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0041-1337/04/7705-698/0

TRANSPLANTATION

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Vol. 77, 698-702, No. 5, March 15, 2004

Printed in U.S.A.

## SOLITARY RENAL ALLOGRAFTS FROM PEDIATRIC CADAVER DONORS LESS THAN 2 YEARS OF AGE TRANSPLANTED INTO ADULT RECIPIENTS

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**Background.** Transplantation of solitary pediatric renal allografts from donors 2 years of age or younger into adult recipients is controversial.

**Methods.** Between 1998 and 2001, 15 solitary renal allografts from pediatric donors 2 years of age or younger were transplanted into adult recipients. Thirty-three en bloc renal allografts transplanted between 1994 and 2001 were used for comparison. En bloc kidneys were considered for separation if they measured greater than or equal to 6 cm in length. Renal function (creatinine clearance [CrCl]) was estimated using the Cockcroft-Gault formula.

**Results.** Two-year graft survival for the solitary and en bloc groups were 93% and 77%, respectively ( $P=0.405$ ). Five grafts were lost because of arterial thrombosis (four en bloc and one solitary). Ureteral complications occurred in three grafts in the en bloc group. One-year postoperative CrCl of the surviving solitary ( $n=14$ ) and en bloc ( $n=26$ ) grafts were  $51.4 \pm 26.2$  mL/min and  $55.1 \pm 27.5$  mL/min ( $P>0.05$ ), respectively. Donor weight and kidney length were greater in the solitary group ( $14.3 \pm 3.5$  kg and  $6.3 \pm 0.4$  cm, respectively) compared with the en bloc group ( $10.8 \pm 2.6$  kg and  $5.9 \pm 0.3$  cm, respectively) ( $P=0.001$ ).

and  $P<0.001$ ).

**Conclusions.** Separation of en bloc pairs into solitary allografts can be considered when the graft measures greater than or equal to 6 cm in length and donor weight is greater than or equal to 14 kg. The transplantation of solitary pediatric kidneys into adult recipients is successful, and the majority of pediatric en bloc allografts can be separated before transplantation.

Since the first description of a pediatric en bloc renal allograft transplanted into an adult recipient in 1972, there has been an attempt to expand the cadaveric donor pool by using smaller en bloc allografts from younger donors (1-4). Transplantation of en bloc renal allografts from pediatric donors younger than 2 years of age into adult recipients is technically challenging and has a higher rate of early vascular and urologic complications when compared with older controls (2-4). However, the 5- and 10-year graft survival rates for these small donor allografts are similar to the adult cadaveric experience (3). With improvements in surgical technique, prolonged graft survival, and knowledge of the technical complications that arise through the use of these small allografts, there has been a desire to expand the donor pool even further by selectively separating en bloc pairs of kidneys, allowing each kidney to be transplanted into different adult recipients.

Even though the practice of separation of en bloc pairs from donors younger than 2 years of age further increases the donor pool, it remains controversial and potentially increases the risk of technical complication and hyperfiltration injury (5, 6). Graft survival in these small solitary organs has been

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Received 21 August 2003. Accepted 26 September 2003.

DOI: 10.1097/01.TP.0000114462.10593.9F

shown by some to be worse than larger grafts from older donors (5, 6). Others have shown that 1-year solitary allograft survival from donors younger than 4 years of age is similar to that of adult donors (7, 8). Few investigators have directly compared the outcomes between solitary and en bloc allografts from small pediatric donors transplanted into adult recipients (9). In addition, there are few data comparing en bloc and solitary allografts from donors younger than 2 years of age. We present our outcomes of solitary renal allografts from donors younger than 2 years of age transplanted into adult recipients. The solitary group was retrospectively compared with en bloc renal allografts transplanted at our institution.

