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Outcomes of small pediatric donor kidney transplants according to donor weight

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SUMMARY

A small pediatric deceased donor (SPD) weight cutoff whether to transplant as en bloc (EB) or single pediatric (SP) kidney is uncertain. Using UNOS/OPTN data (2000–2019), 27 875 SPDs were divided by (i) EB (11.4%) or SP (88.6%) and (ii) donor weight [≤10 (5.4%), >10–15 (8.3%), >15–18 (3.7%), >18–20 (2.9%), and >20 kg (79.7%)]. SP >20 kg and adult deceased donors (grouped by Kidney Donor Profile Index, KDPI, <30, 30–85, and >85) were used as references. The primary outcome was 10-year graft failure. In SP <10 kg, the hazard ratio (HR) for overall graft failure was 1.64 (1.38–2.20) compared with EB <10 kg, and 1.45 (1.18–1.80) compared with SP >20 kg. In SP >10–15 kg, HR was 1.31 (1.12–1.54) compared with EB >10–15 kg, and 1.04 (0.91–1.18) compared with SP >20 kg. In SP >15 kg, the risk was the same as SP >20 kg. Ten-year overall graft survival of SP 12 kg was comparable to SP >20 kg (62% vs. 57%). Ten-year death censored graft failure of SP >10–15 kg (70%) and SP >15–18 kg (70%) was like the adult donors with KDPI 30–85 (67%). In conclusion, we recommend single kidney transplants from SPDs with weight >12 kg to adult recipients in centers with experience in SPD transplants to optimize organ utilization.

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Key words
donor weight, graft survival, small pediatric donor

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Introduction

A small pediatric donor (SPD) is defined by a weight <20 kg at the time of the procurement and corresponds to a donor age of 6-year-old or less based on pediatric growth tables [1]. These donors may be considered "marginal" because of the increased risk of vascular and urologic complications that can lead to early graft failure. Small donor arteries and veins, and a delicate vascular anastomosis contribute to increased thrombotic events [2,3]. Other complications, such as postsurgical bleeding because of the use of prophylactic anticoagulation and urinary leaks, may occur [4]. Moreover, the reduced mass of SPD kidneys may lead to an imbalance between donor and recipient body size, and may be associated with an inadequate kidney function and possibly reduced graft survival because of hyperfiltration injury [5,6]. To minimize this problem, we consider recipient size at the time of organ allocation, and small pediatric kidneys are directed to small size recipients [7,8]. Alternatively, donor kidneys may be transplanted as a pair (en bloc, EB) in one recipient. EB transplants resulted in better kidney transplant outcomes when compared with single pediatric (SP) kidney transplants

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[9,10], but at the cost of one less potential recipient transplant.

Transplantation of small pediatric donor kidneys as single or EB has been a subject of discussion to optimize the number of transplants without jeopardizing graft survival [11,12]. In 2017, Organ Procurement and Transplantation Network/United Network for Organ Sharing (OPTN/UNOS) committee recommended the procurement of kidneys from small pediatric donors as EB for donors weighing <18 kg, a change from previous recommendations of a donor weight <20 kg. However, the final decision to split kidneys would be from the procuring surgeon based on kidney donor size, kidney size, recipient size, and center expertise [13]. The increased experience of using kidneys from small pediatric donors has led to the increased utilization of kidneys from lower-weight donors as single.

The demand for kidney donors is high in the USA, and the utilization of organs from small pediatric donors can contribute to increasing the donor pool. Based on OPTN/UNOS data, <1-year-old kidneys donors accounted for 1.1%, 0.8%, 1.0% of all USA kidney donors in 2017, 2018, and 2019, respectively. The percentages of <6-year-old were 2.0%, 2.2%, and 1.8% in 2017, 2018, and 2019, respectively. Recent data analysis from the Scientific Registry of Transplant Recipients has shown that only 53% of kidneys from potential pediatric donors aged ≤8 years and weight <30 kg were transplanted [14]. The increased risk of graft failure and the need for more refined surgical techniques have restricted the use of small pediatric donor kidneys to a few transplant centers, reducing their recovery and utilization.

This study was performed to examine the long-term outcome of small pediatric donor kidney transplants as en-bloc or single kidney according to weight categories, to define the risk of graft failure and its association with recipients' characteristics. Our particular interest is in the donor group with <18 kg. Outcomes of lower weight small pediatric kidney donors were also compared with adult deceased donors transplants according to the kidney donor profile index (KDPI). We hypothesize that small pediatric kidneys can be used more often as single kidneys and provide comparable or better long-term graft survival than adult donors and a better option than adult kidneys with high KDPI. This information may be used by transplant physicians when discussing with kidney candidates the benefit and expected outcomes of small pediatric donor kidneys and may incentivize the procurement of small pediatric kidneys and its transplantation as single.

Materials and methods

A retrospective cohort study was conducted using OPTN/UNOS data from 2000 to 2019. All deceased donor kidney transplants, excluding those done outside the USA and multiorgan recipients, were included in the study cohort. Recipients of a kidney from a pediatric deceased donor (≤18 years old) were stratified into weight groups such as ≤10, >10–15, >15–18, >18–20, and >20 kg. These groups were further divided according to single kidney or EB transplants. Adult donors were divided by KDPI, such as ≤30%, 31–84%, and ≥85% (Fig. S1). Transplants with donors weighing between >10 and 15 kg, representing the controversial group in terms of separating kidneys, were re-divided by one kg weight difference, and en-bloc versus single kidneys graft survival was re-examined. Adult deceased donor transplants divided by KDPI were compared with small pediatric kidneys transplants. Recipient, donor, and transplant baseline characteristics, including induction and immunosuppressive medication at discharge, were compared.

