World Journal of Transplantation

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DOI: 10.5500/wjt.v6.i1.239

World J Transplant 2016 March 24; 6(1): 239-248
ISSN 2220-3230 (online)

ORIGINAL ARTICLE

Retrospective Cohort Study

Single *vs* dual (*en bloc*) kidney transplants from donors ⩽ 5 years of age: A single center experience

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Author contributions: All of the authors contributed to this paper; Al-Shraideh Y, Farooq U, El-Hennawy H, Khan M, Doares W, Kaczmorski S, Hairston G, Brim E, Mangus M and Stratta RJ participated in research design; Al-Shraideh Y, Farooq U, Farney AC, Palanisamy A, Rogers J, Orlando G, Reeves-Daniel A, Doares W, Gautreaux MD and Stratta RJ participated in writing of the paper; Al-Shraideh Y, Farooq U, Palanisamy A, Khan M, Reeves-Daniel A, Doares W, Kaczmorski S, Iskandar SS and Stratta RJ participated in performance of the research; Al-Shraideh Y, El-Hennawy H, Rogers J, Hairston G, Brim E, Mangus M and Stratta RJ participated in data collection and analysis.

Institutional review board statement: The study was reviewed and approved for publication by our (Wake Forest University Health Sciences) Institutional Review Board.

Informed consent statement: All study participants or their legal guardian provided written informed consent about personal and medical data collection prior to study enrollment.

Conflict-of-interest statement: All of the Authors have no conflict of interest related to the manuscript.

Data sharing statement: The original anonymous dataset is available on request from the corresponding author at: rstratta@wakehealth.edu.

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Received: June 12, 2015
Peer-review started: June 15, 2015
First decision: September 16, 2015
Revised: October 14, 2015
Accepted: December 1, 2015
Article in press: December 2, 2015
Published online: March 24, 2016

Abstract

AIM: To compare outcomes between single and dual *en bloc* (EB) kidney transplants (KT) from small pediatric donors.

METHODS: Monocentric nonprospective review of KTs from pediatric donors ⩽ 5 years of age. Dual EB KT was defined as keeping both donor kidneys attached to

the inferior vena cava and aorta, which were then used as venous and arterial conduits for the subsequent transplant into a single recipient. Donor age was less useful than either donor weight or kidney size in decision-making for kidney utilization as kidneys from donors < 8 kg or kidneys < 6 cm in length were not transplanted. Post-transplant management strategies were standardized in all patients.

RESULTS: From 2002-2015, 59 KTs were performed including 34 dual EB and 25 single KTs. Mean age of donors (17 mo *vs* 38 mo, $P < 0.001$), mean weight (11.0 kg *vs* 17.4 kg, $P = 0.046$) and male donors (50% *vs* 84%, $P = 0.01$) were lower in the dual EB compared to the single KT group, respectively. Mean cold ischemia time (21 h), kidney donor profile index (KDPI; 73% *vs* 62%) and levels of serum creatinine (SCr, 0.37 mg/dL *vs* 0.49 mg/dL, all P = NS) were comparable in the dual EB and single KT groups, respectively. Actuarial graft and patient survival rates at 5-years follow-up were comparable. There was one case of thrombosis resulting in graft loss in each group. Delayed graft function incidence (12% dual EB *vs* 20% single KT, P = NS) was slightly lower in dual EB KT recipients. Initial duration of hospital stay (mean 5.4 d *vs* 5.6 d) and the one-year incidences of acute rejection (6% *vs* 16%), operative complications (3% *vs* 4%), and major infection were comparable in the dual EB and single KT groups, respectively (all P = NS). Mean 12 mo SCr and abbreviated MDRD levels were 1.17 mg/dL *vs* 1.35 mg/dL and 72.5 mL/min per 1.73 m^2 *vs* 60.5 mL/min per 1.73 m^2 (both P = NS) in the dual EB and single KT groups, respectively.

CONCLUSION: By transplanting kidneys from young pediatric donors into adult recipients, one can effectively expand the limited donor pool and achieve excellent medium-term outcomes.

Key words: Donor age; Donor weight; *En bloc* kidney transplant; Kidney donor profile index; Single kidney transplant; Small pediatric donor

Core tip: We evaluated outcomes in 59 kidney transplants (KT) from young pediatric donors ⩽ 5 years of age including 34 dual *en bloc* (EB) and 25 single KTs. Mean donor age and weight were significantly lower in the dual EB compared to the single KT group. Actuarial graft and patient survival rates at 5-years follow-up were comparable as were other outcomes. With appropriate recipient selection, excellent mid-term results can be attained by transplanting kidneys from small pediatric donors into adult recipients, which effectively expands the limited donor pool. Kidney donor profile index is predictive of survival for single KT but is not accurate for predicting dual EB KT outcomes from young pediatric donors.

