Original Article

Single kidney transplantation from pediatric deceased donors in China: the outcomes and risk factors of graft survival

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Background: Pediatric deceased donors offer great potential for expanding the organ donor pool. The utilization of pediatric donor kidneys has been explored by numerous transplant centers; however, the transplant outcome and risk factors have not been well elucidated. The aim of this study was to demonstrate the safety and risk factors of transplant outcome from pediatric deceased donors.

Methods: We retrospectively analyzed 484 cases of single kidney transplantation (SKT) with pediatric donor kidneys performed at our center from January 2012 to March 2021. The recipients were grouped by age: child (≤12 years; n=143), adolescents (12–18 years; n=86), and adults (≥18 years; n=255). The overall prognosis of the recipients was analyzed, and the post-transplant outcomes were compared among the three groups and assessed by univariate and multivariate analyses using the Cox proportional risk model.

Results: The median follow-up time was 26.7 months. The 1- and 3-year patient survival rates were 98.7% and 96.8%, respectively. The 1- and 3-year death-censored graft survival (DCGS) was 96.1% and 92.7%, respectively. The overall estimated glomerular filtration rates (eGFRs) at 1 and 3 years were 80.0±24.5 and 84.2±25.2 mL/min/1.73 m^2; the 3-year eGFR of the three groups were comparable and all were over 80 mL/min/1.73 m^2. Rejection was an independent risk factor for death-censored graft failure within 3 years after transplantation [hazard ratio (HR) =3.85; P=0.001], and was the primary cause of graft losses in the adolescent group. Thrombosis was more common within 1-month post-transplant in the child recipients (P<0.05), and its incidence was higher in recipients with donor body weight (DBW) ≤11 kg.

Conclusions: SKT from pediatric donors could achieve decent outcomes. Rejection was an independent risk factor of graft survival, especially for adolescent recipients. Child recipients may compromise early transplant outcomes due to vascular thrombosis, which might be related to small (DBW ≤11 kg) pediatric donors.

Keywords: Kidney transplantation; pediatric donor; survival analysis; rejection; vascular thrombosis

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Introduction

In recent years, the prevalence of end-stage renal disease (ESRD) has increased (1). Kidney transplantation is preferable to dialysis because of its superior long-term survival rates and better quality of life among recipients. However, an imbalance between donors and potential recipients has been aggravated by the rapid growth of ESRD patients on the waiting list, which has outpaced the collection of donor kidneys. Nonetheless, the donor pool had expanded due to an increase in the number of pediatric donors over the past few years (2-8). This expansion alleviates the conflict between the high demand among ESRD patients and the lack of donor organs. As there are currently no established criteria regarding the allocation of kidneys from pediatric donors, the practice and requirements differ in various countries.

According to the Organ Procurement and Transplantation Network (OPTN) and the Australia and New Zealand Organ Donation Registry (ANZOD), the proportion of pediatric donors has exceeded 10%, and the overall prognosis is also satisfactory (2,7-13). Moreover, studies indicated that the prognosis of kidneys from pediatric donors is comparable to or better than that of adult donors (14,15). Considering the numerous donations from pediatric donors, there is a pressing need to better utilize these kidneys. The allocation criteria for pediatric kidneys vary among different countries, and many centers give priority to pediatric recipients according to national policy (16-18). In China, regulations regarding organ sharing reflect the national priority of giving pediatric donor organs to children since August 2018. While there are challenges with preoperative matching, operation protocol, and long-term care after surgery, a few transplant centers have been exploring the rational utilization of pediatric donor kidneys. Many donor and recipient factors, such as donor type, pre-transplant weight status, donor-recipient size matching, blood type, hyperuricemia, hyper-filtration injury and primary disease have been found affecting renal allograft survival in different studies (19-23). However, risk factors of kidney transplantation from pediatric deceased donors have not been well explored. In the clinical setting, there are notable differences in donor-recipient size matching, transplant surgery, perioperative management, post-transplant complications and allograft survival when pediatric kidneys are transplanted to children or adult recipients. Therefore, survival analysis from the perspective of recipients age may provide specific information facilitating the improvement of transplant outcome of pediatric donor kidneys.

Compared with en bloc kidney transplantation (EBKT) from pediatric donors, single kidney transplantation (SKT) can better utilize the scarce donor pool. Moreover, the SKT surgical procedure for kidneys from pediatric donors is similar to that of adult donors, and it is more convenient to place only one kidney into the iliac fossa, especially in young child recipients. Therefore, SKT does not require a long training period. Studies have also reported that for surgery involving pediatric donors, the prognosis of SKT was comparable to that of EBKT (24-28). Kidneys from donors with low donor body weight (DBW) can be used for EBKT, but there are also centers performing SKT procedures, which provide more transplant opportunities for ESRD patients. Our center carried out SKT from pediatric donors in the early stages in China, and our experiences are worth summarizing. In this retrospective cohort study, we analyzed the 3-year curative effect of SKT and explored the associated risk factors of using pediatric donors in different recipient-age groups, aiming to improve the efficacy of SKT from pediatric donors. We present the following article in accordance with the STROBE reporting checklist (available at https://tp.amegroups.com/article/view/10.21037/tp-22-547/rc).

Highlight box

Key findings

- SKT from pediatric donors can achieve decent outcomes.
- Rejection is an independent risk factor of graft survival, especially for adolescent recipients.
- Child recipients may compromise early transplant outcomes due to vascular thrombosis, which may be related to small (DBW ≤11 kg) pediatric donors.

What is known and what is new?

- Pediatric deceased donors offer great potential for expanding the organ donor pool, but the transplant outcome and risk factors have not been well elucidated.
- This study demonstrated the safety, as well as the risk factors of the transplant outcome from pediatric deceased donors.

What is the implication, and what should change now?

- Our study revealed the risk factors of SKT from pediatric donors, and provided evidence that kidneys from pediatric donors can expand the donor pool.