The primary outcome was 10-year overall graft survival (OGS). OGS was calculated from the time of kidney transplantation to re-transplantation, return to dialysis, death, or end of follow-up. Death censored graft survival was also used to compare outcomes of single small pediatric kidneys with adult kidneys of different KDPIs. Death censored graft survival was calculated from the time of kidney transplantation to re-transplantation, return to dialysis, or end of follow-up. Post-transplant complications as rejection in the first year of transplantation delayed graft function, need for dialysis in the first week after transplant, primary nonfunction, and transplant failure 90 days post-transplant were reported. Studies using OPTN/UNOS, as de-identified data, were approved by UCLA Institutional Review Board and defined as not requiring review. This study complies with the Helsinki and Istanbul Declaration.

Statistical analysis

Baseline donor, recipient, and transplant characteristics were compared using the Kruskal-Wallis test for continuous variables and the Chi-square test for categorical variables. The results were shown in absolute numbers and percentages. Kaplan-Meier product-limit method was used to generate survival curves and Cox proportional regression model was used to define the risk of overall graft failure (OGF) and death censored graft failure. The proportional assumption of the model was respected when comparing groups. Logistic regression

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was used to define the risk of delayed graft function, primary nonfunction, and rejection at one-year post-transplant.

Recipient, donor, and transplant characteristics were treated as independent risk factors to the outcome and included in the adjusted multivariate model. Covariates included in the multivariate model were recipient weight, diabetes and hypertension, transplant year, use of mechanical perfusion, use of induction, panel reactive antibodies, cold ischemia time, time in dialysis, sex, human leukocyte antigen (HLA) mismatch, recipient body mass index (BMI), recipient hepatitis B and C serum status, recipient age, use of steroids, cytomegalovirus (CMV) serum status and re-transplantation. We built the multivariate model in stages. First by running the model with all covariates, then excluding those with a $P > 0.1$, and in the final multivariate analysis keeping only co-variates with a $P < 0.05$. We expressed the results as hazard ratio (HR) or odds ratio (OR) with their 95% confidence intervals (CI) and associated *P*-values. All *P*-values were 2 tailed and were significant if <0.05. STATA software version 11 (StataCorp, College Station, TX, USA) was used in all statistical analyzes.

Results

Donor, recipients, and transplant characteristics

Donor, recipients, and transplant baseline characteristics of small pediatric kidney donors by weight groups and divided by en-bloc or single donor transplants are shown in Table 1. Comparison of the groups revealed a statistical difference between all baseline characteristics. An increased cold ischemia time and in the distance from procurement, hospital to the transplant center in the lowest weight donor categories, particularly in the <10 kg group, which suggest that these kidneys were not transplanted locally. KDPI was also higher in the lower weight groups. Lower weight groups used more induction with anti-thymocyte globulin (ATG) and fewer re-transplants were done. Recipients of lower weight and BMI were more common in the lower weight groups when compared with >20 kg. There was an increase in the numbers of EB kidney transplants in the <10 kg group.

Transplant outcomes

Transplant complications

Delayed Graft function, primary nonfunction, and rejection at one year were examined and presented in Table S1. Delayed graft function and primary nonfunction were more incidents in the lower weight groups with increased risk when compared with pediatric single kidney >20 kg. The risk of primary nonfunction was almost 5× higher in <10 kg and 2.5× higher in 11–15 kg single kidney donor transplants relative to >20 kg SP donor kidneys. The rejection rate was slightly lower in the EB low weight groups, with decreased rejection risk after adjusted analysis.

Overall graft survival and risk of graft failure

Donors with weight <10 kg. Overall graft survival analysis showed a survival superiority of EB over single transplants in donors with weight <10 kg (Fig. 1a). The adjusted analysis demonstrated a 60% increased risk of OGF in the single kidney when compared with an EB transplant (Table 2). Single kidneys of <10 kg donors were compared with >20 kg SP kidney donor transplant and OGS was inferior in the <10 kg group with a 45% higher risk of graft failure relative to >20 kg group (Fig. 1a and Table 2). Recipients' risk factors associated with an increased risk of OGF were obese and diabetic recipients (Table S2).

Donors with a weight between >10 and 15 kg. The results of the donor weight group of >10–15 kg revealed inferior OGS of single kidneys when compared with EB transplants. Single kidney survival was also inferior to pediatric donors >20 kg transplants. Examining the Kaplan-Meier curve, a sharp decline at the beginning of the survival curve was observed, indicating an increased graft loss immediately after transplant. After this, the survival curve in the single group assumes a linear decline, but with a less steep decline than high weight pediatric recipients (Fig. 1b). After 10 years, survival in the >10–15 kg single donor group was 54.6% and in the >20 kg group was 57.1% (log-rank test $P < 0.01$). However, after adjustment, the ten-year risk of graft failure was similar between >10–15 and >20 kg single kidney donor transplants [adjusted HR 1.04 (0.91–1.18), $P = 0.54$]. Yet, single kidney risk of failure was 31% higher than en-bloc transplant (Table 2). EB >10–15 kg donor transplants survival curve crossed the >20 kg at 3 years post-transplant, showing a superior graft survival with time. Ten-year graft survival was 65.1% and 57.1% ($P < 0.01$) in the >10–15 kg EB and >20 kg single, respectively. Recipient characteristics associated with increased risk of graft failure in 10–15 kg pediatric kidneys donor transplants were a recipient time in dialysis, morbid obesity (BMI >40), diabetes mellitus, and age over 60 years.

