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Does recipient weight and surgical approach really matter in pediatric renal transplantation?

Eryiğit Eren, Ayhan Dinçkan
Department of General Surgery, Faculty of Medicine, İstinye University, Istanbul, Turkey

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ABSTRACT

Aim: To compare the outcomes between low-weight (<15 kg) and normal-weight (≥15 kg) children who underwent renal transplantation (RT) and investigate the impact of the surgical approach (intraperitoneal or extraperitoneal RT).

Material and Method: This study was designed as an observational single-centre study and was conducted in Istinye University Hospital, Istanbul, Turkey, between January 2018 and June 2021. Data including age, gender, weight, surgical approach (intraperitoneal/extraperitoneal), complications, length of hospital stay, graft and patient survival were collected. Low-weight (LW) and normal-weight (NW) patients were compared. A p value less than 0.05 was considered statistically significant.

Results: Overall, 107 (33 LW and 74 NW) patients aged between 1 and 17 were included. The LW group had a significantly lower age and a significantly longer duration of intensive care unit (ICU), and inpatient floor stays than the NW group ($p<0.001$). Intraperitoneal RT (IRT) was significantly more common in the LW group (57.6% vs 42.4%), while ERT was more frequent in the NW group (87.8% vs 12.2%) ($p<0.001$). Both early complication and mortality rates were significantly higher in the LW group than in the NW group ($p<0.001$ and $p<0.031$). A comparison between the LW and NW patients who underwent ERT revealed that the mean patient age was significantly lower, while the duration of ICU stay was higher in the former than in the latter group ($p<0.001$ and $p<0.004$). However, the length of inpatient floor stay, early-term complication, and mortality rates were similar ($p>0.05$).

Conclusion: The extraperitoneal approach should be encouraged in children weighing less than 15 kg.

Keywords: Renal transplantation, pediatric, low-weight, extraperitoneal, intraperitoneal

INTRODUCTION

Renal transplantation (RT) is the ideal treatment method for pediatric patients with end-stage renal disease (ESRD) (1). Nevertheless, RT can be challenging in children due to size mismatch between donors and recipients (2). Therefore, there is a relatively higher risk of surgical complications, graft loss, and recipient mortality in children than in the adult patient population (3). These risks are amplified particularly in low-weight (LW) children (i.e., children weighing 15 kg or less).

In these children, the traditional surgical approach is intraperitoneal RT (IRT) performed by a midline laparotomy incision (4). Surgeons performing IRT defend that the intraperitoneal space will provide a relatively larger compartment for the insertion of the renal graft, especially for kidneys donated by adult donors (5). On the other hand, some surgeons prefer performing extraperitoneal RT (ERT) in both adults and children irrespective of recipient weight. These surgeons believe that IRT can increase the risk of bowel complications and therefore lengthen the duration of hospital stay (4).

In our pediatric RT program, both IRT and ERT are performed in both LW and normal-weight (NW) (i.e., 15 kg or more) pediatric patient populations. Therefore, our study aimed to compare the outcomes between LW and NW children who underwent RT and investigate the impact of the surgical approach (IRT or ERT) in the results of this comparative analysis.

MATERIAL AND METHOD

Children (age<18) who underwent RT at our center between January 2018 and June 2021 constituted the target population of this study. The study was carried out with the permisson of İstinye University Human Researches Ethics Committee (Date: 10.02.2022, Decision No: 21-90). All procedures were carried out in accordance with the ethical rules and the principles of the Declaration of Helsinki.

Corresponding Author: Eryigit Eren, eryigiteren58@gmail.com
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The transplant program's patient database was reviewed. Patients with incomplete data, those who underwent multi-organ transplantation, or deceased donor en bloc RT were omitted. Demographic parameters such as age, gender, and clinical data, including primary disease, history of RT, pre-RT dialysis status (preemptive/hemodialysis/peritoneal dialysis), recipient weight, recipient body mass index (BMI), donor type (live or deceased donor), donor kidney side (left or right kidney), donor data including age, gender, BMI, glomerular filtration rate (GFR) and renovascular variations, type of surgical approach (IRT/ERT), need for concurrent surgery during RT, intraoperative and early-term complications, length of inpatient floor and intensive care unit (ICU) stay, functional status of the renal graft (functioning/failed) and patient survival one year after transplant were collected from the database. In addition, immunological data such as panel reactive antibody (PRA), and human leukocyte antigen (HLA) mismatch, were retrieved from the database and analyzed. A comparative analysis was performed between LW and NW patients regarding these data parameters. We made a similar comparison within the group of patients who underwent ERT.