Methods

Study design

The research subjects were patients who received SKT from pediatric deceased donors at The First Affiliated Hospital of Sun Yat-sen University between January 2012 and March 2021. The inclusion criteria were as follows: (I) organ recipients who underwent allograft SKT at The First Affiliated Hospital of Sun Yat-sen University; (II) organ recipients who received donor kidneys from citizens after death; (III) organ donors aged <18 years at the time of donation; and (IV) patients who received regular follow-up after operation. The exclusion criteria were as follows: (I) organ recipients who underwent combined/multiple organ transplantation; (II) transplantation with incompatible ABO blood types; (III) organ recipients who received donor kidneys with definite kidney quality problems or constitutional problems; and (IV) recipients who did not meet the postoperative follow-up period of at least 3 months.

Recipients were grouped based on their age at the time of transplantation: child group (≤12 years), adolescent group (12–18 years), and adult group (≥18 years). Informed consent was obtained from patients or their legal guardians, and this study was approved by the Ethics Committee of The First Affiliated Hospital of Sun Yat-sen University (No. [2019]452). The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013) and upheld the principles of the Declaration of Istanbul on Organ Trafficking and Transplant Tourism (29).

Surgical procedures and perioperative management

Kidney procurement from pediatric deceased donors primarily involved the combined recovery of the liver and kidneys, and simple *en bloc* resection of the kidneys (i.e., with no intention of liver harvesting). In this study, *en bloc* donor kidneys were split and trimmed into two single kidneys on the back table. All surgeries were performed according to the SKT procedure, as described previously (11,12).

Multiple approaches were utilized to reduce vasospasm and thrombosis. It is important to minimize stretching and isolation of the donor renal artery during the procurement and back-table surgery of the donor kidneys. Papaverine (3 mg/mL in saline) was injected into the artery before reperfusion and was pumped at 2 mL/h (1.2 mg/mL in saline) continuously for 3–5 days after the transplantation surgery. The renal hilum was infiltrated with lidocaine hydrochloride (20 mg/mL). Depending on the donor-kidney size, surgical drainage, urine properties, and coagulation function of recipients, low molecular weight heparin (LMWH; 50–100 IU/kg/d) was administered for anticoagulation for 3–5 days, followed by oral clopidogrel bisulfate (12.5–75 mg/day) thereafter. During perioperative management, systolic blood pressure was maintained at 120–130 mmHg for recipients whose donors were aged over 5 months or at 110–120 mmHg if the donor was aged less than 5 months.

All recipients received either anti-thymocyte globulin or anti-CD25 monoclonal antibody as induction therapy. The maintenance immunosuppressive regimen consisted of tacrolimus/cyclosporine, mycophenolic mofetil, or enteric-coated mycophenolic sodium with or without steroids.

Data collection

All recipients received regular outpatient visits or telephone follow-up in our study. Clinical data were collected from hospital records including baseline characteristics [donor type, donor age, body weight, height, kidney size, cause of death, warm ischemia time/cold ischemia time (WIT/CIT), recipient age, sex, body weight, height, type of dialysis, and the number of human leukocyte antigen (HLA) mismatches] and postoperative outcomes [patient survival, graft survival, graft function, primary non-function (PNF), delayed graft function (DGF), rejection, vascular and urinary complications, infection, and recurrence of primary diseases]. Graft survival was defined as re-transplantation, graft nephrectomy, return to dialysis irreversibly, or death with a functioning graft. DGF was defined as the need for dialysis within 1 week postoperatively. Biopsies were classified according to the Banff criteria by local pathologists. Graft function was evaluated by serum creatinine (SCr) and estimated glomerular filtration rate (eGFR). The eGFR was calculated using the Modification of Diet in Renal Disease (MDRD) equation based on SCr (>16 years old) or Schwartz equation (≤16 years old) (30,31).

Statistical analysis

Continuous data with normal distribution were presented as mean ± standard deviation (SD), and were compared using one-way analysis of variance (ANOVA) test with the Turkey HSD post-hoc test between groups. Continuous data without normal distribution were expressed as median [interquartile range (IQR)], and were compared

Table 1 Clinical characteristics of the pediatric donors

Recipient group	Overall	Child	Adolescent	Adult	P value
Donor number	308	89	60	159	
Age (years), mean (SD)	7.15 (5.83)	3.81 (4.88)	5.68 (4.97)	9.57 (5.54)	<0.001
Male, n (%)	184 (59.74)	53 (59.55)	36 (60.00)	95 (59.75)	1.000
Body weight (kg), mean (SD)	27.32 (19.47)	17.82 (15.27)	22.62 (15.61)	34.87 (20.09)	<0.001
Body height (cm), mean (SD)	118.07 (37.43)	97.78 (34.65)	111.94 (33.40)	133.12 (34.05)	<0.001
Cause of death, n (%)					0.017
Trauma	130 (42.21)	39 (43.82)	16 (26.67)	75 (47.17)	
Hypoxic-ischemic encephalopathy	24 (7.79)	8 (8.99)	3 (5.00)	13 (8.18)	
Cerebral hemorrhage	22 (7.14)	5 (5.62)	2 (3.33)	15 (9.43)	
CNS tumor	18 (5.84)	3 (3.37)	5 (8.33)	10 (6.29)	
Other	114 (37.01)	34 (38.20)	34 (56.67)	46 (28.93)	
Donor type, n (%)					0.313
DBD	213 (69.16)	64 (71.91)	45 (75.00)	104 (65.41)	
DCD	95 (30.84)	25 (28.09)	15 (25.00)	55 (34.59)	
SCr pre-procurement, n (%)					0.115
High	91 (29.55)	20 (22.47)	16 (26.67)	55 (34.59)	
Normal	217 (70.45)	69 (77.53)	44 (73.33)	104 (65.41)	
WIT (min), mean (SD)	3.21 (4.93)	3.26 (4.76)	2.52 (4.99)	3.45 (5.00)	0.462
CIT (hours), mean (SD)	11.15 (5.88)	11.76 (5.58)	9.95 (3.93)	11.29 (6.60)	0.176