Table 1. Baseline characteristic of the study groups.

	≤10 kg E (*n* = 1288)	≤10 kg S (*n* = 220)	11–15 kg E (*n* = 1367)	11–15 kg S (*n* = 960)	16–18 kg E (*n* = 375)	16–18 kg S (*n* = 649)	18–20 kg E (*n* = 154)	18–20 kg S (*n* = 655)	>20 kg S (*n* = 22 207)
Donor age	0 (0–1)	0 (0–1)	2 (1–2)	2 (1–3)	3 (2–4)	4 (3–5)	4 (3–5)	5 (4–6)	15 (12–17)
Donor weight	8 (6–9)	9 (8–10)	13 (12–14)	14 (12–15)	17 (16–17)	17 (16–18)	19 (19–20)	20 (19–20)	62 (45–74)
DCD (%)	14.2	6.8	9.4	8.8	8.8	10.5	8.4	9.0	11.2
Mech. perfusion (%)	23.6	8.2	11.2	10.7	8.5	10.2	16.2	11.8	25.3
CIT	19 (13–25)	23 (17–28)	17 (11–23)	18 (13–25)	16 (11–23)	17 (12–23)	13 (9–21)	16 (11–23)	16 (11–22)
Distance	272 (56–763)	344 (23–752)	111 (6–393)	91 (7.5–412.5)	107 (4–300)	59 (3–260)	63 (2–198)	63 (2–216)	60 (3–233)
KDPI	76 (68–84)	71 (67–82)	62 (57–73)	60 (55–70)	53 (49–62)	53 (48–63)	55 (46–59)	49 (43–57)	12 (5–26)
PRA	0 (0–4)	0 (0–3)	0 (0–18)	0 (0–10)	0 (0–24)	0 (0–23)	0 (0–40)	0 (0–26)	0 (0–39)
HLA-MM	5 (4–5)	5 (4–5)	5 (4–5)	4 (4–5)	4 (3–5)	4 (4–5)	5 (4–5)	5 (3–5)	4 (3–5)
CNI at discharge (%)	89.2	88.6	92.8	91.1	93.6	92.8	97.4	93.6	93.5
Induction with ATG	63.1	62.1	50.6	47.6	50.5	46.4	51.6	46.9	41.9
Re-transplant	6.1	6.8	8.2	8.6	9.8	10.2	8.4	14.3	15.2
R. gender (male, %)	47.9	54.4	47.5	47.9	46.1	46.4	42.2	45.2	56.2
R. age	48 (35–58)	50 (38–60)	48 (36–58)	49 (37–58)	47 (36–57)	49 (36–59)	49 (42–59)	48 (34–59)	45 (31–56)
R. Race AA (%)	23.8	22.3	30.6	26.3	30.2	39.6	39.6	27.9	30.2
R. BMI	24 (21–26)	23 (21–27)	25 (22–28)	24 (21–28)	24 (22–28)	24 (21–28)	24 (22–27)	25 (22–28)	26 (22–30)
R. weight	64 (56–74)	65 (56–74)	68 (57–80)	65 (57–76)	69 (59–82)	66 (56–78)	69 (59–82)	68 (57–80)	74 (59–89)
Time in D >3 years	47.5	44.5	50.5	51.3	47.5	54.2	49.3	47.2	45.5
R. DM (%)	21.9	25.9	22.0	25.4	21.3	23.6	26.6	22.7	23.1
Frail (%)	3.8	2.7	4.0	2.5	5.1	4.2	5.2	3.7	3.3
CMV (D+/R−)	7.7	7.3	9.1	9.5	11.7	9.1	9.8	9.3	14.2
R. hepatitis C (%)	2.6	2.3	2.7	2.8	3.7	2.8	4.5	2.7	3.3
R. hepatitis B (%)	13.7	15.0	8.4	10.4	10.4	9.4	8.4	8.1	8.1
Transp. yr. 2000–2006	19.9	27.3	31.6	31.5	29.3	26.8	31.2	35.0	38.8
Transp. yr. 2007–2012	33.6	43.2	31.7	29.3	32.8	31.6	31.8	28.4	28.3
Transp. yr. 2013–2019	46.4	29.5	36.7	39.3	37.9	41.6	37.0	36.6	32.9

AA, African American; ATG, thymoglobulin; BMI, body mass index; CIT, cold ischemia time (hours); CMV, cytomegalovirus; CNI, calcineurin inhibitors; D, dialysis; DCD, donor of circulatory death; DGF, delayed graft function; Distance, distance from donor center to transplant center (nautical miles); HLA-MM, human leukocyte antigens mismatches; KDPI, kidney donor profile index; Mech. perfusion, mechanical perfusion; PNF, primary nonfunction; PRA, panel reactive antibodies; R, recipient; STE, steroid; Tranp. yr., transplant year.

The statistical analysis defined significant differences ($P < 0.05$) in baseline characteristics when all groups were compared. Chi-square was used to compare categorical variables and Kruskal-Wallis to continuous variables. Donor weight, CIT, distance, PRA, HLA-MM, recipient age, weight, BMI reported as a median, inter-quartile range (IQR). Weights in kg. Age in years. Frail criteria included total assistance, moribund, very sick, disable, considerable and frequent medical care, "no play", entire limited to very passive activities, in bed, mostly in bed, can dress but lies around much of the day, no active play.