Perioperative Care

Hemodynamic states of the children were continuously monitored during RT surgeries. A central venous catheter was inserted in all cases to measure the central venous pressure (CVP) constantly. The CVP was maintained at levels higher than 15 cmH2O immediately before reperfusion. All children were referred to the pediatric ICU and followed in the ICU for at least 24 hours. Urine output was monitored hourly, and intravenous fluid replacement was performed according to the patients' urine output and hemodynamic status. Renal function tests, including urea, creatinine, and electrolytes, were performed 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 decision regarding referral to the inpatient floor was given by the ICU and transplant surgery teams. Renal function tests were performed daily during the inpatient floor stay.

Standard immunosuppression (IS), including intravenous basiliximab on days 0 and 4 and intravenous methylprednisolone or oral prednisone, tacrolimus, and mycophenolate mofetil (MMF) was given in all cases. Oral prednisone doses were reduced daily, and MMF was replaced with mycophenolate sodium in patients complaining about gastrointestinal symptoms. We preferred anti-thymocyte globulin (ATG) for IS induction in hypersensitized or deceased donor kidney recipients.

The RT surgeries were performed as IRT or ERT according to the surgeon's preference. In IRT, a transperitoneal midline incision was made, and the kidney was transplanted to the retroperitoneal space after colon mobilization. However, in ERT, a Gibson incision was made, and the kidney was transplanted to the iliac fossa after pushing the peritoneum aside for exposure to the iliac vessels. The renal artery was anastomosed to the common iliac artery or aorta by continuous sutures. The common iliac vein or inferior vena cava was preferred for venous anastomosis. The extravesical Lich-Gregoir method with a 5F double J stent insertion was used for all ureteral reimplantation procedures. A Jackson-Pratt surgical drain was routinely used. The primary surgeon gave the decision regarding drain removal based on drain output. The double J stent was removed after the completion of the third postoperative week.

Early surgical complications were defined as complications occurring between the transplant surgery and the patient's discharge.

Statistical Analysis

Data analysis was performed using IBM SPSS Statistics version 25.0 software (IBM Corporation, Armonk, NY, US). In order to investigate whether the normal distribution and, variance homogeneity assumptions were met were analyzed by Shapiro-Wilk and, Levene tests; respectively. Categorical data were expressed as numbers (n) and percentage (%) while quantitative data were given as mean ± SD and median (25th - 75th) percentiles. While the mean differences between groups were compared Student's t test, otherwise, Mann Whitney U test was applied for the comparisons of not normally distributed variables. Pearson's $\chi 2$test was used in the analysis of categorical data unless otherwise stated. On the other hand, in all 2 x 2 contingency tables to compare categorical variables; the Continuity corrected $\chi 2$test was used when one or more of the cells had an expected frequency of 5-25, otherwise, the Fisher's exact test was used when one or more of the cells had an expected frequency of 5 or less. In all R x C contingency tables to compare categorical variables; Fisher Freeman Halton test was used when ¼ or more of the cells had an expected frequency of 5 or less. A p value less than 0.05 was considered statistically significant.

RESULTS

After applying the inclusion and exclusion criteria, 107 patients aged between 1 and 17 were included in this study. Among all, 60 (56%) were male, while 47 (44%) were female. All but 3 patients underwent the first RT. In total, 99 (92.5%) recipients underwent living donor kidney transplantation (LDKT), while 8 (7.5%) received kidneys from deceased adult donors. The results of the comparative analysis between LW and NW children are displayed in **Table 1** and **Table 2**.

