A single-center kidney transplantation experience in children with low weight: is low weight a contraindication?

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Abstract. – **OBJECTIVE:** Kidney transplantation (KT) might be difficult for underweight kids (under 15 kg). Our goal was to convey information on KT in underweight children.

PATIENTS AND METHODS: The study's target population consisted of children (age 18) weighing 15 kg or fewer who received KT at our facility between January 2018 and June 2021. A retrospective analysis was performed on demographic and clinical data, including age, gender, primary disease, pretransplant dialysis status, recipient weight, recipient body mass index (BMI), surgical approach type (intraperitoneal/extraperitoneal), complications, graft status (functioning/failed), patient survival, and immunological data.

RESULTS: There were 94 pediatric KTs completed. Thirty-three patients were included when the selection criteria were applied. The mean recipient weight was 11.45 [6.7-15] kg, and the average patient age was 3.36 [1-7]. Three (9.9%) patients had kidney transplants from dead adult donors, whereas thirty (90.1%) patients underwent live donor kidney transplantation (LDKT). While the intraperitoneal (IPA) technique was used in 19 cases, the extraperitoneal (KT) strategy was used on 14 patients (EPA). The donor BMI was 28.24 [19.6-42] kg/m², and the mean donor weight was 78.13 [55-109] kg. Bridectomy was necessary because five individuals experienced ileus. IPA was performed in each of these patients during LDKT. Following IPA, a 2-year-old patient with a BMI of 16 kg/m² had renal allograft compartment syndrome and required graft nephrectomy.

CONCLUSIONS: Pediatric patients weighing 15 kg or fewer can get kidney transplants successfully. Gastrointestinal problems are relatively uncommon with EPA, even though there is no agreement on the best surgical strategy.

Key Words:
   Kidney transplantation, Low weight patient, Pediatric patient.

Introduction

Kidney transplantation (KT) is the gold standard treatment method for children with end-stage renal disease (ESRD)[1]. However, it can be challenging in children with low weight (i.e., weight≤15 kg) due to smaller vascular anastomoses, smaller cavities for renal implantation, and potential size discrepancies between donors and recipient[2]. These disadvantages can lead to complications and increase the risk of graft loss and even mortality[3].

In low-weight children, the conventional surgical approach is intraperitoneal KT performed *via* a midline laparotomy incision[4]. Surgeons favoring this method believe that the intraperitoneal approach will provide a relatively larger cavity for the placement of the renal graft, mainly if the donor is an adult[5]. On the other hand, it is widely accepted that intraperitoneal KT can be associated with intestinal complications[4].

Although both approaches have supporters, literature regarding pediatric KT in low-weight children is scant[2]. Therefore, our study aimed to present our data concerning pediatric KT in children weighing 15 kg or less.

Patients and Methods

Pediatric patients (age<18) weighing 15 kg or less who underwent KT at our center between January 2018 and June 2021 constituted the target population of this study. The multi-organ transplant program's patient databases were retrospectively reviewed. Patients with incomplete inpatient or follow-up data, those who underwent kidney-pancreas or liver-kidney transplantation, or deceased donors en bloc KT were excluded. In addition, demographic data including age, gen-

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der, and clinical data such as primary disease, pretransplant dialysis status (preemptive/hemodialysis/peritoneal dialysis), recipient weight, recipient body mass index (BMI), type of surgical approach (intraperitoneal/extraperitoneal), complications and graft status (functioning/failed) and patient survival were retrieved from the database. Also, immunological data, including human leukocyte antigen (HLA) mismatch, were included in the database.

Perioperative Care

Special attention was given to the hemodynamic status of the children during KT surgeries. All patients had a central venous catheter to monitor the central venous pressure (CVP) continuously. The anesthesiology team ensured that CVP was higher than 15 cmH$_2$O immediately before reperfusion. All children were extubated in the operating room and referred to the pediatric transplantation intensive care unit (ICU). Per our institutional protocol, all patients were followed in the ICU for at least 24 hours. Urine output was measured hourly, and fluid replacement was performed based on the patients' urine output and hemodynamic status. Blood biochemistry, including renal function tests (i.e., urea, creatinine, and electrolytes), was checked twice daily during the ICU stay. Perfusion of the renal graft was checked by a bedside Doppler ultrasound during the postoperative first day regardless of the patient's urine output. It was repeated during the inpatient stay as needed. The ICU and transplant surgery teams decided to refer to the inpatient floor. Renal function tests were performed daily during the inpatient floor stay.