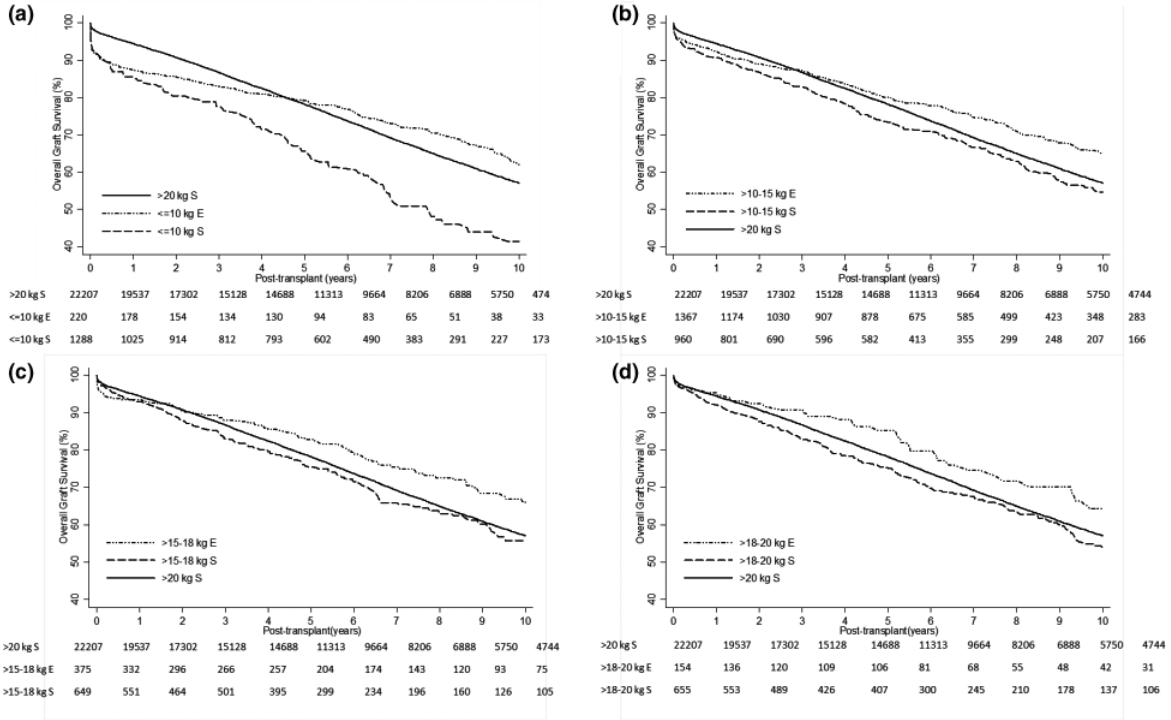

Figure 1 OGS in 10 years of small pediatric donors transplants according to donor weight groups. (a) Log-rank test >20 kg S vs. <10 kg E $P = 0.60$, log-rank test <10 kg E vs. <10 kg S $P < 0.001$. (b) Log-rank test >20 kg S vs. 10–15 kg S $P < 0.01$, log-rank test <10–15 kg E vs. <10–15 kg S $P < 0.001$. (c) Log-rank test >20 kg S vs. >15–18 kg S $P = 0.18$, log-rank test >15–18 kg E vs. >15–18 kg S $P < 0.01$. (d) Log-rank test >20 kg S vs. >18–20 kg S $P = 0.07$, log-rank test >18–20 kg E vs. >18–20 kg S $P < 0.05$.

Table 2. Small pediatric donor single kidney transplant adjusted risk of OGF compared with EB and >20 kg single kidney pediatric donor.

	Reference	aHR	95%CI	*P*-value
<10 kg S	<10 kg E	1.64	1.38–2.20	<0.001
	>20 kg S	1.45	1.18–1.80	<0.001
>10–15 kg S	>10–15 kg E	1.31	1.12–1.54	<0.001
	>20 kg S	1.04	0.91–1.18	0.54
>15–18 kg S	>15–18 kg E	1.27	0.98–1.65	0.07
	>20 kg S	0.99	0.85–1.15	0.91
>18–20 kg S	>18–20 kg E	1.57	1.06–2.21	0.02
	>20 kg S	0.99	0.86–1.16	0.98

Covariates used to adjust the analysis were transplant year, donor of circulatory death, functional state at transplantation, kidney donor profile index, use of induction therapy, panel of reactive antibodies, cold ischemia time, recipient time in dialysis, recipient gender, recipient body mass index, Histocompatibility Leukocytes Antigen mismatch, hepatitis B serum status, hepatitis C serum status, recipient diabetes mellitus, recipient age, recipient and donor Cytomegalovirus status, re-transplant aHR (adjusted hazard ratio), and 95% CI (95% coefficient interval).

In a sub-analysis, single kidney donors were stratified in 10, 11, 12, 13, and 14 kg weight to compare graft survival with the >20 kg single group. The Kaplan-Meier curve demonstrated that donors with weight <12 kg had an inferior survival. Ten-year graft survival in 11 kg (45%) and 12 kg (62%) when compared with >20 kg (57%) single group revealed a *P*-value of 0.05 and 0.81, respectively (Fig. 2). Risk factors associated with OGF restricted to single kidney donors with weight >10–15 kg were recipients with a poor functional status, increased dialysis vintage, diabetes, and age >60 years, as shown in Table S3.

Donors with weight >15–18 and 18–20 kg. Overall graft survival of single kidney transplants in >15–18 and >18–20 kg groups was inferior to EB (Fig. 1c,d). Risk of graft failure after adjusted analysis in >15–18 kg trended ($P = 0.07$) and in the >18–20 kg groups were associated with increased risk ($P = 0.02$) when compared with EB. When >15–18 and >18–20 kg single kidney were compared with >20 kg single kidney transplants, the overall risk of graft failure was not different (Table 2). Characteristics associated with increased risk of graft failure were obesity, increased dialysis vintage, and diabetic recipients. In the 18–20 kg group, male gender, positive hepatitis C status, and recipient age over 60 were also independent risk factors (Table S2).