SD, standard deviation; CNS, central nervous system; DBD, donation after brain death; DCD, donation after cardiac death; SCr, serum creatinine; WIT, warm ischemia time; CIT, cold ischemia time.

using Kruskal-Wallis test between groups and Mann-Whitney test with Bonferroni correction for post-hoc test. Categorical data were presented as counts and percentages, and were compared using chi-square or Fisher's exact test as appropriate. The Kaplan-Meier method was used to analyze the 1- and 3-year patient and graft survival, and the log-rank test was used to compare survival curves between groups. Univariate and multivariate Cox proportional hazards regression analyses were used for assessment of risk factors for graft failure. Variables with a P value <0.20 in the univariate analysis were included in the multivariate analysis. All the tests were bilateral tests, and statistical significance was set at P<0.05. All statistical analyses were performed using SPSS for Windows (version 22.0, IBM Corp., Armonk, NY, USA) and 'R' language for Windows (version 4.1.0), a free software environment for statistical computing and graphics (https://www.r-project.org/).

Results

Population characteristics

This study involved 484 cases of pediatric-donor SKTs, including 229 pediatric recipients and 255 adult recipients. The characteristics of the donors and recipients were summarized in *Tables 1*,*2*, respectively. The donors were predominantly male (n=184, 59.7%) and included a high proportion of donations after brain death (n=213, 69.2%). The average ages of the donors and recipients were 7.15±5.83 and 26.24±17.58 years, respectively. The average body weights of the donors and recipients were 27.32±19.47 and 43.68±19.23 kg, respectively.

As shown in *Table 1*, there was a significant difference in donor age, DBW, and donor body height (DBH) among the three groups (P<0.001), which were significantly higher in the adult group (P<0.001). There was no statistical

Table 2 Clinical characteristics of the recipients

Recipient group	Overall (n=484)	Child (n=143)	Adolescent (n=86)	Adult (n=255)	P value
Age (years), mean (SD)	26.24 (17.58)	7.89 (2.84)	14.47 (1.71)	40.50 (11.91)	<0.001
Male, n (%)	264 (54.55)	70 (48.95)	44 (51.16)	150 (58.82)	0.130
Body weight (kg), mean (SD)	43.68 (19.23)	20.75 (7.43)	38.63 (9.91)	58.24 (11.06)	<0.001
Donor/recipient body weight ratio, mean (SD)	0.65 (0.50)	0.83 (0.70)	0.55 (0.39)	0.58 (0.34)	<0.001
Body height (cm), mean (SD)	147.95 (24.63)	116.02 (18.59)	151.62 (11.52)	164.61 (7.67)	<0.001
Pre-transplant dialysis, n (%)					
Hemodialysis	349 (72.11)	86 (60.14)	58 (67.44)	205 (80.39)	<0.001
Peritoneal dialysis	156 (32.23)	63 (44.06)	32 (37.21)	61 (23.92)	0.001
Pre-emptive transplant	53 (10.95)	17 (11.89)	11 (12.79)	25 (9.80)	0.680
Waiting time since dialysis (days), mean (SD)	635.38 (692.24)	268.06 (248.33)	345.50 (361.26)	783.98 (763.38)	<0.001
Re-transplant, n (%)	23 (4.75)	8 (5.59)	5 (5.81)	10 (3.92)	0.661
HLA-A, B, DR MM number, mean (SD)	3.93 (1.18)	3.81 (1.26)	3.90 (1.03)	4.07 (1.18)	0.215
Induction therapy, n (%)					<0.001
Lymphocyte depleting	342 (70.66)	78 (54.55)	48 (55.81)	216 (84.71)	
Basiliximab	142 (29.34)	65 (45.45)	38 (44.19)	39 (15.29)	
Maintenance regimen, n (%)					0.718
Tac + MPA + Pred	481 (99.38)	142 (99.30)	86 (100.00)	253 (99.22)	
CsA + MPA + Pred	3 (0.62)	1 (0.70)	0 (0.00)	2 (0.78)	
Primary disease, n (%)					<0.001
Glomerulonephritis	367 (75.83)	79 (55.24)	59 (68.60)	229 (89.80)	
FSGS	23 (4.75)	13 (9.09)	5 (5.81)	5 (1.96)	
IgA nephropathy	14 (2.89)	2 (1.40)	5 (5.81)	7 (2.75)	
Other	80 (16.53)	49 (34.27)	17 (19.77)	14 (5.49)	

SD, standard deviation; HLA, human leukocyte antigen; MM, mismatch; Tac, tacrolimus; MPA, mycophenolic acid; Pred, prednisolone; CsA, cyclosporine; FSGS, focal segmental glomerular sclerosis; IgA, immunoglobulin A.

difference between the adolescent group and the child group (P>0.05). DBW distribution suggested statistical differences between the recipient groups (P<0.001), while the DBW of the child group was the lowest (17.82±15.27 kg) (*Table 1*). The overall ratio of the donor-recipient body weight was 0.65±0.50, and the ratio of the child group (0.83±0.70) was higher than those of the adolescent (0.55±0.39; P<0.001) and adult (0.58±0.34; P<0.001) groups.

No significant differences were observed between the groups in terms of donor sex, donor type, donor SCr level, average CIT, recipient sex, preemptive kidney transplantation rate, maintenance immunosuppressive regimens, or HLA mismatch number.