Per our institution's pre-printed orders, a standard immunosuppression protocol consisting of 2 mg/kg anti-thymocyte globulin (ATG) and intravenous methylprednisolone or oral prednisone, tacrolimus, and mycophenolate mofetil was followed in all cases. Corticosteroid doses were decreased daily as per protocol, and mycophenolate mofetil was replaced with mycophenolate sodium in children afflicted with gastrointestinal side effects.

All patients were given antithrombotic prophylaxis with oral or intravenous acetylsalicylic acid (ASA) 2 mg/kg daily for at least 30 days after kidney transplantation. However, recipients with high-risk risk factors such as a history of thrombotic events, multiple vascular anastomoses during transplantation surgery, and congenital nephrotic syndrome were given prophylaxis with intravenous heparin ten units/kg/h for seven days after surgery. Heparin was replaced with ASA at the end of 1 week.

Surgical Approach

Kidney transplantation surgeries were performed by either intraperitoneal (IPA) or extraperitoneal approach (EPA) per the surgeon's preference. A transperitoneal midline incision was made in the IPA, and the renal graft was implanted in the right retroperitoneal space after mobilizing the ascending colon. However, a Gibson incision was made in the EPA, and the graft was transplanted to the right iliac fossa after pushing the peritoneum aside to expose the iliac vessels. The vascular anastomosis sites depended on the size match between the renal graft and the recipient's vessels. The grafted artery was anastomosed to the aorta or common iliac artery continuously.

On the other hand, the inferior vena cava or common iliac vein was selected for venous anastomosis with continuous sutures. All ureteral reimplantation procedures were performed by the extravesical Lich-Gregoir method. A 5F double J stent was routinely inserted during anastomosis. The Foley catheter was removed before completion of the postoperative one week, while the double J stent was removed at the end of the third postoperative week.

Statistical Analysis

This study was designed as a retrospective, observational noncomparative study. The collected quantitative data were cardinal numbers, rates, and percentages. In addition, means and standard deviations were calculated and presented where appropriate. The Statistical Package performed all statistical analyses for Social Sciences (SPSS) software (SPSS v26.0, IBM, Armonk, NY, USA). A p-value less than 0.05 is statistically significant.

Results

Our review revealed that 94 pediatric kidney transplants were performed within the study period. After applying the inclusion and exclusion criteria, 33 patients were included in this study. Among these patients, 19 (57.6%) were male, while 14 (42.4%) were female. All study participants underwent their first kidney transplant during the study period. While 30 (90.1%) patients underwent living donor kidney transplantation (LDKT), three patients (9.9%) were transplanted from deceased adult donors. Thus, none

Table I. Number of HLA mismatches.

Number of patients	Number of HLA mismatches
2 (6%)	0
5 (15%)	1
1 (3%)	2
19 (58%)	3
3 (9%)	4
1 (3%)	5
2 (6%)	6

of the pediatric recipients received a pediatric donor kidney. While IPA was performed in 19 cases, 14 patients underwent KT *via* EPA. Among the 30 patients who underwent LDKT, 27 received a left kidney, while the remaining 3 received a right kidney. While parents were the donors in 23 cases, grandparents were the donors of 7 recipients. While 13 (39%) of the recipients underwent preemptive KT, 10 (30.5%) were on hemodialysis (HD), and the remaining 10 (30.5%) were on peritoneal dialysis (PD).

The mean patient age was 3.36 [1-7] years. They weighed between 6.7 and 15 kg. The mean recipient weight was calculated as 11.45 kg. Mean body mass index (BMI) of the recipients was 17.33 kg/m² [12-24]. On the other hand, mean donor age, donor weight, and renal graft size were 39.23 [23-66] years, 78.13 [55-109] kg, and 110.13 [91-125] mm, respectively. Mean donor BMI was 28.24 [19.6-42] kg/m².

None of the renal grafts, except one with two renal arteries and one renal vein, had renovascular anatomical variations. Panel reactive antibody (PRA) was positive in patients with 33.3% (n=11). The number of HLA mismatches is summarized in Table I.

Primary diseases of the patients leading to ESRD are displayed in Table II.

The mean stay at the inpatient ward was 11.07 [5-26] days, while it was 2.52 [1-12] days in ICU.

The mean follow-up period was 11 [6-24] months. The list of complications detected during the inpatient stay and outpatient clinic follow-up are displayed in Table III.