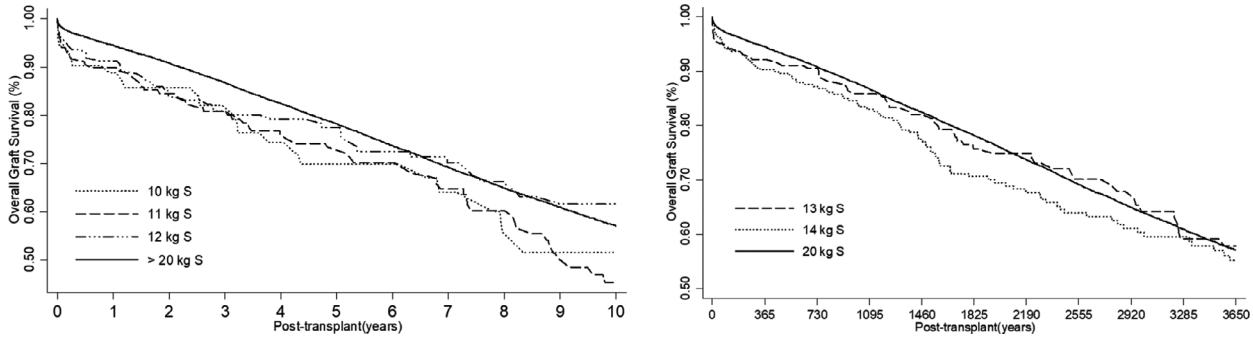

Figure 2 OGS in 10 years of small pediatric donors transplants with a single kidney and weight between 10 and 15 kg compared with a group of single kidney >20 kg. Log-rank test: 10 kg S $P = 0.17$, 11 kg S $P < 0.05$, 12 kg S $P = 0.81$, 13 kg S $P = 0.93$, and 14 kg S $P = 0.07$.

Comparing >10–15 and >15–18 kg groups with adult kidneys divided by KDPI. To obtain a different perspective of small pediatric kidney graft survival, we compared small pediatric donor transplant outcomes with adult donor kidneys stratified by KDPI. We examined overall survival and death censored graft survival given the higher percentage of older recipients, diabetics, and higher BMI in adult donor transplants (Table S4). Figure 3 showed that single kidneys, in the >10–15 and >15–18 kg groups, had superior 10-year OGS (55% and 56%) and death censored graft survival. (70% and 70%, respectively) like adult kidney transplants from deceased donors with a KDPI of 30–85% (OGS 45% and DCGS 66%). In both groups, en-bloc transplant 10-year OGS was superior, and death censored graft survival was like adult KDPI ≤30%.

The risk of graft failure, after adjustment, in both pediatric donor groups regardless of weight was decreased when compared with >85% KDPI adult deceased donor transplant. Risk of death censored graft survival in en-bloc transplants and SP transplants with >10–15 kg weight donors was 52% (HR = 0.48; 95% CI 0.41–0.56) and 33% (HR = 0.67; 95% CI 0.57–0.78) decreased when compared with KDPI >85% adult deceased donor transplants. The risk of death censored graft survival in en-bloc transplants and SP transplants with >15–18 kg weight donors was 55% (HR = 0.45; 95% CI 0.34–59) and 34% (HR = 0.66; 95% CI 0.55–0.79) decreased when compared with KDPI >85% adult deceased donor transplants.

Discussion

Current society guidelines recommend splitting small pediatric kidney donors when the donor weight is >18 kg. In this study, we demonstrate that splitting a pediatric donor kidney at a donor weight >12 kg provided long-term outcomes compared with a pediatric donor >20 kg and adult donors with a KDPI 30–85%. There was an increased risk of graft failure, especially in the early post-transplant period and when using small pediatric donors <10 kg as a single kidney. However, the rate of long-term graft loss was the same, suggesting that concerns regarding hyperfiltration injury are unwarranted. Recipient time on dialysis, diabetes status, age >60, and obesity was associated with an increased risk of graft loss, indicating a need for careful recipient selection for these organs.

The optimal cutoff to split pediatric kidneys may be revisited. One study compiled results from the literature to create a decision model to divide the kidneys from small pediatric donors based on the gain of life years and concluded that split confers an advantage except in donors with weight <10 kg [15]. In a review of the utilization of small pediatric donors for transplantation, the authors suggested a minimum threshold of 15 kg when considering using a single kidney from a pediatric patient [1]. This was mostly based on expert experience than available data. In this study, we showed, based on the US experience, that single kidney transplant results from pediatric donors weighing >12 kg were comparable to those from a pediatric donor group weighing >20 kg. We suggest that 12 kg and more may be the cutoff to consider a single transplant instead of EB kidneys. Our results were limited by the lack of donor kidney size. Kidney size may be used with donor weight in the decision to split the kidney. Uemura *et al.* have shown that pediatric kidneys with size >6 cm provide adequate renal function because of progressive increase in allograft size and can be used as a single transplant [16]. Our results are in line with more recent studies by Suneja *et al.* [14], that defined good outcomes of single >10 kg kidney pediatric donor transplants when compared with en-bloc and ideal donor kidneys. Zhu *et al.*

