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Ten-year experience with infant kidneys transplantated en bloc

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Abstract We analyzed the long-term outcome and function of 78 pairs of infant kidneys transplanted en bloc into adult recipients from February 1987 to February 1997. Donors were 31.2 months old (3.5–60 months), weighed 10.9 kg (5.6–20 kg), and had creatinine levels of 0.3 mg/dl (0.2–0.8 mg/dl). The kidneys had 2.6 (0–6) HLA-A, B, DR, mismatched antigens. Recipients were 36.3 years old (18–78 years), had 3.3% panel-reactive antibodies (0–71%), and weighed 71.5 kg (46–134 kg). Renal revascularization was accomplished by joining the donor aorta and vena cava to the recipient iliac artery and vein, respectively. Cold ischemia time was 23.4 h (16–53 h). Immunosuppression consisted of cyclosporine, azathioprine, steroids, and recently, mycophenolate mofetil. Rejection episodes were treated with steroids, and anti-CD_3 antibodies was used in non-responders. Five en-bloc kidneys thrombosed. Two ureters developed a fistula and were repaired successfully. Five patients underwent dialysis. Death occurred in two patients with infection, six with heart attack and stroke, and one with cancer with excellent graft function. Renal artery stenosis was dilated in seven patients. Six grafts were lost to rejection (one from non-compliance at 20 months). The original disease recurred in three patients with massive proteinuria, despite excellent function. Graft survival at 42 months (1–117 months) was 79%, with serum creatinine levels at 1, 3, and 9 years of 1.2, 1.0, and 0.8 mg/dl, respectively. Creatinine clearance averaged 88 ml/min (34–188 ml/min) and 24-h proteinuria was 146 mg (normal 10–150 mg). In conclusion: (1) en-bloc infant kidneys can be transplanted successfully with excellent long-term function into adults; (2) hyperfiltration injury was not observed; and (3) infant kidneys should be used more frequently.

Key words Infant · En-bloc kidneys · Transplantation · Hyperfiltration

Introduction

Advances in techniques, histocompatibility testing, and never immunosuppressions, have made renal transplantation so safe that 1-year graft survivals of 80–90% have been reported by multiple centers [2, 4, 8, 12]. These results have only stimulated the rate of transplantation and worsened the gap between the number of patients awaiting a kidney transplant (34956 by the UNOS February 1997 report) and the actual number of organs transplanted (11810 organs from 8595 cadaveric and 3215 living donors). To decrease the lack of organs, we started our prospective experience of transplantation of infant en-bloc kidneys in 1987 [4] and demonstrated

that these kidneys were able to grow rapidly and provided excellent renal function at 5 years. This favorable experience has served as an impetus to other centers to use pediatric organs, en bloc [2, 11, 12].

Despite this success, there is still concern that nonimmunologic factors such as adaptive hyperfiltration [1, 13], donor-recipient size mismatch [14, 15], or hypertension may be injurious to the transplants. Cyclosporine nephropathy may also lead to further chronic deterioration of renal function besides the unrelenting effect of chronic immunologic graft attrition. Terasaki et al. [14] reported that small kidneys from 4- to 6-year-old donors and from donors over the age of 60 years do not perform significantly as well as those from the 15- to 45-year-old donor group because of their inadequate mass. Similarly, female kidneys transplanted to large male donors have inferior graft survival and function than the male to female transplants. This can be predicted very early at the time of discharge by the significantly higher creatinine levels. Brenner, based on animal data [13] and kidney weight/body.