Patient and graft survival

The median follow-up time was 26.7 (range, 9.1–109.6) months. The patient survival of this cohort is shown in *Figure 1A*. The 1-, 2-, and 3-year patient survival rates were 98.7%, 98.1%, and 96.8%, respectively. Ten patients died with a functioning graft during the follow-up period, and 50% of whom died of pneumonia. One patient experienced graft loss due to graft rupture and subsequently died of coagulation disorder and severe hemorrhage. There was no significant survival difference among the three groups.

The death-censored graft survival (DCGS) was shown in *Figure 1B*. The 1-, 2-, and 3-year DCGS rates were 96.1%,

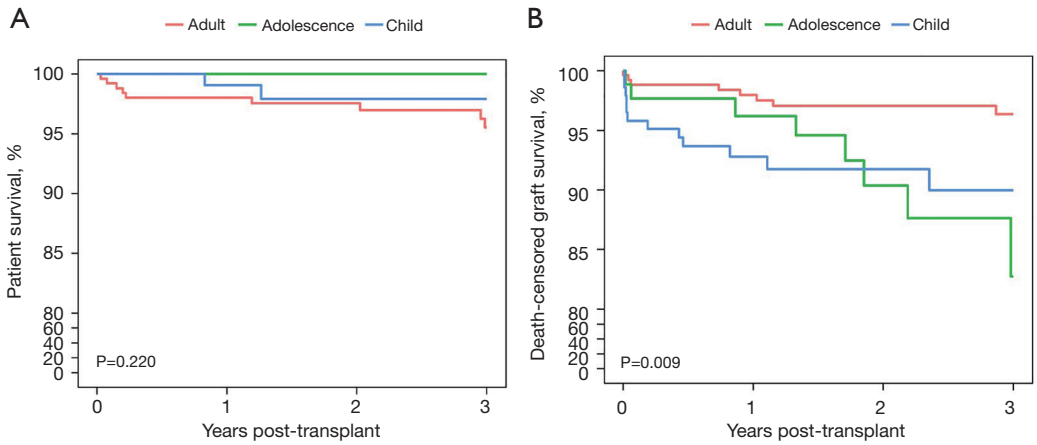

Figure 1 Kaplan-Meier curves of patient and DCGS survival. (A) The patient survival of the adult group, and child group demonstrated no significant differences (P=0.220). (B) The DCGS in the adult group, adolescence group, and child group, demonstrated significant differences (P=0.009). DCGS, death-censored graft survival.

94.4%, and 92.7%, respectively. There was no statistical difference among the three groups (P=0.220). The 1-year DCGS of the child group was 92.8%, which was lower than the adult group (98.0%; P<0.05), but the difference was not statistically significant with that of the adolescent group (96.2%; P=0.379). A statistical difference was observed in the 3-year DCGS among the three groups (P=0.009). The 3-year DCGS of the adolescent group was 82.8%, which was lower than that of the adult group (96.3%; P=0.014), but no statistical differences were observed with that of the child group (90%; P=0.852).

The causes of graft loss included rejection (9/28, 32.14%), surgical-related complications (SRCs, including vascular thrombosis, artery stenosis, and peri-graft hematoma, 11/28, 39.29%), recurrent diseases (3/28, 10.71%), and other complications (5/28, 17.86%). The causes of graft loss in different recipient age groups were summarized in *Table 3* and *Figure 2*. As demonstrated, 12 patients experienced graft loss in the child group, which was attributed to vascular thrombosis (6/12, 50%), rejections (3/12, 25%), recurrence of primary disease (2/12, 16.67%), and BK polyomavirus (BKV) infection (1/12, 8.33%). Eight recipients lost their graft function in the adolescent group, with rejections (4/8, 50%) being the main reason for the loss of function. Graft rupture due to graft bleeding (3/8, 37.5%) and recurrence of primary disease (1/8, 12.5%) also contributed to graft loss. For adult recipients, rejection (2/8, 25%), vascular thrombosis (1/8, 12.5%), graft rupture (1/8, 12.5%), and other complications (4/8, 50%) were the causes of graft loss.

Notably, the 1-month DCGS decreased markedly in the child group (95.8%), as six child recipients developed thrombosis within 1-month post-operatively, which led to graft failure (6/12, 50%) in the child group at that phase. However, the DCGS subsequently stabilized, and the 1-year (92.8%) and 1-month DCGS of the child group were relatively similar. Meanwhile, in the adolescent group, the 1-year DCGS was 96.2% but this rate dropped after 1 year. Further analysis showed that 60% (3/5) of the graft losses were caused by rejections at this phase, leading to a 3-year DCGS of 82.8% in the adolescent group, which was lower than that of the 1-year DCGS in the adolescent group.

Recovery of graft function

PNF was not observed postoperatively in any of the three groups. Seventy-two patients developed DGF and relied on dialysis for transition (72/484, 14.90%). Five of these patients experienced graft loss due to vascular thrombosis or renal rupture within 30 days postoperatively. *Figure 3A* indicated that the overall eGFR increased steadily after surgery. The eGFRs at 1, 6, and 12 months were 59.7±24.7, 74.8±23.5, and 80.0±24.5 mL/min/1.73 m^2, respectively. For the next 2 years, the average eGFR maintained stability above 80 mL/min/1.73 m^2, demonstrating a satisfactory graft function. The average eGFR of each group at 1-, 2-, and 3-year postoperatively was shown in *Figure 3B*. The eGFR of the child group at 1 year was higher than those of the adolescent and adult groups; however, the eGFR was similar between all groups at 3 years postoperatively.

Table 3 Reasons for graft loss among the different age groups

Groups	Age (days)			Total
	0–30	31–360	361–1,080	
Rejection, n	1	2	6	9
Child	0	1	2	3
Adolescent	0	1	3	4
Adult	1	0	1	2
SRCs, n	10	0	1	11
Child	6	0	0	6
Adolescent	2	0	1	3
Adult	2	0	0	2
Recurrent disease, n	0	2	1	3
Child	0	2	0	2
Adolescent	0	0	1	1
Adult	0	0	0	0
Other, n	0	3	2	5
Child	0	1	0	1
Adolescent	0	0	0	0
Adult	0	2	2	4

SRC, surgical-related complication.