Al-Shraideh Y, Farooq U, El-Hennawy H, Farney AC, Palanisamy A, Rogers J, Orlando G, Khan M, Reeves-Daniel A, Doares W, Kaczmorski S, Gautreaux MD, Iskandar SS, Hairston G, Brim E, Mangus M, Stratta RJ. Single *vs* dual (*en bloc*) kidney transplants from donors ⩽ 5 years of age: A single center experience. *World J Transplant* 2016; 6(1): 239-248 Available from: URL: http://www.wjgnet.com/2220-3230/full/v6/i1/239.htm DOI: http://dx.doi.org/10.5500/wjt.v6.i1.239

INTRODUCTION

The burgeoning crisis between organ demand and supply, particularly in kidney transplantation (KT), has fueled initiatives to safely and successfully expand the limited donor pool. Since 2002, the kidney waiting list has doubled from 50000 to > 100000 candidates and waiting times have increased from a median of 3 to > 5 years[1]. At present, nearly 30% of patients waiting on the kidney list have been on dialysis for at least 6 years[1]. For patients awaiting KT, only 48% will ever actually receive a KT[1,2]. Since 2004, the total number of KTs [both from living and deceased donors (DD)] performed each year in the United States has remained static and ranges has between 16000 and 17000[1]. In the last decade, the total number of kidney DDs has slowly increased from 6325 to 7547 annually commensurate with a decrease in living donors. Among these DDs, the annual number ⩽ 5 years of age range from 200 to 300, which accounts for approximately 4% of kidney DDs[3]. The prolonged waiting times for KT and associated longer periods on dialysis have been associated with significant morbidity and mortality[4].

Dual *en bloc* (EB) KT was first described by Carrel[5] in 1908 in a xenograft model. Transplantation of dual EB pediatric DD kidneys into an adult was first reported in 1972[6]. Historically, transplantation of small, pediatric, DD kidneys into adults was reported to be technically challenging and associated with vascular and urinary complications, acute rejection, delayed graft function (DGF), and the development of hyperfiltration injury[7-11]. For these reasons, many transplant centers were reluctant or refrained completely from utilizing kidneys from small pediatric donors because they were considered "marginal"[12-14]. However, several studies in the new millennium have demonstrated that excellent outcomes could be achieved with dual EB KT secondary to improvements in donor management, organ recovery and preservation techniques, antibody identification and crossmatch methodology, recipient selection and management, surgical techniques and immunosuppression[15-20].

Consequently, dual EB KT has become more widely accepted and has been extended to include both donation after cardiocirculatory death (DCD) donors and infant donors < 5 kg body weight[21]. However, the lower limits of acceptable age or body

weight for single KT are currently unknown and many pediatric kidneys from donors either < 5 years or < 20 kg are transplanted dual EB rather than split into two recipients. Because dual EB KT halves the number of potential transplant recipients, in the past decade there has been growing interest in single KT from small pediatric donors[22-26]. Whereas dual EB KT maximizes graft function, single KT maximizes resource availability[27-29]. A few comparative studies of single *vs* dual EB KTs from pediatric donors into adult recipients have been published both from registry and monocentric analyses[30-33]. The aim of this study was to report our monocentric retrospective data spanning 12.5 years with dual EB *vs* single KT from small pediatric donors ≤ 5 years of age in patients receiving standardized management algorithms.

MATERIALS AND METHODS

Study design

We conducted a retrospective chart review of all DD KTs performed from small pediatric donors ≤ 5 years of age at our center from 7/02-1/15 with a mean follow-up of 56 mo. During this 12.5 year study period, a total of 59 DD KTs met the entry criteria and were categorized into dual EB and single KT groups for purposes of comparison.

Definitions

Dual EB KT was defined as keeping both donor kidneys attached to the aorta and inferior vena cava, which were then used as arterial and venous conduits for the subsequent transplant into a single recipient. DGF was defined as the need for dialysis for any reason in the first week post-transplant. Renal allograft loss was defined as death with a functioning graft (DWFG), allograft nephrectomy, return to dialysis, kidney re-transplantation, or return to the pretransplant serum creatinine (SCr) level in a preemptively transplanted patient.

Donor evaluation and selection

In order to estimate the donor creatinine clearance (CrCl), the Cockcroft-Gault calculation was used. We relied mainly on the donor body weight and actual kidney size and anatomy to determine whether or not to use the kidneys either for dual EB, single KT or not at all. In our dual EB KT experience, the youngest donor age was 5 mo (7.7 kg body weight) and the lowest donor weight was 6.8 kg (7 mo of age). Donor age was less useful than either donor weight or kidney size in our decision-making for kidney utilization as we usually refused kidneys from donors < 8 kg or kidneys < 6 cm in length. In our single KT experience, the youngest donor was 15 mo of age and lowest donor weight was 13.0 kg. However, similar to our lower limits of donor acceptability for dual EB KT, size of the vessels (aorta and inferior vena cava for dual EB, renal artery and vein for single KT) was the ultimate factor that determined whether kidneys could be separated and safely transplanted into two recipients. In contrast to our adult DD KT experience, machine preservation of small pediatric donor kidneys was rarely performed.

