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Pediatric renal transplantation; 10 years experience

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ABSTRACT

Objective: Although renal transplantation (RT) is the first treatment option for children with end-stage renal failure, the number of transplanted children remains low compared to adults. Experience of the individual pediatric transplant center is very important in the prognosis of pediatric transplant recipients. In this study, our pediatric RT experience was presented.

Material and Methods: We retrospectively analyzed the data of 27 patients who had RT in our clinic between April 2009 and April 2019.

Results: Fifteen of the patients were males, and mean age of all patients was 12.36 ± 4.18 years (range 4-17 years). The most frequent etiology for end-stage renal disease (ESRD) was vesicourethral reflux. Eighteen (66.7%) of the transplanted kidneys came from cadaveric donors and 9 (33.3%) from live donors. One patient had preemptive RT and one patient had a re-RT. Twenty-two patients were on peritoneal dialysis program and four patients were on hemodialysis program. Mean dialysis time before transplantation was 29 (3-104) months. Bleeding was the most common surgical complication. Delayed graft function developed in four patients, and all of their grafts were from cadaveric donors. Rejection developed in 12 of our patients, graft loss was observed in only four of them. Considering all patients, graft survival rates were 100% in the 1st and 3rd years, and 92% in the 5th year.

Conclusion: Pediatric RT program is difficult to establish, maintain and develop. Complications after transplantation are not uncommon; therefore, early detection and appropriate management are needed. Strategies are still needed to increase post-transplant success.

Keywords: Pediatric, end-stage renal disease, renal transplantation

INTRODUCTION

Chronic kidney disease (CKD) refers to a condition associated with irreversible kidney damage that can progress to end-stage renal failure (ESRD). Although it is relatively rare in children, it can be regarded as an independent clinical condition in part due to its distinct features. Today, progression to ESRD can result in cardiovascular and developmental problems, which can be devastating and can even lead to mortality. Each year, approximately 5-10 children per million in the age-related population are initiated on renal replacement therapy (RRT), and mortality in children with ESRD may be 30 times higher than in the healthy age-related population (1,2). As in the adult age group, the permanent treatment of ESRD in the pediatric group is kidney transplantation. Significant developments have been made in this area recently. The availability of better immunosuppressant drugs, advances in perioperative care and infection management are the main reasons for increased success (3,4). In addition, the frequency of complications such as delayed graft function (DGF), acute rejection (AR) and postoperative infection rates have decreased in the last 20 years (5). Long-term results of pediatric renal transplantation (RT) have been an important problem requiring adequate treatment and follow-up for years (6-9). An important question posed by clinicians is how pediatric transplant recipients will be managed in the long term once they reach adulthood. The answer is not clear yet, and data on the long-term outcomes of pediatric RT are still limited. The aim of this study was to share our 10-year pediatric renal transplant results.

MATERIAL and METHODS

Study Design

In the retrospective analysis of pediatric RT patients followed in our center between April 2009 and April 2019, follow-up data were collected until April 2021. Demographic features (number of patients, gender, age of recipient at transplantation), clinical

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data (end-stage renal failure etiology, previous RRT type, donor type, length of hospital stay, follow-up time after RT, lowest creatinine values, graft loss and death) and complications (perioperative and postoperative surgical complications) were analyzed.

Definitions

DGF was defined as the need for dialysis in the first week after transplantation. The cases considered as rejection were included in the analysis. Graft loss was defined as permanent conversion to dialysis.

Statistical Analysis

A descriptive statistical analysis was performed. Categorical variables were presented as frequency and percentage. All statistical analyzes were performed using SPSS software version 22 for Windows (SPSS Inc., Chicago, IL, USA). Approval was obtained from the ethics committee of our center for this retrospective study.

RESULTS

In our center, RT was performed in 27 pediatric patients in the last 10 years. Cadaveric donor RT was performed in 18 of 27 patients. Basic demographic data and clinical characteristics of the patients are given in Table 1. Mean age at the time of transplantation was 12.36 ± 4.18.

ESRD etiologies are shown in Table 2. The most common reason of ESRD was vesicourethral reflux. Twenty-two patients were on peritoneal dialysis (PD) and four patients were on hemodialysis (HD) program. Mean dialysis time was 29 (3-104) months. A patient who developed ESRD due to Alport Syndrome underwent preemptive transplantation.

Table 1. Pre-transplant patient characteristics

Female/Male	12/15
Transplantation age	12,4 (2-17)
Hemodialysis (HD) Peritoneum dialysis (PD) Preemptive transplantation	4 22 1
Mean HD/PD time (month)	36.3
Living donor Deceased donor	9 18

Table 2. Chronic kidney disease etiology of transplanted children (Number of patients)

Vesicoureteral reflux	8
Unknown etiology	5
Polycystic kidney disease	3
Cystinosis	2
Urological disorders	2
MPGN Type 2 FSGS	1 1
Alport Syndrome	1
Nephronophthisis	1
Hypertension	1
Distal renal tubular acidosis	1

One of our patients had a RT in another center four years ago due to polycystic kidney disease, and a RT was performed again in our clinic after graft loss.