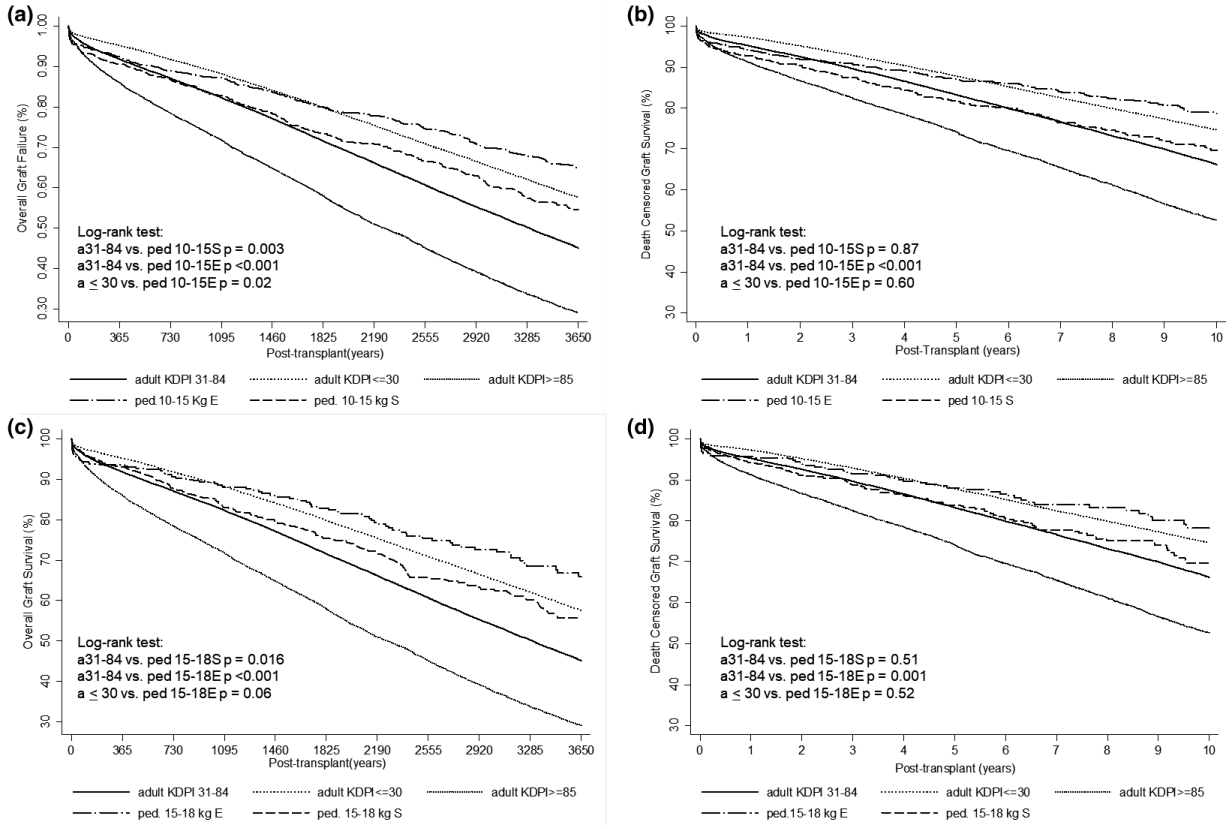

Figure 3 (a–c) OGS in 10 years of small pediatric donor transplants with weigh between 10 and 15 kg (a) and 18–20 kg stratified by single or en-bloc, and adult donor transplants according to KDPI. (b–d) Death censored graft survival in 10 years of small pediatric donor transplants with weigh between 10 and 15 kg (a) and 18–20 kg stratified by single or en-bloc, and adult donor transplants according to KDPI.

[17] showed that kidneys from small pediatric donors (aged 8–36 months) had a similar renal function and graft survival when compared with donors aged 3–12 years.

Two major concerns on utilizing small pediatric kidneys as single kidneys are early graft loss and the concept of poor long-term graft function because of hyperfiltration injury. Based on our survival analysis, early graft loss in SPD is a significant complication. The Kaplan-Meier curve analyzing SPD outcomes revealed a sharp decline in graft survival weeks after transplant because of thrombotic events and consequent graft loss. However, the concern for poor long-term function because of hyperfiltration injury is questionable. Our analysis demonstrated that after the initial loss, the Kaplan-Meier curve was parallel to the pediatric group with the largest kidney mass (>20 kg) and a slower decline compared with deceased adult donors' kidneys, as indicated by the crossing survival lines. Transplant center expertise in utilizing SPD kidneys is important as may lead to superior outcomes when compared with less experienced ones. Using small pediatric kidneys only in selected centers will minimize early graft loss. Recovery technique is also important with a report that transplant technique can be improved, and thrombosis minimized by providing an adequate aortic patch with the renal artery [17,18]. Data, as we presented, showed that small pediatric kidneys mainly when split (single kidneys) travel long distances, which may suggest that they are being shipped to specific centers. In our dataset, we do not have individual center information and we could not confirm this hypothesis or study the association of center volume with outcomes. The existence of a few transplant centers engaged in SPD transplants may remove the stimulus to procure small pediatric kidneys mainly in areas where local centers do not use these donors. A proposal would be to have at least one local center trained and engaged in the transplant of small pediatric donors, which may incentivize procurement. However, traveling long distances, which translated into longer cold ischemia time was not an independent factor associated with graft failure, and long distances should not be a limitation to procurement and transplant of SPD kidneys. This data argues

against the idea of graft loss because of hyperfiltration and may not be a reason to avoid SPD transplants.