Recipient selection

Whenever possible, based on allocation criteria, we attempted to select patients < 60 years of age for small pediatric donor kidneys. We specifically avoided selecting pediatric recipients < 12 years of age. Early in our experience, we transplanted 2 teenagers (ages 13 and 15 years), both of whom suffered early graft loss [one thrombosis secondary to recurrent fulminant focal segmental glomerulosclerosis (FSGS), one severe rejection secondary to noncompliance]. Consequently, we subsequently decided to consider the pediatric age group (who already receive priority towards young adult donors) as an exclusion criterion to KT from small pediatric donors at our center.

Similar to donor assessment, body weight was more useful in adult recipient selection than age. We attempted to select recipients < 180-200 lbs. in weight in order to avoid large mismatches between kidney and recipient size. In addition, we selected low immunological risk patients including primary transplants with a 0% panel reactive antibody (PRA) level, matching for human leukocyte antigens (HLA), and compatible B and T cell flow cytometry crossmatches in accordance with guidelines promulgated by the United Network for Organ Sharing (UNOS)[34,35]. Reasons for selecting low immunological risk patients included concerns regarding the success of treating early acute rejection in the setting of limited nephron mass (prior to kidney growth) coupled with the hazards of performing biopsies on small pediatric donor kidneys.

All KTs from small pediatric donors were performed with informed consent from the recipient, acknowledging that there might be higher risks of DGF and technical complications unique to transplanting these types of kidneys. Other considerations in appropriate recipient selection included favorable vascular anatomy (no severe concentric iliac atherosclerosis), adequate bladder capacitance and function (to accommodate 2 ureteral anastomoses), no chronic anti-coagulation (warfarin or clopidogrel) or history of thrombophilia, adequate cardiac function and reserve (ejection fraction > 40%-50%, no atrial fibrillation or significant valvular disease), absence of either significant pulmonary or systemic hypertension, no orthostasis or history of hypotension, no prior pelvic/retroperitoneal surgery or irradiation, and absence of high risk for recurrent kidney disease.

Surgical techniques

Donor kidneys were recovered dual EB with aorta, inferior vena cava and bilateral ureters in continuity; no attempt was made to perform any dissection

Table 1 Donor, transplant and recipient characteristics

Mean ± SD	Dual *en bloc* KT *n* = 34	Single KT *n* = 25	*P* value
Donor age (yr)	1.4 ± 0.8	3.3 ± 1.2	< 0.001
Donor gender: Male	17 (50%)	21 (84%)	0.01
Donor: African American	13 (38%)	7 (28%)	NS
Donor weight (kg)	11.0 ± 2.6	17.4 ± 3.1	0.046
Import organ (non-local)	17 (50%)	14 (56%)	NS
Calculated CrCl (mL/min)	99 ± 50	111 ± 60	NS
Pre-retrieval SCr (mg/dL)	0.37 ± 0.26	0.49 ± 0.24	NS
DCD donors	6 (17.6%)	3 (12%)	NS
Cause of death: Trauma	19 (56%)	11 (44%)	NS
Cold ischemia time (h)	21.0 ± 7.8	20.9 ± 6.4	NS
KDPI (%)	73.2 ± 9.1	62.2 ± 10.4	NS
HLA-mismatch	4.2 ± 1.4	4.2 ± 1.4	NS
0-Antigen mismatch	0	1 (4%)	NS
0% PRA	30 (88%)	24 (96%)	NS
PRA > 40%	2 (5.9%)	1 (4%)	NS
CMV donor+/recipient-	5 (14.7%)	2 (8%)	NS
Retransplant	1 (3%)	3 (12%)	NS
Recipient age (yr)	38.0 ± 12.1	45.7 ± 16.1	0.040
Recipient gender: Male	21 (62%)	13 (52%)	NS
Recipient: African American	17 (50%)	12 (48%)	NS
Recipient weight (kg)	72.2 ± 14.7	75.2 ± 12.0	NS
Recipient with diabetes	6 (17.6%)	6 (24%)	NS
Preemptive transplant	4 (11.8%)	5 (20%)	NS
Duration of dialysis Pretransplant (mo)	41.2 ± 27.2	43.5 ± 32.6	NS
Waiting time (mo)	25.2 ± 13.6	25.4 ± 27.2	NS

CrCl: Creatinine clearance; KT: Kidney transplantation; SCr: Serum creatinine; DCD: Donation after cardiac death; KDPI: Kidney Donor Profile Index; HLA: Human leukocyte antigen; PRA: Panel reactive antibody; NS: Not significant.