Materials and methods

Between February 1987 and February 1997, 78 adult recipients received cadaveric, en-bloc pediatric kidneys. Organs were harvested from heart-beating donors using standard in-situ aortic cooling with University of Wisconsin solution. Proximal suprarenal sections of the donor aorta and the vena cava of the en-bloc allografts were oversewn with fine monofilament polypropylene sutures. All lumbar and non-renal tributaries were suture ligated. Sixty cubic centimeters of University of Wisconsin solution stained with two ampules of indigocarmine were used to inject both distal aorta and vena cava to detect leakages, which were controlled by sutures. The indigocarmine "angiogram" used in conjunction with a renograffin angiogram further allowed determination of the compliance and the vascularization of the kidneys. The organs were used if they had low resistance to the flush and were well vascularized. Care was taken not to skeletonize the renal pedicles to avoid devascularization of the kidneys and ureters. Revascularization was accomplished by end to side anastomoses of the distal donor aorta and vena cava to the external iliac vessels in all except three instances, where the proximal donor aorta was anastomosed to the hypogastric artery in two patients and the iliac artery in the third. Kidneys were implanted in the right iliac fossa in all except six cases where they were transplanted in the opposite side [4]. Ureteroneocystostomies were performed in the Lich fashion through a common tunnel [5]. Both ureters were supported by a single 4.7F double-pigtail catheter which was left in place for 6 weeks and removed in the outpatient department by cystoscopy [6].

Simultaneous triple immunosuppression therapy with cyclosporine, azathioprine, and prednisolone was used in the majority of patients. Mycophenolate mofetil was introduced in mid-1995, at a dose of 2 g/day. Currently, all patients have been converted to cyclosporine emulsion. Rejection episodes were treated with methylprednisolone, 3 mg/kg, for 3–5 days. Anti-lymphoblast and anti-CD_3 cell antibodies were used only for steroid-resistant rejection episodes. Only one highly sensitized patient was transplanted. Minnesota anti-lymphocyte globulin was used in two patients as a quadruple drug. Efforts were developed to control postoperative systolic blood pressure very tightly to the neighborhood of 100 mm Hg to avoid subjecting the infant kidneys to hypertension. This clinical necessity excluded all patients with severe cardiovascular disease. Parameters studied sequentially consisted of the determination of kidney volume [3] and renal hemodynamics by gray scale ultrasound and Doppler Duplex examinations, glomerular filtration rates by Technetium DTPA, creatinine, 24-h creatinine clearance, and proteinuria [9].

Table 1 En-bloc pediatric kidneys: donor demographics ($n = 78$, data shown as average values and range)

Age	31.2 months (3.5–60 months)
Weight	10.9 kg (5.6–20 kg)
Initial serum creatinine	0.3 mg/dl (0.2–0.8 mg %)
Cold ischemic time	23.4 h (16–53 h)
Type of cold storage	Five Euro Collins, 73 University of Wisconsin solution

Table 2 Recipient characteristics (*PRA* panel-reactive antibodies)

Age	36.3 years (18–78)
Weight	71.5 kg (46–134)
PRA	3.3% (0–71%)
HLA-A, B, DR mismatch	2.6 (0–6)
Follow-up	42 months (1–117)

Results

Seventy-eight pediatric en-bloc kidneys were transplanted into adult recipients. Donor demographics (Table 1) showed only one 5-year-old 20-kg underdeveloped baby with multiple congenital malformations. His kidneys measured only 6.5 cm in length. Other donors were 24 months old or younger, weighed around 11 kg, and had serum creatinine levels of 0.3 mg %. The majority of kidneys were preserved in University of Wisconsin solution and were transplanted after an average 23.4 h of cold ischemia. Recipient characteristics (Table 2) showed an average 36.3-year-old patient weighing 71.5 kg, with low panel-reactive antibodies and low HLA-A, B, DR mismatching. Only one patient was septuagenarian. Only one patient was highly sensitized (71%). The patients were followed up for 42 months. The original cause of renal failure is summarized in Table 3.

