really believe that we can do a lot for infants with renal failure, and even obtain better graft survival rates than for older age groups. For example, to place this in perspective, the lowest-risk age group undergoing kidney transplantation is the adult group aged 18 to 45 years. Adult recipients of living-related grafts in this age group have only a 68% graft survival at 7 years nationally; whereas in our current analysis of UNOS national data, infants, despite their complexity, have the potential for considerably better long-term graft survival. So, as was emphasized yesterday, and also by Dr Millan today, what it really takes to bring infants and small children to a normal life with transplantation is a closely integrated, experienced, multidisciplinary team. I think Dr Debas would be pleased to hear this, following his comments earlier this morning. There should be a multidisciplinary team that has a disease-based practice that preserves and considers it critically essential that patient, parent, and physician relationships are cherished and carefully preserved.

IN OTHER AMA JOURNALS

ARCHIVES OF INTERNAL MEDICINE

The Educational Value of Autopsy in a Residency Training Program

Steven Durning, MD; Lannie Cation, MD

Background: Historically, the autopsy has been an indispensable educational tool. Over the past several decades, however, the national autopsy rate has declined and the educational role of autopsy in modern medicine is being questioned.
Objective: To assess the educational value of autopsy attendance in an internal medicine residency program.
Methods: We performed a retrospective review of all autopsies performed on the general internal medicine teaching service between October 1996 and September 1998. Premortem and postmortem diagnoses were determined and compared and attending physician surveys were reviewed.
Results: Eighty-eight deaths occurred during the study period. Twenty-nine (33%) patients underwent autopsy. All autopsies were observed by the primary team and the attending physician completed an autopsy survey on each patient. An unexpected pathological diagnosis directly contributing to death was detected in 10 (34%) patients at autopsy. Additional unexpected pathological diagnoses were discovered in 23 (79%) cases. Attending physician surveys revealed that all 10 unexpected diagnoses contributing to death were observed by the primary team at the time of autopsy. Autopsy attendance was rated as a valuable educational experience in 27 cases (93%).
Conclusion: Autopsy is a valuable educational tool and autopsy attendance should remain an integral part of internal medicine residency training. (*2000;160:997-999*)

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