along the aorta, vena cava or renal hila in the donor. Back bench preparation of the dual EB specimen included oversewing the supra-renal vena cava and aorta with careful, meticulous dissection of the infra-renal vena cava and aorta with individual ligation of lumbar and mesenteric branches. Minimal dissection was performed in the renal hila in order to preserve any accessory vessels. Perinephric fat was left on the kidneys and suture fixation of the upper poles antero-medially was performed to maintain correct graft orientation. The dual EB allograft was transplanted extraperitoneally with end-to-side anastomoses between the distal donor vena cava and the right external iliac vein and between the distal donor aorta and the right external iliac artery. Separate parallel extravesical ureteroneocytostomies over two small (3.5-4 French) indwelling stents were performed to the dome of the bladder, attempting to make the ureters as short as possible. Single pediatric donor kidneys were transplanted in a fashion similar to standard adult KT using an extraperitoneal approach, the distal external iliac vessels as targets, and generous vena caval and aortic cuffs or patches around the orifices of the renal vein and artery, respectively. Ureteroneocystostomy was performed in an extravesical fashion over a single indwelling double-J ureteral stent (5-6 French), again attempting to make the ureter as short as possible without tension. Both EB and single pediatric allografts were affixed either to the lateral pelvic wall or retroperitoneum using perinephric fat or capsule as needed in order to avoid torsion.

Immunosuppression and post-transplant management

Nearly all DD KT patients received either rabbit antithymocyte globulin or alemtuzumab induction as previously reported[34-36]. Daily immunosuppression maintenance therapy included mycophenolate mofetil, tacrolimus, and either early corticosteroid withdrawal or rapid tapering as previously reported[36]. Ultrasound-guided percutaneous kidney biopsies were performed to evaluated renal allograft dysfunction and to diagnosis and grade acute rejection. However, because of small kidney size and the theoretical risk for a higher complication rate, we did not perform surveillance kidney biopsies in these patients. All patients received surgical site, anti-fungal, anti-viral, and anti-Pneumocystis prophylaxes as previously published[34-36]. Most patients received aspirin as prophylaxis but anti-coagulation agents were not specifically administered. Infections were categorized as major if the patient required hospitalization for either diagnosis or treatment. SCr levels were used to determine renal allograft function. In addition, the abbreviated modification of diet in renal disease (MDRD) formula was used to determine glomerular filtration rate (GFR)[37].

Statistical analysis

Both retrospective and prospective data were analyzed and confirmed by medical record review with approval from the Wake Forest University Health Science Institutional Review Board. Statistical review of the study was performed by a biomedical statistician. Actual graft and patient survival rates were reported, and actuarial and death-censored graft survival rates were also established using Kaplan-Meier methodology with comparisons using the log-rank test. A two-tailed *P* value of < 0.05 was considered significant.

RESULTS

From 2002-2015, we performed 59 KTs from young pediatric donors ⩽ 5 years of age including 34 dual EB and 25 single KTs. The majority of dual EB KTs (23/34 = 68%) were performed since 2010 whereas the majority of single KTs (16/25 = 64%) were performed prior to 2010. Mean age of donors (17 mo *vs* 38 mo, *P* < 0.001), mean weight (11.0 kg *vs* 17.4 kg, *P* = 0.046) and male donors (50% *vs* 84%, *P* = 0.01) were lower in the dual EB compared to the single KT group, respectively (Table 1). All but 4 of the dual EB KT donors were ⩽ 2 years of age whereas all but 6 of the single KT donors were ⩾ 3 years of age. Organ import (52%), DCD donors (15%), mean cold ischemia (21 h) and terminal SCr levels (0.37 mg/dL *vs* 0.49 mg/dL, all *P* = NS) were comparable

Table 2 Results

Mean ± SD	Dual *en bloc* KT *n* = 34	Single KT *n* = 25	*P* value
Patient survival	32 (94.1%)	20 (80%)	0.12
Graft survival	31 (91.2%)	17 (68%)	0.04
Follow-up (mo)	52 ± 38	74 ± 41	NS
Death-censored graft survival	31/33 (93.9%)	17/21 (81%)	0.19
DWFG	1 (3%)	4 (16%)	0.15
Months to DWFG	15	54 ± 6.5	NS
Delayed graft function	4 (11.8%)	5 (20%)	NS
# Days to SCr < 3.0 mg/dL	4.7 ± 4.5	8.9 ± 7.2	NS
Initial length of stay (d)	5.4 ± 2.9	5.6 ± 3.4	NS
Acute rejection in 1st year	2 (5.9%)	4 (16%)	NS
Surgical complications	1 (2.9%)	1 (4%)	NS
12 mo SCr (mg/dL)	1.17 ± 0.3	1.35 ± 0.3	NS
12 mo GFR (mL/min per 1.73 m^2)	72.5 ± 18.4	60.5 ± 18.1	NS
4 yr SCr (mg/dL)	1.0 ± 0.4	1.17 ± 0.4	NS
4 yr GFR (mL/min per 1.73 m^2)	81 ± 21.9	64.4 ± 18.1	NS

KT: Kidney transplantation; SCr: Serum creatinine; DWFG: Death with a functioning graft; GFR: Glomerular filtration rate; NS: Not significant.