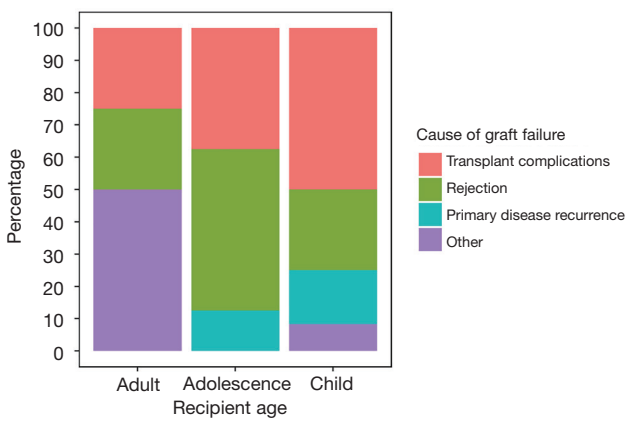

Figure 2 The causes of graft loss in the different recipient age groups.

Post-transplant complications

All postoperative complications were summarized in *Table 4*. The most common postoperative complication among the recipients was infection (168/484, 34.71%). Within 3 years post-transplant, pulmonary infection accounted for 17.36% of the total number of complications (84/484), leading to 5 deaths, and the incidence of urinary infections was up to 12.40%. Rejection affected 40 cases (8.26%) in total, and child (14/143, 9.79%) and adult (16/255, 6.27%) recipients had a relatively lower risk of rejection than adolescent recipients (10/86, 11.63%). Three adolescent recipients (3/4, 75%) developed graft loss resulting from rejection after 1 year postoperatively. Once rejection occurred, it appeared easier to develop graft loss in adolescent recipients (four graft losses from 10 rejections, 4/10, 40%) and child recipients (four graft losses from 14 rejections, 4/14, 28.57%) than in adult recipients (one graft losses from 16 rejections, 1/16, 6.25%).

Regarding SRC, the child (13/143, 9.09%) and the adolescent (8/86, 9.30%) groups had higher incidences than the adult group (12/255, 4.71%). Among SRCs, the overall incidence of vascular thrombosis was low in our cohort (10/484, 2.07%), but all cases occurred within 1-month post-transplant and were more commonly observed in the child group (7/10, 70%). In addition, this may have led to

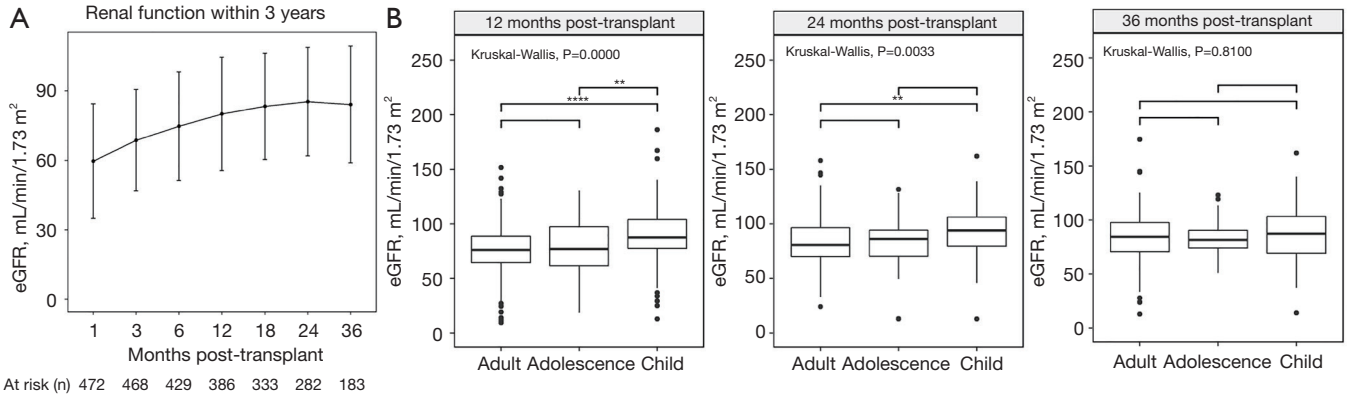

Figure 3 Recovery of graft function. (A) Post-transplant eGFR of all recipients. (B) The average eGFR of each group at 1, 2, and 3 years. eGFR was expressed as the mean and 95% CI. **, P<0.01; ****, P<0.0001. eGFR, estimated glomerular filtration rate; CI, confidence interval.

Table 4 Post-transplant complications in the recipients

Complications	Overall (n=484)	Child (n=143)	Adolescent (n=86)	Adult (n=255)	P value
PNF, n (%)	0 (0.00)	0 (0.00)	0 (0.00)	0 (0.00)	–
DGF, n (%)	72 (14.88)	18 (12.59)	16 (18.60)	38 (14.90)	0.464
Infection, n (%)					
Pulmonary infection	84 (17.36)	31 (21.68)	12 (13.95)	41 (16.08)	0.241
Urinary infection	60 (12.40)	25 (17.48)	11 (12.79)	24 (9.41)	0.064
Other infection	86 (17.77)	36 (25.17)	14 (16.28)	36 (14.12)	0.020
Biopsy-proven rejection, n (%)					
ABMR	10 (2.07)	3 (2.10)	3 (3.49)	4 (1.57)	0.557
TCMR	18 (3.72)	7 (4.90)	4 (4.65)	7 (2.75)	0.488
Mixed-rejection	12 (2.48)	4 (2.80)	3 (3.49)	5 (1.96)	0.703
SRCs, n (%)					
Vascular thrombosis	10 (2.07)	7 (4.90)	1 (1.16)	2 (0.78)	0.018
Artery stenosis	12 (2.48)	4 (2.80)	3 (3.49)	5 (1.96)	0.703
Peri-graft hematoma	13 (2.69)	4 (2.80)	4 (4.65)	5 (1.96)	0.409
Ureteral stenosis, n (%)	9 (1.86)	5 (3.50)	2 (2.33)	2 (0.78)	0.148
Urinary leak, n (%)	2 (0.41)	1 (0.70)	0 (0.00)	1 (0.39)	0.725
Recurrence of primary disease, n (%)	20 (4.13)	8 (5.59)	5 (5.81)	7 (2.75)	0.269
Cause of death, n (%)					0.541
Pneumonia	6 (1.24)	1 (0.70)	0 (0.00)	5 (1.96)	
Malignancy	3 (0.62)	1 (0.70)	0 (0.00)	2 (0.78)	
Others	2 (0.41)	0 (0.00)	0 (0.00)	2 (0.78)	