Five patients had developed ileus, which necessitated bridectomy. Of note, all of these cases underwent IPA during LDKT. Four patients were afflicted with urinary tract infections. Two of these patients received kidneys from deceased donors. A 2-year-old female patient with a BMI of 16 kg/m² who underwent LDKT *via* IPA developed a renal allograft compartment syndrome and had to undergo graft nephrectomy on postoperative day 8. She was managed with an open abdomen until she died from septic shock in the ICU on a postoperative day 16. A 4-year-old male patient developed lymphoma 18 months after an LDKT. This patient was on standard triple immunosuppression until he was diagnosed with lymphoma. However, the immunosuppression protocol had to be reduced to treat lymphoma, and he lost the graft short before his death in the 24th month after surgery. Two patients had antibody-mediated rejection episodes successfully treated with plasmapheresis. These patients were positive for PRA before LDKT with a 4 HLA mismatch. Finally, two patients had acute cellular rejection episodes, which responded well to pulse steroid treatment. All four patients who had rejection underwent LDKT with EPA, and they were all diagnosed by ultrasound-guided percutaneous graft biopsies. One patient had a wound site infection which was successfully treated with daily dressing changes and wound care.

Discussion

Kidney transplantation is not only the gold standard treatment method for ESRD in adults but also the standard gold treatment for ESRD in chil-

Table II. Primary diseases of the patients and concurrent surgeries during kidney transplantation.

Primary disease	Numbers and percentages	Concurrent surgery during KT
Nephrotic Syndrome (NS)	11 (33.3%)	Bilateral nephrectomy in 3 Finnish-type NS cases
Hypoplastic kidney	6 (18.2%)	Bilateral nephrectomy in 1 case with dysplasia
Posterior urethral valve Mitrofanoff procedure in 2 cases	6 (18.2%)	Bilateral nephrectomy in 2 cases with dysplasia
Polycystic kidney disease Right nephrectomy in 2 cases	5 (15.5%)	Bilateral nephrectomy in 1 case
Reflux nephropathy	2 (6%)	Bilateral nephrectomy in 2 cases
Primary Hyperoxaluria	1 (3%)	
Unknown	2 (6%)	

Table III. List of complications and brief explanations regarding management.

Complications	Number of patients	Management
İleus	5	5 patients underwent bridectomy
UTI	4	All responded to conservative management
RACS	1	Underwent graft nephrectomy, died due to sepsis
Malignancy	1	PTLD, lost the graft and subsequently died
Rejection	4	All acute, 2 cellulars, 2 AMR, all responded to treatment
Wound infection	1	Responded well to conservative management
Graft failure	2	1 due to RACS and 1 due to cessation of IS
Mortality	2	1 due to sepsis and 1 PTLD

RACS: Renal allograft compartment syndrome, CNS: Central nervous system, AMR: Antibody-mediated rejection, IS: Immunosuppression, UTI: Urinary tract infection, PTLD: Post-transplant lymphoproliferative disease

dren[2]. It was shown that KT treated growth retardation and developmental delay and increased the quality of life in children with ESRD[6]. Although the success of KT surgery is increasing in the pediatric patient population with increasing experience, it is widely accepted that it is significantly more challenging in children with low weight[6]. This challenge mainly originates from the size mismatch between the renal graft and the recipient's abdominal cavity. This size discrepancy is also believed to increase the risk of renal allograft compartment syndrome (RACS), which constitutes a high risk for graft thrombosis and subsequent graft loss[7]. Due to these reservations, most transplant surgeons prefer the traditional IPA in KT to believe that this approach will provide a sizeable operative field for renal implantation and facilitate the exposure to the great vessels for vascular anastomoses.

On the other hand, the popularity of EPA, the traditional approach for adult patients, has increased during the last few years[2]. Surgeons favoring this approach lean on the fact that most kidney transplantation surgeons use the EPA from their experience with the adult patient population. They can avoid gastrointestinal complications with this approach. Although there is no consensus regarding the optimal approach, it is known that there is an increasing demand for KT in the low-weight (i.e., weight<15 kg) pediatric patient population[2].

Due to their low weight, this subgroup of patients is at the risk of potential complications from size mismatches, such as RACS and cardiovascular complications[8,9]. In addition, other potential complications from the graft's growth and aging constitute additional challenges[10]. Since some surgeons are reluctant to perform KT in this patient population due to these reservations, studies conducted with these patients and reporting favorable outcomes are of significant value.