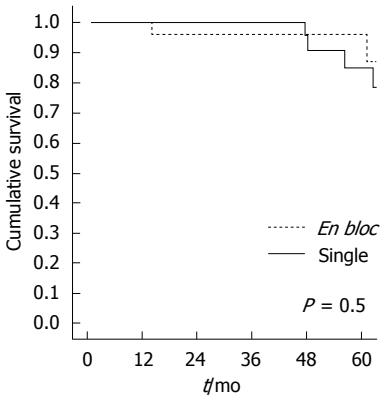

Figure 1 Actuarial patient survival rates among recipients of dual *en bloc* *vs* single kidney transplantation from young pediatric donors.

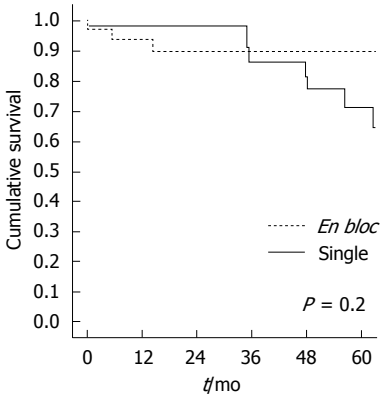

Figure 2 Actuarial graft survival rates among recipients of dual *en bloc* *vs* single kidney transplantation from young pediatric donors.

in the dual EB and single KT groups, respectively. The longest cold ischemia times were 45 h for a dual EB and 35 h for a single KT. Only one donor (in the dual EB group) had evidence for acute kidney injury with a terminal SCr level > 1.0 mg/dL. In the single KT group, both kidneys from the same donor were transplanted at our center in 6 cases (12 KTs). Mean kidney donor profile index (KDPI) was 73% for dual EB *vs* 62% for single KT donors (*P* = NS).

Other than mean recipient age (38 dual EB *vs* 46 years single KT, *P* = 0.04), there were no differences in recipient variables between groups (Table 1). Nearly 50% of recipients were African American. With a mean 52 mo follow-up in dual EB compared to 74 mo follow-up in single KT recipients, actual graft (91% *vs* 68%, *P* = 0.04) and patient (94% *vs* 80%, *P* = 0.12) survival rates were slightly higher in dual EB compared to single KT recipients, respectively (Table 2). Death-censored kidney graft survival rates were 93.9% and 81% (*P* = 0.19), respectively. Actuarial patient and graft survival rates are shown in Figures 1 and 2 (*P* = NS). Survival rates were similar up to 4 years follow-up in the each group after which time graft survival decreased in the single KT group. There was no influence of recipient gender or ethnicity on outcomes.

As previously mentioned, patients #3 and #4 in our dual EB KT experience were both teenagers who developed early graft failure (at 5 mo secondary to noncompliance and at 2 d secondary to thrombosis related to fulminant recurrence of FSGS, respectively). Patient #3 subsequently died 5 years later secondary to a hemorrhagic stroke (in the absence of retransplantation because of a high PRA level); the only other death (and graft loss) in the dual EB KT group was a 28 years old male who experienced DWFG at 15 mo post-transplant; the cause of death was unknown. However, one patient developed a near 50% lower pole infarction of one kidney secondary to a missed accessory renal artery that was managed expectantly without sequela. Another patient developed a partial lower pole infarction of the left kidney secondary to a missed accessory renal artery that was also successfully managed expectantly. A third patient developed a lower pole infarct of the right kidney secondary to a missed accessory renal artery and underwent allograft nephrectomy of the left kidney on post-operative day #1 because of venous thrombosis. Fortunately this latter patient has acceptable renal function from the remaining right kidney and no evidence of a ureteral complication with limited follow-up. One recipient developed dual ureteral strictures at 15 mo following dual EB KT secondary to acute cellular and antibody-mediated rejection related to medication noncompliance. The strictures were initially managed with percutaneous nephrostomies followed by placement of chronic internalized ureteral stents that are changed at frequent intervals.

In the single KT group, there were 5 deaths (4 DWFGs) occurring at a mean of 70 mo post-KT; none occurred until 4 years or more post-KT. Causes of

death include 2 strokes, 2 pneumonias/respiratory failure, and one unknown. There were 8 graft losses including 4 DWFGs, 2 secondary to acute and chronic rejection, 1 chronic allograft nephropathy and one early thrombosis. There were no urological or other surgical complications in either group.

During this same period in time, we performed 758 standard criteria donor (SCD) KTs (excluding young pediatric donors) in 722 recipients with an age mean of 50.4 years. With 63 mo mean follow-up, actual patient and graft survival rates in SCD KT recipients were 83.9% [P = 0.15 compared to dual EB (94%), P = NS compared to single KT (80%)] and 70.4% [P = 0.006 compared to dual EB (91%), P = NS compared to single KT (68%)], respectively. The kidney graft survival rate (censored for death) following SCD KT was 79.6% [P = 0.04 compared to dual EB (93.9%), P = NS compared to single KT (81%)]. From 2008-2015, we performed 180 living donor KTs in 179 patients with an age mean of 47.4 years. With a 40 mo mean follow-up, actual patient and graft survival rates were 92.7% [P = NS compared to dual EB (94%), P = 0.05 compared to single KT (80%)] and 88.9% [P = NS compared to dual EB (91%), P = 0.01 compared to single KT (68%)], respectively. The kidney graft survival rate (censored for death) following living donor KT was 93.6% [P = NS compared to dual EB (93.9%), P = 0.065 compared to single KT (81%)].