Recipient sensitization and reduction in the chance of a second transplant is another concern of early loss caused by thrombosis of small pediatric single kidneys. Higher sensitization after brief exposure to a thrombosed living donor kidney was associated with a 37% reduction in the chance of a second transplant [19]. In young adults, the recipient's sensitization was higher after a failed first deceased donor when compared with a living donor, with consequent delay to a second transplant [20]. Early graft loss in adult kidney recipients was associated with high mortality rates in the first few months after transplantation, low re-listing rates, and increased risk of a subsequent early graft loss [21,22]. However, the risk of long-term mortality was higher if one remained on the waiting list [21]. The risk associated with early graft loss must be disclosed to recipients of small kidney donors and weighted against a longer wait for a second offer.

Improving the use of SPD kidneys is an important part of increasing the donor pool. Compared to kidneys from adult donors with a KDPI >85%, a group considered by many as "marginal", the adjusted risk of graft failure was decreased in pediatric small kidneys weighing 10–15 or 15–18 kg, which shows that a small kidney from a pediatric donor is a better option than an adult transplant from a deceased donor KDPI >85%. Given the ongoing efforts to reduce discard from adult donor kidneys with a KDPI >85%, further attention and studies should be conducted on the discard and use of SPDs.

Recipient selection is an important aspect in transplanting small pediatric donor kidneys. Our multivariate analysis has shown that long-term graft survival is reduced when small pediatric kidneys were transplanted in frailer, older, individuals with longer dialysis vintage, diabetic, and higher BMI recipients. Recipients' characteristics were more related to patient survival than graft survival, re-enforcing the importance to match kidneys and recipients per expected lifetime. A consideration would be to offer SPD kidneys to a selected group of recipients with low morbidity and longer expected survival. Currently, organs with a KPDI < 20% are preferentially allocated to recipients with the best predicted post-transplant survival. However, SPD kidneys carry an inflated KDPI, resulting in their placement into an alternate allocation algorithm. A critic of this KDPI based rule is that a high KDPI in pediatric donors is because of low weight, height, and age but kidneys are histologic pristine, and as shown in this study hyperfiltration injury is of limited impact. This is in stark comparison to high KDPI adult kidneys, which often present some chronic kidney injury [23,24]. Considering the high thrombosis rate, one issue is the transplantation of SPD into pediatric recipients, where vascular anastomosis involving small-donor arteries may increase the risk of thrombosis [25]. There is a lack of clear recommendations on the outcomes of small pediatric kidney transplants in pediatric recipients. Matching donor and recipient size may apply to optimal graft survival, mainly in transplanting small pediatric kidneys. Our study was not designed to examine the association of donor and recipient weight or size relation with transplant outcome; however, we found that a recipient with BMI >30 was associated with increase graft failure. Therefore, we do not recommend transplanting small pediatric kidney donors to adult obese recipients.

While we showed that single SPD kidneys from pediatric donors >10–15 kg have comparable outcomes to adult donor kidneys with a KDPI 30–85%, en-bloc kidneys transplanted fared much better. Our results showed a pediatric donor group of weight between 10 and 18 kg en-bloc transplantation had similar ten-year death censored graft survival when compared with adult deceased donor transplants with a KDPI <30%. A previous single-center study compared outcomes of pediatric en-bloc with living donors and concluded that graft survival was similar [26]. From a strictly utilitarian point of view, SPD should be transplanted en-bloc. However, we believe a small reduction in long-term outcomes, which is still comparable to "standard" adult donors, is an acceptable tradeoff to increase the number of kidney transplants.

Limitations of this study were inherent to the retrospective nature of the analysis. It is also limited by the information available in the database. Despite the use of a multivariate model, residual confounders can still exist. We did not have details on possible surgical damage and surgery complications that can affect pediatric donor kidney transplant outcomes. We did not have access to individual center data and cannot include center volume into the multivariate model. Multivariate analysis was not used to examine some outcomes, as the proportional haze method would be violated.

In conclusion, we recommend considering a single kidney transplant from pediatric donors with a body weight >12 kg to selected adult recipients from deceased donors (nondiabetic, nonobese, under 60 years of age, and shortened dialysis vintage), especially at a center with experience in transplanting pediatric donors. The time of cold ischemia is not independently related to

graft failure, and these kidneys can be transported to an experienced center. This strategy will increase the number of kidney transplants without significantly compromising the long-term outcome of the transplant. We have mainly linked the risk of early transplant failure in pediatric kidney donors to anatomical and surgical complications. The solution to minimizing complications is to create a regional center of excellence to accept pediatric transplants to optimize results and to ensure the transplantation of these organs at the time of procurement.

Authorship

MSS, and ELL: research idea and study design. MSS, ELL, SB, PH, and HAG: data analysis/interpretation. MSS: statistical analysis. SB, and HAG: supervision or mentorship. Each author contributed important intellectual content during manuscript drafting or revision and agrees to be personally accountable for the individual's contributions and to ensure that questions about the accuracy or integrity of any portion of the work, even one in which the author was not directly involved, are appropriately investigated, and resolved.

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Conflicts of interest

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SUPPORTING INFORMATION

Additional supporting information may be found online in the Supporting Information section at the end of the article.

Figure S1. Cohort formation.

Table S1. Post-transplant complications.

Table S2. Recipient risk factors associated with overall graft failure per weight group of small pediatric donor transplants.

Table S3. Risk factors associated with overall graft failure in pediatric single kidney with weight >10–15 kg.

Table S4. Baseline characteristic of the study groups.