#### PATIENTS AND METHODS

Between 1998 and 2001, eight en bloc pediatric (donors  $\leq 2$  years of age) renal allografts were separated, resulting in 15 solitary renal allografts being transplanted into 15 adult recipients at our institution. One solitary pediatric allograft was sent to a different institution for transplantation after separation at our institution and was not available for analysis. Thirty-three en bloc renal allografts from pediatric donors 2 years of age or younger transplanted between 1994 and 2001 were used for retrospective comparison (Table 1). For both groups combined, the mean donor age was  $18.4 \pm 6.3$  months (range, 2–24 months) and the mean recipient age was  $49.4 \pm 14.6$  years (range, 18–75 years). The mean weight for the donors was  $12.1 \pm 3.4$  kg (range, 4.2–22.0 kg) and the mean weight for the recipients was  $67.9 \pm 18.2$  kg (range, 48.2–81.3 kg). Because the practice of separation of en bloc pairs began at our institution after 1997, the mean follow-up for the solitary group was shorter ( $17.1 \pm 11.2$  months) compared with the en bloc group ( $35.1 \pm 27.5$  months).

All allografts were procured from heart-beating donors, with a mean cold ischemia time of  $23.6 \pm 9.2$  and  $24.8 \pm 7.8$  hr in the solitary and en bloc groups, respectively. The en bloc allografts were transplanted using the intact donor aorta and inferior vena cava as previously described (1–4). En bloc pediatric kidneys were prepared on a separate table in the operating room over ice slush using at least  $2.5 \times$  optical loupe magnification. The suprarenal ends of the aorta and inferior vena cava were closed with running 6-0 nylon suture. If the suprarenal aorta was cut too close to the renal artery orifices on procurement, a distal infrarenal aorta segment was transposed to the suprarenal aorta to allow closure without compromise of the renal artery orifices. All lumbar and gonadal vessels were ligated with 4-0 silk suture. Through a modified Gibson incision in the recipient, the external iliac vessels were exposed by means of an extraperitoneal approach. The donor inferior vena cava and aorta

were anastomosed to the recipient external iliac vessels using running 6-0 nylon. Special attention was directed toward ensuring proper orientation of the donor vessels with these small kidneys because of their propensity to rotate and compromise vascular flow. Ureters were anastomosed to the bladder separately using an extravesical technique. Ureteral stents were placed if the ureteral blood supply appeared questionable or if the attending surgeon preferred.

En bloc kidneys were considered for separation only after close inspection in the operating room, and this decision was never made before the arrival of the organs at our institution. On the basis of previous experience by the senior author (S.T.B.), en bloc pediatric kidneys measuring greater than 6 cm in length were considered for separation. However, the final decision to separate en bloc kidneys was left to the attending transplant surgeon on call. Separation was performed on a separate table in the operating room over ice slush, using a donor aortic patch for each renal artery, a vena caval cuff for the left renal vein, and a vena caval extension graft for the right renal vein. Extreme care was used in the preparation of the right renal vein extension graft, because experience has shown that there is a tendency to narrow the orifice of the vein as it enters the vena cava. If care is not taken to allow sufficient distance between the oversewn vena cava and the renal vein orifice, the thin-walled right renal vein is easily compromised. Engraftment was achieved by means of the iliac vessels in the recipient through an extraperitoneal surgical approach. The ureters were stented only if they appeared ischemic.

All patients received induction therapy with anti-T-cell agents, including basiliximab, antithymocyte globulin, Thymoglobulin (SangStat Medical Corporation, Menlo Park, CA), or OKT3. Generally, before 1996, all patients received antithymocyte globulin, and after that, most patients received OKT3 or Thymoglobulin, until 1999, when basiliximab was used unless a patient was undergoing retransplantation or was at high risk for rejection, in which case they received Thymoglobulin or OKT3. Before 1996, all patients received cyclosporine A-based immunosuppression and then tacrolimus after 1996. All of the recipients in the solitary graft group received basiliximab induction with tacrolimus-based therapy thereafter. Tacrolimus was begun after transplantation after the serum creatinine level dropped below 4 mg/dL. Mycophenolate mofetil was introduced after 1996, and prednisone was generally given to most patients. Patients with episodes of biopsy-proven allograft rejection were treated with high-dose corticosteroids, anti-T-cell agents, or both.