In one of these studies, Becker et al[11] reported their experience with 40 pediatric patients weighing less than 11 kg. At the same time, 24 of these patients received kidneys from deceased donors, and 16 received kidneys from live donors. These authors had the chance to compare the graft survival between these two groups and noted no significant difference between the study groups. Despite this finding, they stated that LDKT should be preferred in these patients since it allowed them to electively proceed with KT, perform a preemptive KT with a short cold ischemia time, and find a relatively young donor with low HLA mismatch. In our study, only 3 of our patients were transplanted from deceased donors, and our duration of follow-up ranged between 6 months and two years. Of note, two grafts were lost during follow-up, and both of these recipients had live donors. Approximately 82% of our recipients received kidneys from donors with ≤3 HLA mismatches. Thirty-nine percent of our patients were transplanted preemptively.

None of the donors -including the deceased donors- was pediatric donors in our study. Thus, all KT surgeries analyzed in this study should be considered KT from adult donors to low weight (weight≤15 kg) pediatric recipients. While the mean donor BMI was 28.24 kg/m^2, the mean recipient BMI was 17.33 kg/m^2. Similar to the significant difference between BMIs, mean donor and recipient weights were also significantly different (78.13 vs. 11.45 kg). These data and the mean renal graft size (i.e., 110.13 mm) indicate a size mismatch between donors and recipients.

Parekh et al[9] focused on the cardiovascular complications of KT in children. They noted that maintaining the central venous pressure at a level

higher than 15 cmH$_2$0 was crucial for early graft survival. Our institutional protocol was in line with this approach, and only 2 of our 33 patients experienced early graft failure. Thus, our early graft failure rate was relatively low (i.e., 6%).

According to the American Society of Transplantation (AST) pediatric committee, there is no consensus regarding KT's lower age and weight limit in pediatric recipient[12,13]. However, it was suggested that pediatric KT was relatively safer in children older than six months with a weight of higher than 6 kg[12,13]. Our youngest recipient was one year old and weighed 6.7 kg. Muramatsu et al[14] reported their experience regarding LDKT in pediatric patients weighing less than 15 kg. All donors in this study were adults, and while 24 patients underwent KT *via* IPA, 27 went through KT by an EPA approach. They calculated the donor kidney and recipient abdominal cavity volumes by performing computerized tomography scans before KT and comparing the patients who underwent IPA and EPA, which revealed that patients in the IPA group were younger and shorter with relatively lower weights. However, the two groups were similar regarding complication rates. They noted that the lower weight limit for EPA was 11.6 kg, and they had to perform simultaneous native nephrectomies in 56.9% of their cases since there was limited space for graft implantation. We performed concurrent native nephrectomy procedures in our series in 11 (33.3%) cases. However, 6 of these procedures were performed due to other indications, such as Finnish type nephrotic syndrome in 3 and renal dysplasia in 3 cases. Among the remaining 5 cases, 3 underwent bilateral nephrectomy, and 2 cases went through right-sided nephrectomy due to limited space for implantation. We had only 1 case of RACS in our series. This patient underwent IPA and weighed 8 kg during LDKT. Her primary disease was polycystic kidney disease, and a bilateral nephrectomy was performed simultaneously with LDKT. In this case, bilateral nephrectomy was not performed only to gain extra space; it was also performed since the patient had a history of recurrent pyelonephritis due to the polycystic kidneys.

Nevertheless, she developed RACS and had to undergo graft nephrectomy due to graft thrombosis. This 2-year-old patient received a kidney from a donor with a BMI of 42 and a kidney size of 121 mm. Considering that the highest BMI was 42, the largest renal graft size

was 125 cm in our series, and the recipient had a BMI of 16, it can be stated that there was a significant size mismatch in this case. Muramatsu et al[14] reported 2 cases of ileus, which necessitated bridectomy; both cases were in the IPA group. In our cohort, 5 cases of ileus requiring bridectomy were detected. In line with the report of Muramatsu et al[14], these cases underwent KT *via* IPA[14].

Furness et al[15] reported their results concerning KT by EPA in pediatric patients weighing less than 15 kg. This cohort included 29 patients, 13 of whom underwent deceased donor KT. They noted that four renal grafts were lost; however, only two failed for KT-related reasons. One of these patients developed vascular thrombosis, while the other lost the graft due to acute rejection. In line with this, we had 1 case of graft failure due to thrombosis in our series.