REFERENCES

1. Damji S, Callaghan CJ, Loukopoulos I, *et al*. Utilisation of small paediatric donor kidneys for transplantation. *Pediatr Nephrol* 2019; **34**: 1717.
2. Bresnahan BA, McBride MA, Cherikh WS, Hariharan S. Risk factors for renal allograft survival from pediatric cadaver donors: an analysis of united network for organ sharing data. *Transplantation* 2001; **72**: 256.
3. Singh A, Stablein D, Tejani A. Risk factors for vascular thrombosis in pediatric renal transplantation: a special report of the North American Pediatric Renal Transplant Cooperative Study. *Transplantation* 1997; **63**: 1263.
4. Beetz O, Weigle CA, Nogly R, *et al*. Surgical complications in pediatric kidney transplantation-Incidence, risk factors, and effects on graft survival: a retrospective single-center study. *Pediatr Transplant* 2021; **25**: e13871.
5. Miller AJ, Kiberd BA, Alwayn IP, Odutayo A, Tennankore KK. Donor-recipient weight and sex mismatch and the risk of graft loss in renal transplantation. *Clin J Am Soc Nephrol* 2017; **12**: 669.
6. Yamakawa T, Kobayashi A, Yamamoto I, *et al*. Clinical and pathological features of donor/recipient body weight mismatch after kidney transplantation. *Nephrology* 2015; **20**(Suppl 2): 36.
7. Sui M, Zhao W, Chen YU, *et al*. Optimizing the utilization of kidneys from small pediatric deceased donors under 15 kg by choosing pediatric recipients. *Pediatr Transplant* 2016; **20**: 39.
8. Englesbe MJ, Lynch RJ, Heidt DG, *et al*. Early urologic complications after pediatric renal transplant: a single-center experience. *Transplantation* 2008; **86**: 1560.
9. Dharnidharka VR, Stevens G, Howard RJ. En-bloc kidney transplantation in the United States: an analysis of united network of organ sharing (UNOS) data from 1987 to 2003. *Am J Transplant* 2005; **5**: 1513.
10. Satterthwaite R, Aswad S, Sunga V, *et al*. Outcome of en bloc and single kidney transplantation from very young cadaveric donors. *Transplantation* 1997; **63**: 1405.
11. Mo H, Ko H, Chung CTY, *et al*. Single versus en bloc kidney transplant from donors less than or equal to 15 kg to pediatric recipients. *Pediatr Transplant* 2021; **25**: e13719.
12. Hoyer DP, Dittmann S, Büscher A, *et al*. Kidney transplantation with allografts from infant donors-Small organs, big value. *Pediatr Transplant* 2020; **24**: e13794.
13. Organ Procurement and Transplantation Network. Improving en bloc kidney allocation. Kidney committee Board briefing paper-en bloc. December 2017. Available from: https://optn.transplant.hrsa.gov/governance/public-

comment/improving-en-bloc-kidney-allocation-2/. Access date 5/21/2019.
14. Suneja M, Kuppachi S, Katz D, Hunsicker L. Small split pediatric kidneys to expand the donor pool: an analysis of scientific registry of transplant recipients (SRTR) data. *Transplantation* 2019; **103**: 2549.
15. Laurence JM, Sandroussi C, Lam VW, Pleass HC, Eslick GD, Allen RD. Utilization of small pediatric donor kidneys: a decision analysis. *Transplantation* 2011; **91**: 1110.
16. Uemura T, Liang J, Khan A, *et al*. Outcomes of transplantation of single pediatric renal allografts equal to or more than 6 cm in length. *Transplantation* 2010; **89**: 710.
17. Zhu L, Fu C, Chen S, *et al*. Successful single-kidney transplantation in adult recipients using pediatric donors aged 8 to 36 months: comparable outcomes with those using pediatric donors aged >3 years. *Transplantation* 2019; **103**: 2388.
18. Mohanka R, Basu A, Shapiro R, Kayler LK. Single versus en bloc kidney transplantation from pediatric donors less than or equal to 15 kg. *Transplantation* 2008; **86**: 264.
19. Adler JT, Markmann JF, Yeh H. Renal allograft thrombosis after living donor transplantation: risk factors and obstacles to retransplantation. *Clin Transplant* 2016; **30**: 864.
20. Phonphok K, Homkrailas P, Duong T, *et al*. Time to second kidney transplantation in young adults after failed pediatric kidney transplant. *Pediatr Transplant* 2020; **24**: e13800.
21. Hamed MO, Chen Y, Pasea L, *et al*. Early graft loss after kidney transplantation: risk factors and consequences. *Am J Transplant* 2015; **15**: 1632.
22. de Kok MJ, Schaapherder AF, Mensink JW, *et al*. A nationwide evaluation of deceased donor kidney transplantation indicates detrimental consequences of early graft loss. *Kidney Int* 2020; **97**: 1243.
23. Chen LX, Francalacci LC, Bang H, De Mattos A, Perez RV, Jen KY. Histopathologic findings on implantation renal allograft biopsies correlate with kidney donor profile index and 30-day serum creatinine. *Transplant Proc* 2019; **51**: 639.
24. del Moral Martín RMG, Retamero Díaz JA, Cava Molina M, *et al*. Validation of KDRI/KDPI for the selection of expanded criteria kidney donors. *Nefrologia* 2018; **38**: 297.
25. Wang C-S, Greenbaum LA, Patzer RE, *et al*. Renal allograft loss due to renal vascular thrombosis in the US pediatric renal transplantation. *Pediatr Nephrol* 2019; **34**: 1545.
26. Sureshkumar KK, Habbach A, Tang A, Chopra B. Long-term outcomes of pediatric en bloc compared to living donor kidney transplantation: a single-center experience with 25 years follow-up. *Transplantation* 2018; **102**: e245.