PNF, primary non-function; DGF, delayed graft function; ABMR, antibody mediated rejection; TCMR, T cell mediated rejection; SRC, surgical-related complication.

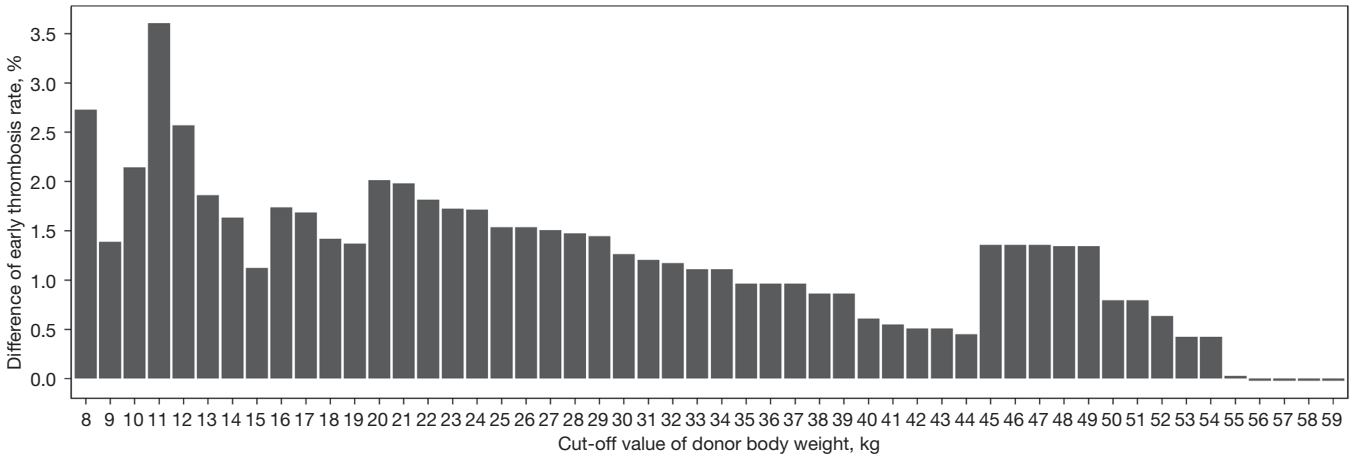

Figure 4 The thrombosis rate difference between the recipient groups according to different DBW cut-off level. Early thrombosis rate differences were observed between the lower and higher DBW groups of each cut-off value. Early thrombosis rates were higher in the lower DBW group for every cut-off value. DBW, donor body weight.

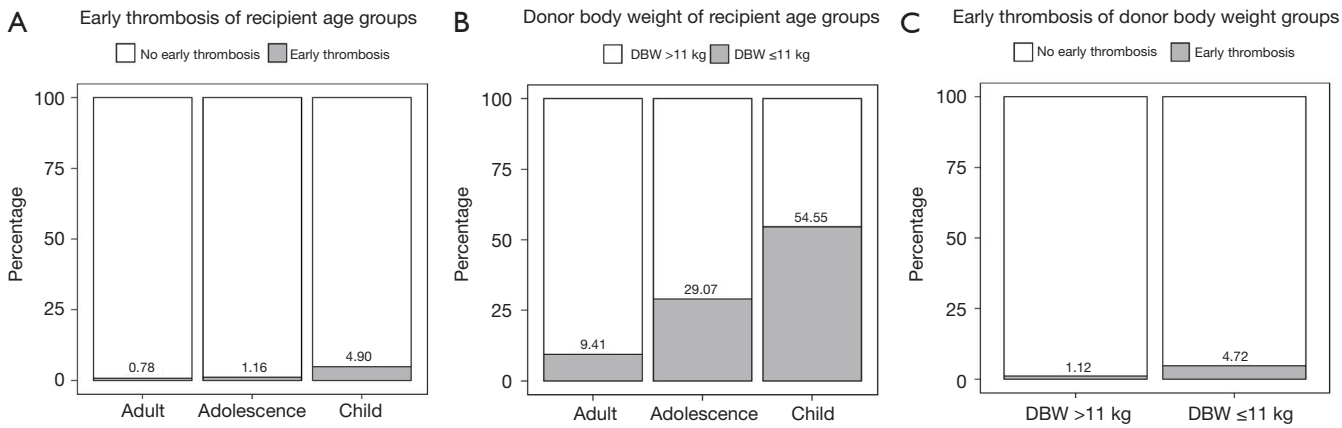

Figure 5 The relationship between DBW and early thrombosis after kidney transplantation. (A) The early thrombosis of different recipient age groups. (B) DBW of the recipient age groups. (C) The early thrombosis of DBW groups. DBW, donor body weight.

graft loss at an early stage (within 1-month post-transplant) in the child group, as mentioned. For further analysis, the recipients were assigned to groups according to different DBW cut-off levels; according to the different rates of early thrombosis between the groups, 11 kg, as the highest value, was set as the cut-off value (*Figure 4*). *Figure 5A* showed that the thrombosis rate of child recipients was the highest among the three groups (4.9%), as child recipients possessed 54.55% kidneys from DBW ≤11 kg (*Figure 5B*). Also, the thrombosis rate was higher in recipients from DBW ≤11 kg (6/127, 4.72%) than those from DBW >11 kg (4/357, 1.12%) (*Figure 5C*). *Figure 6* revealed an increasing trend of the DBW and donor age and a declining trend of thrombosis rate in recent years.