Table 1. Demographic and clinical characteristics of cases compared regarding body weights

	<15 kg (n=33)	≥15 kg (n=74)	p-value
Age (years)	3 (2-4)	13 (10-16)	<0.001†
Gender			0.675‡
Boys	20 (60.6%)	40 (54.1%)	
Girls	13 (39.4%)	34 (45.9%)	
Height (cm)	80.0 (73.5-87.0)	140.5 (124.5-155.0)	<0.001†
Weight (kg)	11.0 (10.0-13.0)	37.5 (25.0-45.5)	N/A
Body mass index (kg/m²)	17.2 (14.4-19.0)	17.6 (16.0-20.8)	0.254†
Second transplantation	0 (0.0%)	3 (4.1%)	0.551¶
Diagnosis			0.215¥
Nephrotic syndrome	13 (39.4%)	16 (21.6%)	
Lower urinary system pathology	5 (15.1%)	16 (21.6%)	
Polycystic kidney disease	3 (9.1%)	5 (6.8%)	
Focal segmental glomerulosclerosis	0 (0.0%)	9 (12.1%)	
Atrophic kidney	2 (6.1%)	4 (5.4%)	
Other	3 (9.1%)	5 (6.8%)	
Unknown	7 (21.2%)	19 (25.7%)	
Dialysis status			0.005§
Preemptive1	16 (48.5%)a	18 (24.3%)a	
Hemodialysis2	9 (27.3%)b	45 (60.8%)b	
Peritoneal dialysis	8 (24.2%)	11 (14.9%)	
History of abdomen surgery	4 (12.1%)	9 (12.1%)	>0.999¶
Surgical approach			<0.001‡
Intraperitoneal	19 (57.6%)	9 (12.1%)	
Extraperitoneal	14 (42.4%)	65 (87.9%)	
Concurrent surgery	23 (69.7%)	14 (18.9%)	<0.001‡

† Mann Whitney U test, ‡ Continuity corrected χ2 test, ¶ Fisher's exact test, ¥ Fisher Freeman Halton, § Pearson's χ2 test. N/A: Not applicable.1 p=0.024 for the comparison in terms of preemptive, 2p=0.003 for the comparison in terms of hemodialysis.

Table 2. Demographic and clinical characteristics of cases compared regarding body weights – continued

	<15 kg (n=33)	≥15 kg (n=74)	p-value
Donor's age	36.0 (30.0-46.0)	39.0 (35.0-49.0)	0.109†
Donor's gender			0.889‡
Male	14 (42.4%)	34 (45.9%)	
Female	16 (48.5%)	35 (47.3%)	
Cadaver	3 (9.1%)	5 (6.8%)	
Donor's height (m)	1.65±0.089	1.66±0.078	0.726¶
Donor's weight (kg)	78.2±15.2	77.4±13.3	0.787¶
Donor's body mass index (kg/m2)	28.8±5.5	28.3±5.3	0.710¶
Kidney size	110.1±8.0	107.5±9.6	0.199¶
Localization			0.026¥
Right	2 (6.7%)	20 (29.4%)	
Left	28 (93.3%)	48 (70.6%)	
Donor's GFR	114.3±21.9	107.7±17.3	0.112¶
Short term complication	14 (42.4%)	9 (12.1%)	<0.001¥
Mortality	4 (12.1%)	1 (1.4%)	0.031§
Duration of mortality (months)	0.36 (0.21-18.1)	N/A	N/A
Failed graft	1 (3.0%)	1 (1.4%)	N/A
Mismatch			0.562#
0	2 (6.1%)	7 (9.5%)	
1	3 (9.1%)	9 (12.1%)	
2	1 (3.0%)	8 (10.8%)	
3	20 (60.6%)	32 (43.2%)	
4	4 (12.1%)	14 (18.9%)	
5	1 (3.0%)	2 (2.7%)	
6	2 (6.1%)	2 (2.7%)	
PRA 1 positivity	3 (9.1%)	12 (16.2%)	0.385§
PRA 2 positivity	9 (27.3%)	21 (28.4%)	>0.999¥
Vascular variation			0.269§
Single artery – single vein	32 (97.0%)	66 (89.2%)	
Double artery – single vein	1 (3.0%)	8 (10.8%)	
Length of ICU stay	1 (1-3)	1 (1-1)	<0.001†
Hospitalization	9 (7-14)	7 (6-9)	<0.001†

†Mann Whitney U test, ‡ Pearson's χ2 test, ¶ Student's t test, ¥ Continuity corrected χ2 test, § Fisher's exact test, # Fisher Freeman Halton test, GFR: Glomerular filtration rate, PRA: Panel reactive antibody, ICU: Intensive care unit, N/A: Not applicable.