Perioperative surgical complication was seen in one patient, and a re-anastomosis was performed after thrombosis developed following arterial anastomosis. Five patients needed surgery again due to bleeding during hospitalization. Three of these patients were operated in the first 24 hours postoperatively. Only one of the bleeding was from vascular anastomosis, and four patients had leakage from the operation area. In one of our patients, venous drainage problem developed due to vascular torsion in the transplanted kidney, and no additional intervention was required after de-torsion.

DGF was seen in four patients, all of them were cadaveric transplants. At the same time, three of the patients with DGF needed reoperation in the first 24 hours due to bleeding.

Median length of hospital stay was 7 (4-21) days. One of our patients, who underwent reoperation due to bleeding and developed a lymphocele, was hospitalized for 21 days. Mean follow-up period of the recipients was 66.07 ± 37.97 months, 12 patients had rejection and five patients had graft loss. While the reason of graft loss was chronic rejection in 4 of the patients, one patient returned to dialysis due to focal segmental glomerulosclerosis (FSGS) recurrence. Protocol biopsy was not performed in any of our patients during clinical follow-up, our diagnoses were supported by biopsy in patients who were considered rejection and were unresponsive to treatment. Of those who experienced loss of graft due to rejection, three were living donors. Considering all patients, graft survival rates were 100% in the 1st and 3rd year and 92% in the 5th year.

During follow-up, five patients needed reoperation. The most common indication for reoperation was transplanted kidney ureter pathologies. In four of these patients, the cause of ESRD was VUR. Three patients had ureteral stricture, and two patients had reflux into the transplanted ureter. In patients with stenosis, ureteroneocystostomy was performed as a surgical treatment, and graft loss occurred in two of these three patients in the long term.

DISCUSSION

RT is the most effective treatment for children with ESRD (10). All over the world, there is a prominent increase not only in frequency but also in success in pediatric RT in parallel with the advances in immunosuppression and surgical techniques. The most important causes of ESRD in the pediatric group are chronic pyelonephritis and vesicoureteral reflux (VUR). Other common causes are chronic glomerulonephritis and FSGS (11).

The effect of etiology on graft survival has been reported in some studies (12), but not in others (13). The pathology that causes ESRD and the risk of recurrence may have significant effects on the need for additional urological intervention and donor selection. Although hemodialysis seems to be a more common treatment method before RT, the number of PD patients in our center is increasing in parallel with the advances in PD programs. Although PD is more physiological than HD, its use depends on many external factors. Various factors related to parental willingness, insufficient asepsis conditions in home environments, lack of necessary materials and solutions, limit the practice of PD. PD is associated with a lower risk of DGF and cardiovascular mortality in adult transplant recipients, but with a higher risk of infectious complications (14) and increased graft loss due to vascular thrombosis (15). Preemptive RT is considered the most suitable choice for adult and pediatric patients with ESRD. In this study, 3% of our patients had not undergone dialysis before RT. Amaral et al. have reported better results in terms of graft and patient survival in children with preemptive transplants compared to children exposed to dialysis. To reach RT earlier, appropriate patients, educated parents and timely hospital admission are required (16). Different dialysis time intervals before transplantation have been reported in the literature. Haberal et al. have reported 7.6 months and Mir et al. 22 months (11). This period was 29 months in our series. Although pediatric RT has generally been reported to be limited to older children in developing countries, the youngest child transplanted in our cohort was four years old. Other 26 patients were over five years of age. The pediatric RT center, located in a pediatric hospital with multidisciplinary facilities, is especially necessary for younger patients. (even to infants weighing <5 kg or <6 months) (17).

Living donor transplants, having fewer technical failures than cadaveric donor transplants, are also associated with longer term graft survival. Early graft function was excellent in most of our patients (85.1%). While DGF was observed in four patients, the primary nonfunctioning graft did not occur. It has been clearly reported that both the cadaveric donor and the pediatric population have a significant effect on the incidence of DGF (18). Fortunately, only one of our patients with DGF experienced graft loss.

Surgical complications, acute or chronic rejections and post-transplant infections are the main causes of mortality and morbidity. Vascular thrombosis and stenosis in the transplant renal artery have been well known in pediatrics since the emergence of RT. In our series, one patient developed perioperative renal artery thrombosis. After the diagnosis was made by Doppler ultrasonography, re-anastomosis was performed. The patient who did not develop DGF was discharged on the postoperative 15th day. Another patient was re-operated upon the detection of a venous drainage problem causing DGF, and torsion was observed in the transplanted kidney. Since the arterial and venous flow was uneventful after detorsion, no additional vascular intervention was performed. There was no graft loss due to vascular complications in either recipient. Our vascular complication rate (7.4%) is lower than that reported by Gargah et al. as 8.5% (19).