The recurrence of primary disease (20/484, 4.13%) and urological complications (11/484, 2.27%) were comparable between the groups (P>0.05). Five patients ultimately experienced graft loss, including four patients with recurrent focal segmental glomerular sclerosis (FSGS) and one patient with recurrent immunoglobulin A (IgA) nephropathy.

Graft survival risk factors

The recipient and donor risk factors were analyzed for overall DCGS, and the results were presented in *Table 5*.

Table 5 Univariate and multivariate analysis of risk factors affecting DCGS of recipients

Variables	HR (95% CI, P) (univariable)	HR (95% CI, P) (multivariable)
DBW ≤11 kg	3.08 (1.47–6.47, P=0.003)	1.91 (0.82–4.45, P=0.137)
Adolescence recipient	3.55 (1.33–9.50, P=0.012)	2.46 (0.87–6.98, P=0.091)
Child recipient	3.27 (1.33–8.02, P=0.010)	2.09 (0.75–5.81, P=0.156)
CIT ≤10 hours	0.63 (0.30–1.33, P=0.224)	–
DCD donor	1.82 (0.87–3.84, P=0.114)	–
Male recipient	0.61 (0.29–1.30, P=0.202)	–
Dialysis	1.79 (0.42–7.54, P=0.429)	–
ATG induction	0.54 (0.24–1.18, P=0.123)	–
Normal donor creatine	0.85 (0.39–1.85, P=0.687)	–
Donor/recipient body weight ratio ≤0.5	1.13 (0.54–2.38, P=0.746)	–
Donor/recipient body height ratio ≤0.8	1.75 (0.79–3.87, P=0.166)	–
HLA MM ≤4	1.75 (0.58–5.31, P=0.324)	–
Rejection	4.88 (2.20–10.79, P<0.001)	3.85 (1.71–8.66, P=0.001)

DCGS, death-censored graft survival; HR, hazard ratio; CI, confidence interval; DBW, donor body weight; CIT, cold ischemia time; DCD, donation after cardiac death; ATG, antithymocyte globulin; HLA, human leukocyte antigen; MM, mismatch.

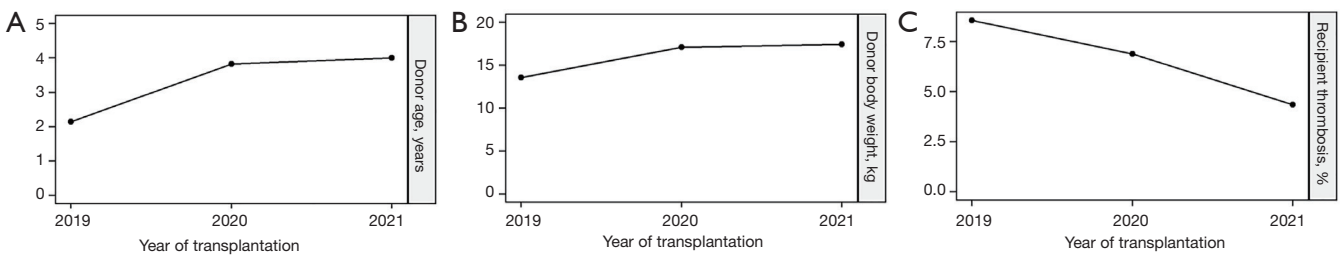

Figure 6 In recent years, the thrombosis rate declined as the donor age and DBW increased. (A) Donor age, (B) DBW, (C) thrombosis rate changes in recent years. DBW, donor body weight.

Univariate analysis revealed that DBW ≤11 kg [hazard ratio (HR) =3.08; 95% confidence interval (CI): 1.47–6.47; P=0.003], adolescent recipient group (HR =3.55; 95% CI: 1.33–9.50; P=0.012), child recipient group (HR =3.27; 95% CI: 1.33–8.02; P=0.010), and rejection (HR =4.88; 95% CI: 2.20–10.79; P<0.001) were risk factors for DCGS. In multivariate analysis, only rejection (HR =3.85; 95% CI: 1.71–8.66; P=0.001) was observed to be a significant risk factor for poor DCGS.

Discussion

In this large-sample size cohort of SKT from pediatric deceased donors, we reported the outcomes of SKT receiving pediatric donor kidneys, and more importantly discovered the specific risk factors of renal allograft survival among recipients of different ages. In this study, the overall 1-, 2-, and 3-year DCGS were 96.1%, 94.4%, and 92.7%, respectively. The graft survival was comparable or superior to the previously reported outcomes (25,26,32). The eGFR at 1 year after transplant was 80.0±24.5 mL/min/1.73 m^2 and maintained stable thereafter during this study, indicating that satisfactory renal allograft function was obtained from the pediatric deceased donors. Survival analysis revealed rejection as a strong independent risk factor (HR =3.85) for the 3-year DCGS of pediatric donor kidneys. Moreover, a significant decrease in the DCGS 1 year after transplantation was observed in the

adolescent group, which was mainly attributed to rejection (accounting for 60% of graft losses). We also identified vascular thrombosis as the main cause of graft loss in the very early phase (<30 days) after transplantation in the child group, and recipients who received kidneys from DBW ≤11 kg had a higher rate of thrombosis. These findings suggest that specific measures should be taken to further improve the transplant outcomes of pediatric donor kidneys by targeting risk factors for different recipient ages.