There were 33 patients in the LW and 74 patients in the NW group. The LW group had a significantly lower age, height, and a significantly longer duration of ICU and inpatient floor stays than the NW group (p<0.001). In addition, the rate of preemptive RT was significantly higher in the LW group, while the rate of hemodialysis (HD) patients was higher in the NW group (p=0,024 and p=0.003). Two groups were similar regarding the rate of peritoneal dialysis (PD) (p=0,369).

The comparison regarding the surgical approach revealed that IRT was significantly more common in the LW group (57,6% vs. 42,4%) while ERT was more frequently performed in the NW group (87,8% vs. 12,2%) (p<0.001). In addition, the rate of concurrent surgeries was significantly higher in the LW group than in the NW patient group (p<0.001). The most common simultaneous procedure was unilateral or bilateral nephrectomy of native kidneys in the entire cohort (35 of 107 cases; 32,7%). While the left donor kidney was transplanted more frequently in the LW group, the right kidney was used significantly more often in the NW group (p=0.026).

The comparison of complication rates revealed that both early complication and mortality rates were significantly higher in the LW group than in the NW group (p<0.001 and p<0.031). The most common complications were ileus (n=5), followed by urosepsis (n=4), wound infections (n=3), and renal allograft compartment syndrome (RACS) (n=1). Four patients (2 due to urosepsis, 2 due to cardiac failure) in the LW and one (due to urosepsis) in the NW group died during early-term follow-up. There was no difference between the LW and NW groups regarding other analyzed data parameters (p>0.05) (Tables 1 and 2). One patient in the LW group had graft thrombosis due to RACS, while another patient in the NW group experienced graft failure due to rejection. Although a similar comparison was not possible in the IRT group due to low patient numbers, our study also included a comparative analysis of the demographic and clinical data of the LW and NW patients who underwent ERT (**Tables 3** and **4**).

Table 3. Demographic and clinical characteristics of cases with extraperitoneal approach compared regarding body weights

	<15 kg (n=14)	≥15 kg (n=65)	p value
Age (years)	3 (3-4)	13 (11-16)	<0.001†
Gender			>0.999‡
Boys	7 (50.0%)	34 (52.3%)	
Girls	7 (50.0%)	31 (47.7%)	
Height (cm)	80.0 (79.5-86.2)	142.0 (125.0-155.0)	<0.001†
Weight (kg)	11.0 (9.9-12.1)	38.0 (25.0-46.0)	N/A
Body mass index (kg/m2)	16.2 (13.9-19.0)	17.7 (16.0-20.4)	0.085†
Second transplantation	0 (0.0%)	3 (4.6%)	>0.999¶
Diagnosis			0.311¥
Nephrotic syndrome	7 (50.0%)	15 (23.1%)	
Lower urinary system pathology	1 (7.1%)	10 (15.4%)	
Polycystic kidney disease	2 (14.3%)	4 (6.1%)	
Focal segmental glomerulosclerosis	0 (0.0%)	9 (13.9%)	
Atrophic kidney	0 (0.0%)	4 (6.1%)	
Other	1 (7.1%)	5 (7.7%)	
Unknown	3 (21.4%)	18 (27.7%)	
Dialysis status			<0.001¥
Preemptive1	9 (64.3%)	14 (21.5%)	
Hemodialysis2	2 (14.3%)	43 (66.2%)	
Peritoneal dialysis	3 (21.4%)	8 (12.3%)	
History of abdomen surgery	1 (7.1%)	7 (10.8%)	>0.999¶
Concurrent surgery	11 (78.6%)	5 (7.7%)	<0.001¶

† Mann Whitney U test, ‡ Continuity corrected χ2 test, ¶ Fisher's exact test, ¥ Fisher Freeman Halton. N/A: Not applicable.1 p=0.003 for the comparison in terms of preemptive, 2 p<0.001 for the comparison in terms of hemodialysis.