Estimated renal function (creatinine clearance [CrCl]) was calculated using the Cockcroft-Gault formula and ideal body weight. Cumulative graft and patient survival curves were calculated using the Kaplan-Meier method, and the log-rank test was used to compare the

TABLE 1. Donor and recipient demographics<sup>a</sup>

	Solitary (n=15)	En bloc (n=33)	P value
Mean follow-up (mo) <sup>a</sup>	17.1±11.2	35.1±27.5	0.018
Donor-to-recipient weight ratio (%)	22	16	<0.001
Recipient			
Mean age (yr) <sup>a</sup>	46.8±14.4	50.4±14.8	0.474
Mean weight (kg) <sup>a</sup>	65.2±16.3	69.2±23.5	0.792
Female (%)	47	45	0.728
Male (%)	53	55	0.728
Donor			
Mean age (mo) <sup>a</sup>	22.4±2.1	16.0±6.7	0.001
Mean weight (kg) <sup>a</sup>	14.3±3.5	10.8±2.6	0.001
Mean kidney length (cm) <sup>a</sup>	6.3±0.4	5.8±0.3	<0.001
Cold ischemia time (hr) <sup>a</sup>	23.6±9.2	24.8±7.8	0.677
Terminal creatinine (mg/dL) <sup>a</sup>	0.45±0.28	0.39±0.29	0.497
Total HLA mismatch	2.92±2.14	3.59±1.78	0.304

<sup>a</sup> Mean±SD.

curves between the solitary and en bloc groups. Graft loss was defined as resumption of dialysis, allograft nephrectomy, or patient death. Delayed graft function was defined as the requirement for postoperative dialysis. The Wilcoxon rank sum test was used to compare CrCl between the two groups. Multivariate analysis was used to identify factors affecting survival. Donor weight and age, graft size, recipient weight, cold ischemia time, cause of donor death, and human leukocyte antigen (HLA) typing were compared between the two groups.

## RESULTS

The mean donor age and weight for the solitary group (age,  $22.4 \pm 2.1$  months; weight,  $14.3 \pm 3.5$  kg) was greater ( $P=0.001$ ) compared with the en bloc group (age,  $16.0 \pm 6.7$  months; weight,  $10.8 \pm 2.6$  kg). The en bloc group had eight donors younger than 12 months of age (Table 1). The mean recipient weight for both groups was below 70 kg secondary to the tendency to select smaller patients for these small pediatric allografts. The mean donor-to-recipient weight ratio (percentage) was significantly greater ( $P<0.001$ ) in the solitary group (22%) compared with the en bloc group (16%). All of the en bloc grafts that were separated into solitary renal allografts were greater than or equal to 6 cm in length, and the mean length of the kidneys left as en bloc pairs ( $5.8 \pm 0.3$  cm) for transplantation was significantly less ( $P<0.001$ ) than those that were separated ( $6.3 \pm 0.4$  cm). Recipient age and weight, donor cold ischemia time and terminal creatinine, and total HLA mismatching were similar between the solitary and en bloc groups. Only one patient in the study had a previous transplant (the patient had received a cadaveric kidney 5 years earlier that was lost to chronic rejection). This patient currently has a functioning en bloc graft and experienced no episodes of acute rejection postoperatively.

Overall 2-year graft survival (Fig. 1) for the solitary ( $n=15$ ) and en bloc groups ( $n=33$ ) was 93% and 77%, respectively ( $P=0.405$ ). Two-year graft survival for transplants performed after 1998 (Fig. 2) for the solitary ( $n=15$ ) and the en bloc ( $n=25$ ) groups was 93% and 83%, respectively ( $P=0.695$ ). There were no patient deaths in either group. The only solitary graft loss was caused by an acute renal artery

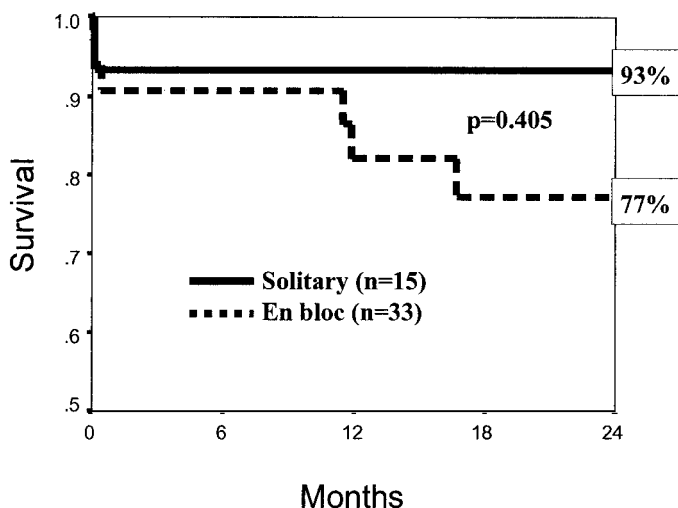


FIGURE 1. Overall 2-year graft survival in the solitary and en bloc groups.