Venous thrombosis occurred in five patients int he short postoperative period. Ureteral leaks developed in two patients and were repaired successfully. One leak was secondary to cytomegalic virus disease of the ureter diagnosed by electron microscopy. Five patients required dialysis and regained normal function. No primary non-function was observed. Renal artery stenosis was

Table 3 *Etiology of end-stage renal disease*

Disease	Number of patients
Glomerulonephritis	31
Diabetes	10
Glomerulosclerosis	8
Polycystic disease	7
Membranoproliferative glomerulonephritis	5
Undetermined	11
Miscellaneous	6

Table 4 Functional characteristics of the transplanted kidneys. The volume of both kidneys is expressed in cubic centimeters and calculated by the formula (length × width × thickness) determined by gray scale ultrasound examination. Actual creatinine clearance determined from 24-h urine collection was 88 ml/min (34–188 ml) [*CR* serum creatinine, *GFR* glomerular filtration rate determined by Technetium DTPA scan (Gates technique), *RI* resistive index determined by Doppler Duplex ultrasound examination (normal 0.5–0.7)]

Year	CR	GFR	RI	Volume
1	1.2	111	0.62	120
2	1.0	100	0.63	220
3	1.0	115	0.63	360
9	0.8	114	0.64	380

diagnosed in seven patients who had lateralized decreased function revealed by a Captopril scan as well as failure of growth of the affected side. These lesions were confirmed by angiographic studies and were successfully ballooned between 12 and 30 months. Most lesions occurred at the origin of the renal artery as a kink, resulting from overgrowth of the kidneys. Three kidneys thrombosed following the angioplastic procedures, resulting in a slight increase in serum creatinine levels. They were watched conservatively and subsequently became atrophied. No transplant nephrectomy was required.

Rejection was responsible for loss of graft in six patients despite the additional use of antibodies. Recurrent disease (confirmed by biopsy in two) was observed in three patients who maintained excellent blood pressure control and normal serum creatinine levels despite massive proteinuria. Death occurred in two patients from infection, in six patients from cerebrovascular accident, and in one patient from hepatoma. All grafts had normal function at the time of the patient's demise. Actual graft survival is 79% at the end of the 10-year experience.

The functional characteristics of the kidneys are presented in Table 4. Creatinine clearance averaged 88 ml/min and proteinuria 146 mg/24 h.

Discussion

Although the technique of transplantation of double pediatric kidneys en bloc has been established and successful, one word of caution has to be said about organ procurement and selection since, within the same period, 30 double infant kidneys were discarded because of injuries to renal arteries, veins, absence of proximal aortic cuff, devascularization of the pelvis and ureter, short ureters, high resistance on flushing with University of Wisconsin perfusate, and poor indigocarmine "angiogram" confirmed by a renograffin table angiogram. Despite the fact that all the pediatric donors were also liver donors, it is still possible to preserve the superior mesenteric artery take off to permit proximal aortic closure [4]. The use of a homograft was not necessary. Also the distal aorta could have been lengthened had the perfusing cannula been inserted in the iliac artery rather than in the aorta itself.

Whether the intraperitonealization of the medial kidney [4] allowed the kidneys to grow fully without vascular distortion is unknown, but the low incidence of renal artery stenosis in this series is noteworthy.

The growth of the kidneys has been increasing steadily, even after the third year post-transplantation, and provided the recipient with a normal renal mass since the volume of one adult kidney is 260 ± 110 ml [9]. This has contributed to a serum creatinine level of 0.8 ml/dl and a normal creatinine clearance which cannot be attained even with a perfect adult kidney transplant.

Renal hyperfiltration literature, which has been related most to small animal models of five-sixths nephrectomy [1, 13], and to analyses of registries [14, 15], did not take into account the normal processes of growth of the normal amount of nephrons transplanted still continuing in the recipient, provided the kidneys were protected from hypertension and from immunologic attrition. Nephron dosing at the time of transplant, and not renal mass dosing, appeared the primary cause of the 10-year success of en-bloc infant kidney transplant. In view of these data we conclude that the correct procurement and the use of infant kidneys transplanted en bloc may improve the lack of organs.

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