Table 4. Demographic and clinical characteristics of cases with extraperitoneal approach compared regarding body weights – continued

	<15 kg (n=14)	≥15 kg (n=65)	p-value
Donor's age	35 (27.5-58.5)	40 (35-48.5)	0.509†
Donor's gender			>0.999‡
Male	6 (42.9%)	28 (43.1%)	
Female	7 (50.0%)	33 (50.8%)	
Cadaver	1 (7.1%)	4 (6.1%)	
Donor's height (m)	1.61±0.077	1.66±0.075	0.075¶
Donor's weight (kg)	76.8±18.8	77.3±13.8	0.924¶
Donor's body mass index (kg/m2)	29.5±7.2	28.2±5.2	0.539¶
Kidney size	109.9±5.9	107.7±9.7	0.433¶
Localization			0.017¥
Right	0 (0.0%)	19 (31.1%)	
Left	13 (100.0%)	42 (68.9%)	
Donor's GFR	112.3±19.9	107.7±16.4	0.382¶
Short term complication	4 (28.6%)	8 (12.3%)	0.210¥
Mortality	1 (7.1%)	1 (1.5%)	N/A
Failed graft	0 (0.0%)	1 (1.5%)	N/A
Mismatch			>0.999‡
0	1 (7.1%)	6 (9.2%)	
1	2 (14.3%)	8 (12.3%)	
2	1 (7.1%)	6 (9.2%)	
3	7 (50.0%)	27 (41.5%)	
4	3 (21.4%)	14 (21.5%)	
5	0 (0.0%)	2 (3.1%)	
6	0 (0.0%)	2 (3.1%)	
PRA 1 positivity	2 (14.3%)	11 (16.9%)	>0.999¥
PRA 2 positivity	4 (28.6%)	20 (30.8%)	>0.999¥
Vascular variation			0.338¥
Single artery–single vein	14 (100.0%)	57 (87.7%)	
Double artery–single vein	0 (0.0%)	8 (12.3%)	
Length of ICU stay	1 (1-2)	1 (1-1)	0.004†
Hospitalization	7 (6-12.5)	7 (6-8)	0.211†

†Mann Whitney U test, ‡ Fisher Freeman Halton test, ¶ Student's t test, ¥ Fisher's exact test, GFR: Glomerular filtration rate, PRA: Panel reactive antibody, ICU: Intensive care unit, N/A: Not applicable.

There were 79 patients in this group. This analysis revealed that the mean patient age and height were significantly lower, while the duration of ICU stay was higher in the LW group than in the NW group (p<0.001 and p<0.004). However, the length of inpatient floor stay was similar between the two groups (p=0,211). While the rate of preemptive RT was significantly higher in the LW group, the rate of the patients on HD at the time of RT was significantly higher in the NW group (p=0.003 and p<0.001). The two groups were not different regarding the rates of patients on PD at the time of RT (p=0.401). The rate of concurrent surgery was significantly higher in the LW group than in the NW group (p<0.001). While the left kidney was more often transplanted in the LW group, the right kidney was significantly more commonly used in the NW group (p=0.017). Although the rate of early-term complications was relatively higher in the LW group than in the NW group, the difference was statistically insignificant (p=0.210). The mortality rates were also similar between these two groups (p>0.05). There was no difference between the groups concerning other data parameters.

DISCUSSION

Renal transplantation is the preferred method in the treatment of ESRD in children (1). It was reported that RT at an early age positively affected patients' survival and increased the longevity of the renal allograft (2). Also, an early RT saves the child from a long period of dialysis therapy and its adverse effects (3). Therefore, RT is considered a valuable treatment option in LW pediatric patients, despite the small caliber of the major vessels and the potential size mismatch between the donor and the recipient. Traditionally, IRT is preferred for children weighing less than 15 kg (2). This approach has advantages such as consenting more space for the renal allograft and facilitating the closure of the abdominal wall (5).

On the other hand, IRT is believed to have disadvantages, including increased risks of ileus and twisting of the renal allograft due to its hypermobility in the abdominal cavity (6,7). Thus, ERT became popular in some transplantation centers (8-15). These centers believe ERT provides advantages such as the reduced

risk of gastrointestinal complications, ease of access to the graft for percutaneous biopsy, and the ability to use the peritoneal cavity when dialysis is needed after RT. In our pediatric RT center, RT is performed in both NW and LW children by intraperitoneal or extraperitoneal approach according to the surgeon`s preference. Therefore, we compared the clinical data and short-term outcomes of the LW and NW children who underwent IRT or ERT in our center.