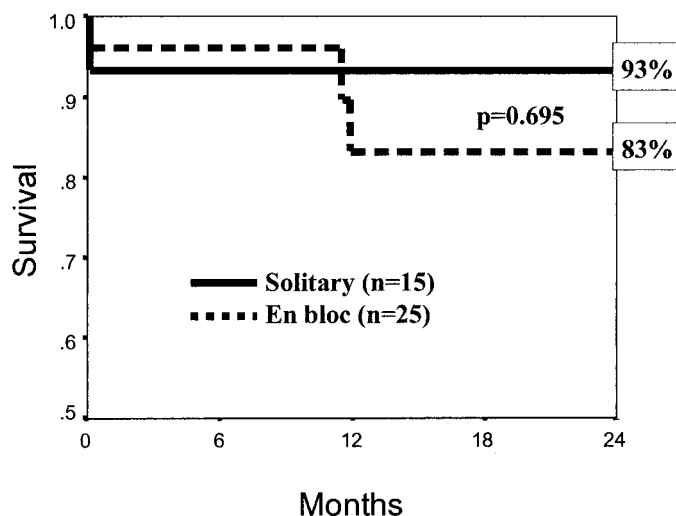


FIGURE 2. Two-year survival for grafts transplanted after 1998 in the solitary and en bloc groups.

thrombosis occurring 2 days after transplantation. Seven grafts were lost in the en bloc group: renal artery thrombosis (four cases), chronic rejection (two cases), and acute rejection (one case). Using multivariate analysis, donor weight and age, graft size, recipient weight, cold ischemia time, cause of donor death, and HLA typing did not influence graft loss secondary to vascular thrombosis or immunologic loss (Table 2). Terminal donor creatinine and delayed graft function were the only covariates found to predict graft loss ( $P=0.036$  and  $P=0.016$ , respectively). Terminal donor creatinine was higher in grafts lost ( $0.66$  mg/dL) compared with those grafts not lost ( $0.41$  mg/dL). When episodes of acute rejection were compared to the entire group of patients with grafts lost (eight patients), statistical significance was not reached ( $P=0.664$ ). However, when compared with those grafts lost secondary to immunologic rejection (three patients), the incidence of acute rejection did predict immunologic graft loss ( $P=0.021$ ). Total HLA mismatching did tend to be higher in those grafts lost (4.6) compared with those that survived (3.1), but this was not found to be statistically significant ( $P=0.066$ ). Excluding the data for the solitary allograft that was transplanted at an outside institution, 14 recipients currently have functional solitary renal allografts as a result of the separation of eight en bloc pairs that more commonly would have been used in only eight recipients.

Delayed graft function occurred in 6 patients in the solitary group and 13 patients in the en bloc group (Table 2), of which 1 (17%) and 4 (31%) patients lost their grafts, respectively. However, it must be noted that all of the patients that lost their grafts because of vascular thrombosis were considered to have delayed graft function. In addition, only one patient that lost their graft not because of vascular thrombosis but because of acute rejection experienced delayed graft function. Episodes of biopsy-proven acute rejection occurred in 4 patients (27%) in the solitary group and 13 patients (39%) in the en bloc group ( $P=0.378$ ). After 1998, episodes of biopsy-proven acute rejection occurred in three patients (25%) in the solitary group and eight patients (36%) in the en bloc group ( $P=0.461$ ). Biopsy-proven immunologic graft loss occurred in three patients (two because of acute rejection and one be-