The DGF rate (12% dual EB *vs* 20% single KT, P = NS) was slightly lower in dual EB KT recipients. Duration of hospitalization (mean 5.4 d *vs* 5.6 d) and the one-year incidences of acute rejection (6% *vs* 16%), operative complications (3% *vs* 4%), and major infection were comparable in the dual EB and single KT groups, respectively (all P = NS). Mean 12 mo SCr and aMDRD levels were 1.17 mg/dL *vs* 1.35 mg/dL and 72.5 mL/min per 1.73 m^2 *vs* 60.5 mL/min per 1.73 m^2 (both P = NS) in the dual EB and single KT groups, respectively. At 4 years follow-up, the corresponding values were 1.0 mg/dL *vs* 1.17 mg/dL and 81 mL/min per 1.73 m^2 *vs* 64.4 mL/min per 1.73 m^2 in the dual EB and single KT groups, respectively.

DISCUSSION

Historically, kidneys from donors at the extremes of age have been considered as marginal organs for KT because of concerns regarding technical complications and long-term functional outcomes[38]. Most of the recent expansion in organ donation has occurred at the older extreme of age[1]. However, unlike kidneys from older donors, kidneys transplanted from pediatric donors into adult recipients have the capacity to grow to a normal adult renal size within a few months of KT and represent an under-utilized resource[39]. Both conversion and utilization rates are lower with younger DD age[3,31,33]. Small pediatric donor KT is gaining wider acceptance but is still regarded as controversial by some and is not universally accepted. The total number of nephrons in each kidney (estimated at a mean of approximately 1.0 million) is attained by 36 wk of gestation; subsequent renal "growth" occurs by hypertrophy rather than increases in nephron number[40,41]. Excellent outcomes with pediatric dual EB KT have been published from recent reports, which in theory reduces concerns regarding functional outcomes and graft longevity because of the potential for growth coupled with the increased nephron mass associated with transplantation of both kidneys[20,31-33]. However, there exists a persistent unwillingness to separate small pediatric donor kidneys for KT into two recipients, and no consensus exists as to when single KT can be safely and successfully performed[42-46].

Previous studies have suggested that pediatric dual EB KT should be performed for donors < 10 kg whereas "splitting" kidneys for use in two recipients is appropriate when the donor is > 20 kg in size[20,24,26]. However, donors weighing between 10-20 kg represent a "gray area" in achieving the proper balance between utilization and outcomes[31,33]. In a large retrospective UNOS registry analysis of donors < 10 years of age from 1995-2007, Kayler *et al*[24] reported that kidneys from donors with a 15-19, 10-14, and < 10 kg body weight were used for dual EB KT in 40%, 65%, and 86% of adult recipients, respectively[24]. In a subsequent UNOS registry analysis of donors < 10 years of age spanning 1987-2007, Sureshkumar *et al*[25] reported that kidneys from donors with a 10-13, 13-15, 15-20, and > 20 kg body weight were used for dual EB KT in 63%, 49%, 24%, and 4% of adult recipients, respectively. In addition, they noted that although pediatric dual EB kidneys functioned "better" than single kidneys for all pediatric donor weight groups studied, "acceptable" graft outcomes could be achieved with single KT from donors > 10 kg because the graft failure risk declined above this donor size.

In 2011, Laurence *et al*[26] constructed a decision analysis model based on existing literature in order to predict outcomes (expressed as life years) for waitlist patients according to whether they underwent dual EB or single KT from a pediatric donor. At all ages of recipients studied, the combined projected life years of both recipients of solitary KTs exceeded the projected life years of a dual EB KT. However, for recipients of kidneys from donors < 10 kg, there was an estimated net loss of life years following solitary KT irrespective of recipient age group.

Other studies have reported that outcomes following dual EB KT are comparable to those achieved following living donor KT whereas outcomes following single KT from pediatric donors are comparable to those achieved following SCD KT and superior to those achieved following ECD KT[27,43,45,46]. In our experience, we likewise found that dual EB KT outcomes were comparable to concurrent living donor KT and superior to SCD KT at our center whereas outcomes following single KT from pediatric donors were inferior to living donor KT and similar to those achieved following SCD

KT. Although these findings may be explained in part by variations in recipient age, differences persisted even when we censored for DWFG.