Rejection is increasingly recognized as an important influencing factor that can lead to poor post-transplant prognosis (33,34). In our multivariate model, rejection was observed to be the only risk factor for graft loss. Moreover, our research illustrated a rapid decline in the DCGS rate from 1- (96.2%) to 3-year (82.8%) post-transplant in the adolescent group. Rejection was the main cause of graft loss in this phase, leading to a relatively unsatisfactory long-term prognosis in the adolescent group. The underlying mechanisms of higher rejection incidences and the subsequent poor prognosis remain unclear. One of the chief culprits was non-adherence to medication. Two adolescent recipients in our cohort had once refused or forgot to take the immunosuppressants and developed rejection soon afterward, resulting in graft loss. Adolescents are a special population of kidney transplant recipients. They begin to assume responsibility for their healthcare and become less dependent on their families. It has been reported adolescent recipients after transplantation might have increased susceptibility to psychological illnesses and are prone to develop non-adherence to immunosuppressive medications, which might lead to rejection (35-38). In the adolescent group, 40% (4/10) of patients with rejection eventually progressed to graft loss, whereas this number was 28.57% (4/14) in the child group and 6.25% (1/16) in the adult group. This result indicates that rejection is more difficult to treat once it occurs or when it is diagnosed. Non-adherence-induced rejection often presents an acute and rapid process. Timely diagnosis and intervention are very important to obtain positive outcomes. Delayed detection and diagnosis can impair the responsiveness to anti-rejection therapy and lead to a poor prognosis. Therefore, particular attention should be paid to medication adherence during the age transition of adolescent recipients. Increasing the frequency of follow-up and developing better follow-up tools may also help to reduce rejection (39-41).

Thrombosis is common surgical complication after transplantation of pediatric donor kidneys and often leads to graft loss once it occurs (24,27,42,43). The vascular thrombosis rate in our cohort was 2.07%, which was relatively low. One of the reasons for this lower rate was the meticulous operation throughout the surgical procedure, which helped to reduce vascular stimulation intraoperatively and perioperatively, as lidocaine and papaverine favor vasospasm prevention (44). Additionally, the diameter of the vascular anastomosis can be enlarged using the aortic disc and inferior vena when performing SKT, and the risk of anastomotic stenosis and thrombosis can be significantly reduced (45). However, despite the preventative measures mentioned above, a higher rate of vascular thrombosis was observed in the child group than in the other two groups (4.9% *vs.* 1.16% *vs.* 0.78%, P=0.018). It is notable that the DCGS in the child group decreased markedly to 95.8% within 1 month after transplantation and stabilized at 92.8% thereafter. Vascular thrombosis was the main cause of early graft loss in this group. One explanation for this is that small pediatric recipients might be more prone to suffer thrombosis due to uremic coagulation disorders, as well as fine vessels, especially when the external iliac artery is used for anastomosis. Another more important reason may be the use of smaller pediatric donor kidneys in the child group. The DBW was considerably lower in the child group than in the other two groups (17.82±15.27 *vs.* 22.62±15.61 and 34.87±20.09 kg, P<0.001). DBW ≤11 kg was found to be a strong risk factor for DCGS (HR =3.08; P=0.003), while the proportion of DBW ≤11 kg was notably higher in the child group (54.55%) than in the other groups (29.07% and 9.41%) (*Figure 5B*). Further analysis revealed a recent trend toward a lower incidence of vascular thrombosis as DBW increased (*Figure 6*). These results suggest that increasing the body weight criteria of acceptable pediatric donors for single transplantation may facilitate the reduction of thrombosis and improve early graft survival to some extent, especially in younger pediatric recipients. This has significant implications for pediatric kidney transplant (PKT) in China, as most kidneys of PKT recipients are from pediatric donors. This study may provide insights into optimizing the allocation policy of pediatric donor kidneys.

This study has some limitations that should be noted. Firstly, this is a single-center retrospective study. Although our center is representative of the utilization of pediatric donor kidneys in China, a multicenter study is needed to validate our key findings. Also, the child group was inferior to the other two groups in terms of the early DCGS; however, this should not necessarily be interpreted as a denial of the allocation policy of pediatric kidneys to young children as the apparent bias of DBW among groups. Furthermore,

owing to the lack of an adult donor cohort in this study, we could not compare the outcomes between pediatric and adult donors for pediatric recipients. Therefore, the long-term outcomes of pediatric donor kidneys for recipients of different age groups require further observation.

Conclusions

In this study, we explored the prognosis and safety of SKT receiving pediatric donors. Recipients of different ages might have varying risk factors at different post-transplant phases. Rejection was the only lasting obstacle in our multivariate model and was particularly risky for adolescent recipients at 1–3 years post-transplant. Moreover, child recipients may compromise their postoperative outcomes for thrombosis at an early stage, which may be related to the lower DBW. Hence, paying more attention to medication adherence for adolescent recipients in the early-middle phase after surgery and using kidneys from DBW >11 kg could achieve a better prognosis. Overall, SKT from pediatric donors could achieve satisfactory outcomes. Our study revealed the risk factors of SKT from pediatric donors and provided evidence that kidneys from pediatric donors can expand the donor pool.

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Footnote

Reporting Checklist: The authors have completed the STROBE reporting checklist. Available at https://tp.amegroups.com/article/view/10.21037/tp-22-547/rc

Data Sharing Statement: Available at https://tp.amegroups.com/article/view/10.21037/tp-22-547/dss

Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at https://tp.amegroups.com/article/view/10.21037/tp-22-547/coif). The authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. Informed consent was obtained from patients or their legal guardians, and this study was approved by the Ethics Committee of The First Affiliated Hospital of Sun Yat-sen University (No. [2019]452). The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013) and upheld the principles of the Declaration of Istanbul on Organ Trafficking and Transplant Tourism.

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