In contrast to Furness et al[15], we had 4 cases of acute rejection; however, all rejection episodes responded well to anti-rejection treatments. Nevertheless, while comparing our results with the findings of Furness et al[15], it should be considered that Furness et al published their report in 2001. These authors did not have a case with postoperative ileus. Of note, all cases in this series were performed *via* EPA. In our study, all cases with ileus underwent KT *via* IPA. Furness et al. noted that they performed KT *via* EPA safely even in children weighing 8 kg[15]. This finding is also similar to ours.

Similarly, Vitola et al[16] presented their data regarding KT in children weighing less than 15 kg. Their study included living and deceased donor KT cases, and it concluding that EPA was a valid technique in this patient population[15,16]. Gander et al performed KT *via* EPA or IPA in 44 children weighing less than 15 kg. They demonstrated that the surgical complication or early graft loss rates were not higher than the general pediatric patient population[2]. Finally, Aoki et al[12] compared the outcomes of LDKT *via* EPA with those of LDKT *via* IPA in a study including 100 pediatric recipients weighing less than 15 kg. They concluded that EPA was associated with fewer surgical complications. Since we had a relatively small sample size, we did not compare the outcomes of EPA with IPA in our study.

ElSheemy et al[17] presented their experience with 26 pediatric KT recipients weighing 20 kg or less. They performed EPA in all cases. They reported a vascular complication rate of 7% and

a urological complication rate of 18%. Their graft survival rate was 96% in a 3-year follow-up period. One of their patients died due to lung infection; this series had no other mortality. These authors concluded that EPA was safe in this patient population. In our study, the follow-up period was relatively shorter. Although we did not encounter any urological complications in our series, the significant difference between the follow-up periods should not be ignored while interpreting this finding.

Tanabe et al[18] reviewed their data concerning KT *via* EPA in pediatric patients. Their study population included 32 patients weighing less than 20 kg and 75 patients weighing more than 20 kg. These authors and other published reports noted that the EPA was safe in the pediatric patient population and helped avoid complications such as ileus, intestinal edema, duodenal perforation, abdominal compartment syndrome, and wound evisceration[5,19]. It was also stated that this approach facilitated postoperative enteral feeding and early mobilization. In addition, since the peritoneal cavity is not entered during EPA, patients on PD during the pretransplant period can continue with this treatment if delayed graft function occurs after KT.

Additionally, EPA facilitates exposure to the renal graft for diagnosis or treatment of post-transplant complications such as percutaneous renal graft biopsies or interventional radiologic procedures such as percutaneous drain insertion. Our study, did not have the chance to compare the outcomes of EPA and IPA due to our limited sample size. However, it is worth noting that all of the post-transplant ileus cases in our series had undergone KT *via* IPA. In addition, we performed percutaneous renal graft biopsies in 4 cases subsequently diagnosed with rejection. All these patients had undergone KT *via* EPA, and we did not experience graft biopsy-related complications.

Gomes et al[20] reported that aorta and vena cava inferior should be preferred for vascular anastomosis while transplanting kidneys to low-weight pediatric recipients. Our approach was the same as for this report. Therefore, our series did not encounter any vascular complications regarding donor-recipient vascular size mismatch in our series.

Our study has some limitations that must be considered while evaluating its findings. First, it is a retrospective study. Second, the sample size is relatively small. Due to the small sample size, it was impossible to compare the outcomes between patients who underwent KT *via* EPA and those who went through KT by IPA. Therefore, our co-

hort represented a heterogeneous patient group in this regard. However, since all donors, including the deceased donors, were adults and all recipients weighed 15 kg or less at the time of KT, our findings are valuable in encouraging transplant surgeons and transplant nephrologists to proceed with KT in this patient subgroup. As a third limitation, our follow-up period was relatively short. Thus, we could not include late complications and long-term graft survival data.

Despite the limitations above, we conclude that KT can be safely performed in pediatric patients weighing 15 kg or less. Although currently, there is no consensus regarding the optimal surgical approach, it should be considered that gastrointestinal complications are relatively rare with EPA. Nevertheless, for selecting the ideal surgical approach, all recipients should be evaluated by an individualized approach considering the primary disease for ESRD, past surgical history, the recipient, and renal graft size.

Conclusions

Pediatric patients weighing 15 kg or fewer can get kidney transplants successfully. Gastrointestinal problems are relatively uncommon with EPA, even though there is no agreement on the best surgical strategy.

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