TABLE 2. Multivariate analysis

	Solitary (n=15)		En bloc (n=33)		P value
	GL	GNL	GL	GNL	
No. of patients	1	14	7	26	
Donor					
Mean age (mo)	24.0	22.3	11.5	16.9	0.097
Mean weight (kg)	22.0	13.8	8.6	11.2	0.565
Mean kidney length (cm)	7.0	6.2	5.6	5.8	0.648
Cold ischemia time (hr)	36.0	22.6	22.5	25.2	0.801
Terminal creatinine (mg/dL)	1.0	0.41	0.58	0.36	0.036
Total HLA mismatch	4.0	2.8	4.7	3.3	0.066
Recipient					
Mean age (yr)	46.4	47.3	48.7	53.8	0.573
Mean weight (kg)	65.2	65.2	69.2	69.2	0.219
Donor to recipient weight ratio (%)	34	21	12	16	0.571
Episodes of acute rejection (No. of patients)	0	4	3	10	0.664
Delayed graft function (No. of patients)	1	5	4	9	0.016

GL, Graft loss (all grafts lost in the study); GNL, grafts not lost.

cause of chronic rejection) in the en bloc group and none in the solitary group.

Major and minor surgical complications (Table 3) between the solitary (7% and 20%) and en bloc (18% and 24%) groups were similar ( $P>0.05$ ). Of the four grafts (12%) that experienced vascular complications in the en bloc group, two were caused by donor aorta thrombosis (en bloc grafts explanted), one was caused by donor renal artery thrombosis leading to donor aorta thrombosis after unilateral nephrectomy (en bloc graft explanted), and one was caused by isolated donor renal artery thrombosis, allowing salvage of the contralateral renal unit after ipsilateral nephrectomy. In the solitary group, arterial thrombosis occurred in one graft (7%). Ureteral complications occurred in two grafts in the en bloc group. Both of these grafts came from small (9.0 and 4.2 kg) and young (9.6 and 2.4 months) donors. In both cases, ureteral stents were placed at the time of transplantation. Bilateral distal ureteral necrosis presented within 2 weeks of transplantation as a urine leak. Ureteroureterostomy using native ureter was performed in each case successfully.

The mean CrCl 12 months after transplantation in the surviving solitary (n=14) and en bloc (n=26) grafts was  $51.4\pm 26.2$  mL/min and  $55.1\pm 25.5$  mL/min ( $P>0.05$ ), respectively (Fig. 3). Because the follow-up in the en bloc group was longer, the CrCl in this group was  $69.1\pm 25.5$  mL/min, with a mean follow-up of  $35.1\pm 27.5$  months. Both the solitary and en bloc groups have CrCl curves that are still increasing at the end of the follow-up, and further observation will be

TABLE 3. Postoperative complications

	Solitary (n=15) (%)	En bloc (n=33) (%)	P value
Major complications	1 (7)	6 (18)	0.300
Arterial thrombosis	1 (7)	4 (12)	0.570
Venous thrombosis	0	0	NA
Urologic	0	2 (6)	0.335
Minor complications	3 (20)	8 (24)	0.679
Lymphocele	1 (7)	2 (6)	0.937
Wound complication	2 (13)	3 (9)	0.659
Other	0	3 (9)	0.233

NA, Not applicable.

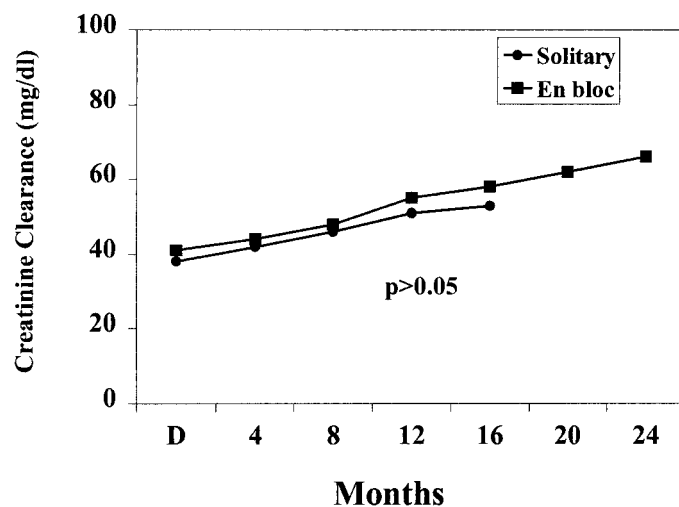


FIGURE 3. Postoperative calculated creatinine clearance (in milligrams per deciliter) in the solitary and en bloc groups. D, Days after surgery.

necessary to ascertain the plateaus for each. The incidence of long-term postoperative proteinuria ( $>0.8$  g/24 hr) at 12 months was similar between the solitary (43%) and en bloc (36%) groups ( $P=0.383$ ).