Acute and chronic rejection has been reported to be associated with decreased graft survival rates (20). Many studies have reported AR rates between 15% and 39% (21). In our series, 12 patients developed rejection, and graft loss occurred in four of these patients. One of the patients with graft loss was with a cadaveric donor. Five-year graft survival rate was 83%, the average graft life was 59.2 months. There was no AR attack in our patients, the reason for graft loss was chronic rejection processes. In one of our patients who underwent transplantation due to FSGS, recurrence developed in the 5th year of the follow-up, and graft loss occurred in the 7th year of the follow-up.

Urinary tract infection (UTI) was the most common post-transplant bacterial infection in our series (seen in 22% of the patients). In previous pediatric reports, the prevalence of post-transplant UTI ranges from 15% to 33% (22).

Several reports show that despite acute graft dysfunction during febrile UTI, long-term renal function is not different between patients with and without infection (23). Other reports reveal worse outcomes in patients with UTI, especially those with recurrent UTIs (24). In our series, only one of the patients who experienced graft loss had recurrent urinary tract infections, but it may not be enough to explain the graft loss with urinary bacterial infection. The effect of UTI on long-term graft outcome continues to be a point where further studies are needed.

Children with ESRD have a shorter life expectancy compared to children without ESRD, and survival rates of these children are approximately 30 times lower than their healthy peers (1). Although recent data show a reduction in mortality for children receiving chronic dialysis, RT remains the treatment of choice for maximizing survival and quality of life (25). Children with ESRD now die mainly from cardiovascular causes and infection rather than kidney failure. The survival rate of our patients was 100%. No transplantation-related mortality was seen in patients whose follow-up was continued after graft loss.

CONCLUSION

Pediatric RT program is difficult to establish, maintain and develop. Complications after transplantation are not uncommon; therefore, early detection and appropriate management are needed. Strategies are still needed to increase post-transplant success. Possible areas for improvement include increasing adherence to medications and follow-up includes systematic surveillance for malignancies and cardiovascular risk, as well as

early effective management of infectious complications that occur during follow-up.

Ethics Committee Approval: This study approval was obtained from İnönü University Health Sciences Non-Invasive Clinical Researches Ethics Committee (Decision No: 2020/932, 14.07.2020).

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Pediyatrik böbrek nakli: 10 yıllık deneyim

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ÖZET

Giriş ve Amaç: Böbrek nakli (BN), son dönem böbrek yetersizliği olan çocuklar için ilk tedavi seçeneği olmasına rağmen, nakledilen çocuk sayısı yetişkinlere göre düşük kalmaktadır. Bireysel pediyatrik nakil merkezinin deneyimi pediyatrik nakil alıcılarının sonuçlarında çok önemlidir. Bu çalışmada pediyatrik böbrek nakli deneyimimiz sunulmuştur.

Gereç ve Yöntem: Nisan 2009 ile Nisan 2019 arasında merkezimizde böbrek nakli yapılan 27 pediyatrik hastamızın verilerini retrospektif olarak inceledik.

Bulgular: 15'i erkek hasta ve ortalama BN yaşları 12,36 ± 4,18 yıl (dağılım 4-17 yıl) idi. En sık son dönem böbrek yetersizliği endikasyonu vezikoüretral reflüydü. Transplante edilen böbreklerin on sekizi (%66,7) kadavra vericiden, 9'u (%33,3) canlı donöründen geldi. Bir hastaya preemptif BN ve bir hastaya da ikinci kez transplant yapıldı. 22 hasta periton diyalizi, 4 hasta hemodiyaliz programındaydı. Ortalama diyaliz süresi 29 (3-104) aydı. Kanama en sık görülen cerrahi komplikasyondu. Dört hastada gecikmiş greft fonksiyonu gelişti, hepsi kadaverik vericiliydi. 12 hastada rejeksiyon gelişirken buna bağlı greft kaybı 4 hastada görüldü. Tüm hastalar göz önüne bulundurulduğunda greft sağkalım oranları 1. ve 3. yılda %100, 5. yılda ise %92'ydi.

Sonuç: Pediyatrik BN programının oluşturulması, sürdürülmesi ve geliştirilmesi zordur. Transplantasyondan sonra komplikasyonlar nadir değildir; bu nedenle erken tespit ve uygun yönetime ihtiyaç vardır. Nakil sonrası başarıyı arttırmak için hâlâ stratejilere ihtiyaç duyulmaktadır.

Anahtar Kelimeler: Pediyatrik, son dönem böbrek hastalığı, böbrek nakli

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