We conducted a retrospective review spanning 12.5 years of our clinical experience in KT from small pediatric donors (defined as ⩽ 5 years of age) and compared outcomes between recipients of dual EB *vs* single KTs. The majority of dual EB KTs (69%) were performed since 2010 whereas the majority of single KTs (64%) were performed prior to 2010. In our dual EB KT experience, the youngest donor age was 5 mo (7.7 kg body weight) and the lowest donor weight was 6.8 kg (7 mo of age). Donor age was less useful than either donor weight or kidney size in our decision-making for kidney utilization as we usually refused kidneys from donors < 8 kg or kidneys < 6 cm in length. Over time, we have become more comfortable with performing dual EB KTs from smaller pediatric donors; 14 of the 34 dual EB donors were < 10 kg body weight and 50% were age ⩽ 12 mo. In our single KT experience, the youngest donor was 15 mo of age and lowest donor weight was 13.0 kg. However, similar to our lower limits of donor acceptability for dual EB KT, size of the vessels (inferior vena cava and aorta for dual EB, renal vein and artery for single KT) and ureters were the ultimate factors that determined whether kidneys could be separated and safely transplanted into two recipients.

Recipient selection is paramount to success in KT from small pediatric donors. Similar to donor assessment, we found that body weight was more useful in adult recipient selection than age. We attempted to select recipients < 180-200 lbs in weight in order to avoid large mismatches between kidney and recipient size in an attempt to minimize the risk of hyperfiltration injury[47-50]. However, we specifically excluded pediatric recipients from consideration after a negative experience with dual EB KT in 2 teenagers who developed early graft loss. Some authors have reported that the risk of graft failure may be higher when transplanting kidneys from small pediatric donors into pediatric recipients[20,24,28,32,43]. The primary reason to avoid transplanting small pediatric donor kidneys into pediatric recipients (in the absence of a primary renal disease with a high recurrence rate) is to avoid anastomosing small donor vessels to small recipient vessels in relatively hypotensive (compared to adults) patients, which may result in early technical failure. At present, 90% of all pediatric DD kidneys are transplanted into adult recipients, 37% of whom are aged 50 years and older[41]. However, recent studies are beginning to question the prohibition of pediatric recipients from receiving pediatric donor kidneys as improving results are being reported and size-matching between donors and recipients seems logical from a functional and growth perspective[21,29].

We have observed that small pediatric donors are assigned relatively high scores in the new KDPI (overall mean 69% in our experience) because of the negative cumulative impact of reduced donor height, weight, and age in the calculation. The UNOS KDPI is derived from the kidney donor risk index that explicitly incorporates 10 donor factors (such as donor age, hypertension, diabetes, ethnicity, height, weight, cause of death, SCr, hepatitis C status, and whether the donation occurred after cardiocirculatory death) to rank order the relative quality of kidneys into a continuous score as defined by an aggregate population relative risk[51,52]. However, many of the KDPI variables do not "fit" for small pediatric donors, particularly in the setting of dual EB KT. For example, the mean KDPI in our single KT experience was 62%, which translates roughly to an expected graft survival rate at 5 years follow-up of 69%. Our observed graft survival rate at 5 years follow-up in this group was 70%. Conversely, the mean KDPI in the dual EB KT group was 73%, which translates roughly to an expected graft survival rate at 5 years follow-up of 66%. However, our observed graft survival rate at 5 years follow-up in this group was 90%. Consequently, one might contend that the KDPI is not applicable in this setting and a new predictive algorithm may be needed not only for dual EB KT in particular but perhaps dual KT in general.

Other important aspects of recipient selection included informed consent and selecting low immunological risk patients (primary transplants with a low PRA level, HLA-matching, negative T and B cell flow crossmatches) so as to avoid the need to either biopsy or treat for acute rejection. Additional recipient "contraindications" to either dual EB or single KT from small pediatric donors included severe pulmonary or systemic hypertension, orthostasis or severe hypotension, low ejection fraction, severe iliac vascular disease, presence of an abnormal urinary bladder (either anatomically or functionally), high risk for recurrent kidney disease, history of thrombophilia or need for anti-coagulation.

Based on this experience, we found that excellent mid-term outcomes can be attained from young pediatric donors; our protocol at present is to perform dual EB KT from donors < 15 kg and single KT from donors ⩾ 15 kg. Limitations of our study design include its retrospective nature and relatively small number of KTs in each group whereas strengths include intermediate-term follow-up and standardized management algorithms pertaining to donor and recipient selection, surgical technique, immunosuppression and post-transplant management. It is well established that small pediatric donor kidneys increase in size and have excellent function in adult recipients provided that technical complications or acute rejection do not occur[8,39,53]. Pediatric donor kidneys appear to have an excess capacity for hypertrophy, which translates into an absolute increase in GFR over time[39,43,46,49,54]. Because pediatric dual EB kidneys have double the nephron mass compared to single KT, studies have shown that these recipients may attain renal function that is similar to or even

better than functional outcomes achieved following living donor KT[43,45,49]. In our experience, renal function improved in both groups from 1 to 4 years following KT but the improvement observed in the dual EB KT group was more notable.