DISCUSSION

Many centers are still reluctant to transplant small pediatric en bloc kidneys into adult recipients. This reluctance is based on reports of increased technical complications (10), graft thrombosis (11), insufficient nephron mass (12), increased incidence of rejection (13), and lower graft survival (13). The present study and others have shown that the transplantation of these small pediatric kidneys into adult recipients is safe and yields graft survival rates similar to adult cadaveric kidneys (2-4). There are few data supporting the use of small solitary pediatric cadaveric kidneys in adult recipients, particularly from donors younger than 2 years of age (6). Many argue against the use of small solitary kidneys, citing a high risk for hyperfiltration injury and technical difficulty. Modlin and associates from the Cleveland Clinic

Foundation studied 60 solitary pediatric grafts, of which 18 were from donors younger than 2 years of age (6). They reported a significantly lower 1-year graft survival rate (48%) in the solitary group compared with ours (93%). The investigators noted an 80% incidence of acute rejection in their grafts 6 months after transplantation, using cyclosporine-based immunosuppression. Our exclusive use of basiliximab induction therapy with tacrolimus-based long-term immunosuppression in the solitary group may explain the lower incidence of acute rejection (27%) and improved 1-year graft survival (93%) in this group. Limiting the incidence of early acute rejection in these small pediatric grafts with aggressive immunosuppressive regimens likely minimizes the onset of focal segmental glomerulosclerosis and proteinuria, which eventually lead to graft loss. This study is not prospective, and the difference in survival between the en bloc and solitary groups is most likely because of differing immunosuppressive regimens and donor quality between the two groups.

The donor age and weight in the solitary group tended to be greater than the en bloc group in our study (Table 1). This is because those en bloc pairs selected for separation into solitary allografts at our institution had a kidney length greater than 6 cm (mean, 6.3 cm) and tended to be from older pediatric donors (mean, 22 months). The 6-cm cutoff chosen was not based on any prior published data but on the personal experience of our senior transplant surgeon (S.T.B.). A combination of strict donor (weight, >14 kg; kidney length, >6 cm) and recipient (weight, <70 kg) selection criteria along with an aggressive immunosuppression regimen led to a 1-year graft survival of 93% for solitary allografts from donors younger than 2 years of age. We made a concerted effort to select recipients from our wait list who weighed less than 70 kg, especially when a solitary pediatric kidney was being used. Even though the recipients of the solitary donor kidneys tended to weigh less (mean, 65 kg) than the recipients of the en bloc kidneys (mean, 69 kg), this difference was not statistically significant ( $P=0.792$ ). There is some evidence in the literature that suggests smaller adult recipients will have a lower risk of developing long-term hyperfiltration injury in these pediatric allografts (14, 15).

Interestingly, the renal function curves in both the en bloc and solitary groups were similar and continued to improve over time. Assuming that the curves continued to show improvement in renal function over time, the en bloc and solitary groups would reach a CrCl greater than 100 mL/min from 6 to 10 years as previously demonstrated by larger en bloc series (3). This observation of improving renal function months after transplantation was also reported by Ratner

and associates (9). Longer follow-up is needed for our solitary and en bloc groups to determine the point at which renal function begins to plateau.

#### CONCLUSION

The use of solitary pediatric kidneys in adult recipients results in no compromise of graft survival. Separation of en bloc pairs can be considered when the renal allograft measures greater than 6 cm in length and the donor weight is greater than 14 kg. The transplantation of solitary pediatric kidneys into adult recipients is successful and the majority of pediatric en bloc allografts can be separated before transplantation.

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