Ghidini et al. (16) retrospectively reviewed the data of 108 children who underwent ERT. They compared the LW (i.e., weighing less than 15 kg) and NW (i.e., weighing 15 kg or more) children regarding early outcomes. These authors reported that the two patient groups had similar overall early complication rates except for venous thrombosis, which was more common in the LW patient group. However, they ascribed this finding to the patient characteristics in the LW group rather than patients` weight per se. In our cohort, 79 patients underwent ERT. The comparison of the LW and NW patients in this group regarding early complication rates did not reveal a significant difference. Of note, one of our LW patients developed graft thrombosis due to RACS. We had to do a graft nephrectomy in this case.

Chiodini et al. (17) reviewed the outcomes of pediatric RT in 72 children weighing 15 kg or less. They reported an early complication rate of 35%; however, these authors did not give any technical details regarding their surgical approach. The 1-year graft survival was 94% in this cohort. In our study, we calculated a similar 1-year graft survival rate (i.e., 97%).

In 2017, Gander and coworkers reported the results of their comparative analysis regarding RT in patients weighing 15 kg or less and those weighing more than 15 kg (18). Overall, their cohort included 164 patients. In the LW group, all but two patients underwent ERT. They noted that the two patient groups were similar regarding complication and graft survival rates. Their 1-year graft survival rate was 81%. However, it should be considered that all renal allografts were received from deceased donors in this study. They concluded that RT was challenging in LW pediatric recipients but was not associated with increased complication and graft failure rates. This finding is in line with ours.

ElSheemy et al. (19) retrospectively analyzed the outcomes of pediatric patients weighing less than 20 kg who underwent live-donor ERT. They had 26 patients with a mean weight of 16,4 kg. In this study, the early complication rate was 26,9%. These authors reported a 3-year graft survival rate of 96% and concluded that excellent graft and patient survival rates could be achieved by ERT in children weighing less than 20 kg. Similarly, Nahas et al. (20) worked on 46 children weighing less than 20 kg and underwent ERT at their center. The mean patient weight was 16,6 kg. While 5 cases had deceased donors, others underwent live donor ERT. These authors reported that 6 (13%) patients had complications during early-term follow-up, and one renal graft was lost due to a surgical complication.

Vitola et al. (21) analyzed the data of 62 children weighing less than 15 kg who underwent ERT. Among these patients, 32 underwent live-related RT, while deceased donor RT was performed in 30 cases. The mean patient weight was 12,3 kg. This study reported a 1-year graft survival rate of 85,2% and concluded that ERT was a valid approach in children weighing less than 15 kg.

Furness et al. (22) retrospectively investigated the clinical data of 29 LW (i.e., weighing less than 15 kg) children who underwent ERT. The mean patient weight was 11,2 in this study. These authors reported that two renal grafts were lost during early-term follow-up due to vascular complications. However, they concluded that ERT was technically feasible in children weighing less than 15 kg.

Our analysis revealed that the length of ICU and hospital stays were significantly longer in the patients with LW. In addition, early-term complication and mortality rates were significantly higher in the LW group than in the NW group. However, the comparative analysis performed within the group of patients who underwent ERT did not show a difference in length of hospital stay and the early-term complication and mortality rates. This finding is in favor of the extraperitoneal approach.

Our study has some limitations that must be considered while evaluating its results. First, it is a retrospective study that might have been affected by the inherent weaknesses of its design. Second, RT surgeries were performed by different transplant surgeons preferring ERT or IRT in LW children. Third, these decisions were not given based on predetermined specific institutional criteria. In addition, long-term outcomes were not included in the analysis.

CONCLUSION

Despite the weaknesses mentioned above, we conclude that RT is a challenging procedure in children weighing less than 15 kg. However, ERT should be encouraged in this patient population, considering that RT is the gold standard renal replacement treatment method, and these patients should not be deprived of the advantages of this approach.

ETHICAL DECLARATIONS

Ethics Committee Approval: The study was carried out with the permisson of İstinye University Human Researches Ethics Committee (Date: 10.02.2022, Decision No: 21-90).

Informed Consent: All patients signed the informed consent forms.

Referee Evaluation Process: Externally peer-reviewed.

Conflict of Interest Statement: The authors have no conflicts of interest to declare.

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Author Contributions: All of the authors declare that they have all participated in the design, execution, and analysis of the paper, and that they have approved the final version.

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