Fortunately, we did not note in our study an increase in technical complications associated with the utilization of small pediatric donor kidneys. There was one thrombosis resulting in early graft loss in each group and no early ureteral complications mandating any re-operation or intervention. A study of UNOS data demonstrated a 5% thrombosis risk among donors between 12 and 17 years of age compared to a 10% rate of vascular thrombosis using donors < 5 years of age[15]. This study also showed inferior outcomes with single grafts from donors > 15 kg compared to using dual EB kidneys from donors < 5 years of age. Other risk factors for inferior outcomes in this study included retransplants, those with a body mass index > 24 kg/m^2, black recipients, and prolonged ischemia time[15]. Some studies have demonstrated that small donor kidneys may have a higher risk of late graft failure if transplanted into large recipients[48,50,55]. Consequently, the relative sizes of the recipient and donor need to be considered. When the donor weight is greater than 14 kg and the individual renal allografts measure greater than 6 cm in length, then separation of EB pairs can be contemplated. Other series have shown that kidneys from donors 1-3 year of age and/or weighing 9-15 kg can be successfully transplanted EB and those from donors > 3 years of age and/or weighing > 15 kg can be successfully transplanted as single grafts[13,30]. Our experience mirrors and supports these previous recommendations. Moreover, we would like to underscore the fact that in the new Kidney Allocation System, the KDPI for small pediatric donor kidneys does not accurately represent the outcomes that can be achieved with dual EB KT.

COMMENTS

Background

The burgeoning crisis between organ supply and demand, particularly in kidney transplantation, has fueled initiatives to safely and successfully expand the limited donor pool. Historically, transplantation of small pediatric donor kidneys into adult recipients was reported to be technically challenging and associated with an increased risk of vascular and urinary complications, acute rejection, delayed graft function, and the development of hyperfiltration injury. For these reasons, many transplant centers are reluctant to transplant kidneys from small pediatric donors, which results in lower conversion and utilization rates among young donors.

Research frontiers

Most of the recent expansion in organ donation has occurred at the older extreme of age. However, unlike kidneys from older donors, kidneys transplanted from small pediatric donors into adult recipients have the capacity to grow to a normal adult renal size and represent an under-utilized resource. Transplantation of kidneys from small pediatric donors is gaining wider acceptance but is still regarded as controversial by some and is not universally accepted. Moreover, criteria for using these kidneys either as single or dual *en bloc* (EB) transplants are evolving. Previous studies have suggested that pediatric dual EB kidney transplants (KT) should be performed for donors < 10 kg whereas "splitting" kidneys for use in two recipients is appropriate when the donor is > 20 kg in size. However, donors weighing between 10-20 kg represent a "gray area" in achieving the proper balance between utilization and outcomes.

Innovations and breakthroughs

The authors conducted a retrospective review spanning 12.5 years of the authors clinical experience in kidney transplantation from small pediatric donors (defined as ⩽ 5 years of age) and compared outcomes between recipients of dual EB *vs* single KT. In the authors' dual EB KT experience, the youngest donor age was 5 mo (7.7 kg body weight) and the lowest donor weight was 6.8 kg (7 mo of age). Over time, the authors have become more comfortable with performing dual EB KT from smaller pediatric donors; 14 of the 34 dual EB donors were < 10 kg body weight and 50% were age ⩽ 12 mo. In the authors' single KT experience, the youngest donor was 15 mo of age and lowest donor weight was 13.0 kg. Recipient selection is paramount to success as we attempted to avoid large mismatches between kidney and recipient size. However, the authors specifically excluded pediatric recipients from consideration. The authors established that dual EB outcomes were comparable to concurrent living donor kidney and superior to standard criteria adult deceased donor KT whereas outcomes following single kidneys from small pediatric donors were inferior to concurrent living donor kidney and similar to those achieved following standard criteria adult deceased donor KT at the center.

Applications

Based on this experience, the authors verified that excellent intermediate-term outcomes can be achieved from young pediatric donors; the authors' current policy is to perform dual EB KT from donors < 15 kg and single KT from donors ⩾ 15 kg. Moreover, the authors have observed that small pediatric donors are assigned relatively high scores in the new Kidney Donor Profile Index (KDPI) because of the negative cumulative impact of reduced donor height, weight, and age in the calculation. In the new Kidney Allocation System, however, the KDPI for small pediatric donor kidneys does not accurately predict outcomes that can be achieved with dual EB KT, suggesting that a new predictive algorithm may be needed in this setting.

Terminology

Dual EB KT are performed by keeping both donor kidneys attached to the aorta and inferior vena cava, which are then used as arterial and venous conduits for the subsequent transplant of both kidneys as a single unit into one recipient. The KDPI is derived from the kidney donor risk index that explicitly incorporates 10 donor factors (such as donor age, hypertension, diabetes, ethnicity, height, weight, cause of death, serum creatinine, hepatitis C status, and whether the donation occurred after cardiocirculatory death) to rank order the relative quality of kidneys into a continuous score as defined by an aggregate population relative risk.

Peer-review

This manuscript of Yousef Al-Shraideh *et al*, exhaustively described a current issue, directly related to the ever-existing problem of acute organ shortage, namely the optimum use of small paediatric donors.

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P- Reviewer: Cantarovich F, Milford DV, Orlando G **S- Editor**: Ji FF
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