Renal Transplantation in Pediatric Patients: Surgical Outcomes of 15 Years of Single-Center Experience

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Abstract

Objectives: **Renal transplant is the most appropriate treatment for adult and pediatric patients with end-stage renal failure.**

Materials and Methods: **Fifty-one pediatric kidney transplants were performed in 49 pediatric recipients from a total of 263 kidney recipients at the Gazi University Transplantation Center (Türkiye) between January 2006 and January 2021. We gathered and analyzed data retrospectively from hospital medical records of pediatric transplant recipients.**

Results: **Kidney grafts were obtained from 18 deceased (35%) and 33 living donors (65%). Among 51 pediatric renal transplants, 10 (19.6%) had complications, with 6 early and 4 late complications. Among 6 early complications posttransplant, 5 were surgical complications (9.8%) and 1 (1.9%) was urologic (1.9%), but no vascular complications were seen. Among 5 surgical complications, 3 (5.8%) were lymphocele and 2 were (3.9%) bleeding complications. Among 4 patients with late complications, 2 had renal artery stenosis and 2 had ureter stenosis. Two patients required re-transplantation because of graft loss from BK virus nephropathy and chronic allograft nephropathy. Among 51 pediatric kidney transplants, 15 recipients (29.4%) presented with 27 cases of infection. Twenty-one acute rejection episodes were seen in 14 of 51 pediatric transplant procedures (27.4%), and 4 humoral rejections occurred in 3 of 51 pediatric transplant procedures (5.8%). In addition, 27 renal transplant patients (52.9%) had normal graft functions at median follow-up of 95 months (98.7 ± 57.7; range, 58-233 mo). Twenty-eight of 51 patients (54.9%) lost kidney grafts over a 15-year follow-up. No graft loss or patient deaths occurred because of surgical complications.**

Conclusions: **In analysis of 15 years of experience in pediatric renal transplants, our results were within results of other series. Pediatric renal transplant is a safe procedure in our department, based on patient and graft survivals, with no graft loss from surgical complications.**

Key words: *Kidney transplantation, Pediatric kidney transplantation, Surgical outcome*

Introduction

Renal transplant is the most appropriate treatment for adult and pediatric patients with end-stage renal failure (ESRF). Obstacles in pediatric patients with ERSF include difficulties proper to that age group, hospitalizations, psychosocial effects of dialysis, immature immune system, and elusive donors that match according to body size. Although renal transplant procedures in pediatric patients arrived later than in adult patients, desired success has been achieved despite these difficulties.

The first successful renal transplant was performed in adult patients in the 1950s and about the end of the 1960s for pediatric patients.[1] In Türkiye, the first successful renal transplant in a pediatric patient was performed by Prof. Haberal and colleagues in 1975.[2]

The most important problem in pediatric patients who are on hemodialysis or peritoneal dialysis because of ESRF is growth and development retardation. Long-term dialysis programs can also result in psychosocial problems and unfavorable effects on quality of life. Successful renal transplant at the right time could prevent the occurrence of these negative effects and prevent complications.

Pediatric patients can catch up to normal growth and development with help from optimum

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immunosuppressive treatment after transplant. Data on resumed growth and development supported opportunities for renal transplant in numerous infants and adolescents with ESRF disease until the 1990s. However, peritoneal dialysis was still the preferred treatment choice for newborns and infants with ESRF. With further developments in immunosuppressive drugs, advancements in pediatric intensive care units, and improvements in surgical techniques in the 1990s, renal transplant became optimum for patients of infant age. Pediatric patients can catch up to normal growth and development with help from optimum controlled immunosuppressive treatment after transplant.[1-3]

Materials and Methods

Of 263 total kidney transplant recipients treated at the Gazi University Transplantation Center (Ankara, Türkiye) between January 2006 and January 2021, 51 pediatric kidney transplants were performed in 49 pediatric transplant recipients. We gathered and analyzed data of pediatric transplant recipients retrospectively from hospital medical records.

Patients received standard surgical techniques.[1] Briefly, for infants and small children weighing 20 kg or less (and in some weighing between 20 and 25 kg), we use a midline transperitoneal approach. In larger children, we use a standard curvilinear right or left abdominal extraperitoneal incision. Renal vessel anastomoses are performed to the aorta and vena cava in children weighing 20 kg or less. In children weighing between 20 and 30 kg, we tend to utilize the common iliac artery and vena cava. In children weighing more than 30 kg, we still tend to use the common iliac artery for the arterial anastomosis with adult size kidney unless the child has a well-developed external iliac artery that will provide good arterial flow to the kidney graft. In larger children, a choice between use of the vena cava or iliac veins for the renal vein anastomosis can be made at the time of surgery. In urethral anastomosis, we use Prof. Haberal's "corner saving open loop continuous suture technique" with 5-0 polydioxanone suture with combination with ureteral double J stent since 2006.[4] All recipients take trimethoprim-sulfamethoxazole for prevention of Pneumocystis pneumonia for 3 months after transplant.

Our immunosuppression protocol has been previously published.[1,5] Briefly, calcineurin inhibitors (CNIs) based on triple regimens were given to all recipients. In high-risk patients (high panel reactive antibody, deceased donors, or patients with multiple transplants), interleukin 2 receptor antagonists were used as induction therapy. Prednisolone dose started at 10 to 15 mg/kg and then was tapered to a maintenance dosage of 5 mg/day by 3 months posttransplant and later to every other day at 5 mg/dL in the first year posttransplant. For patients with delayed graft function, antithymocyte globulin as polyclonal antibody was preferred instead of CNI until the graft function returned to an acceptable level (50% decrease of serum creatine levels in 24 hours or creatine level of <3 mg/dL). Although the initial treatment for acute rejection was pulse steroid, polyclonal agents (generally antithymocyte globulin) were used for patients with steroid-resistant rejection.

All procedures adhered to the ethical standards of the institutional and national research committees and the 1964 Helsinki Declaration and its later amendments or comparable ethical standards. The Local Ethical Committee of Gazi University (reference No. E.951182) approved this study.

We used SPSS software version 20 for statistical analyses. We expressed results as mean values ± SD or as median values with ranges. We analyzed relevant variables with descriptive statistics.

Results

Between January 2006 and January 2021, 51 pediatric kidney transplants were performed in 49 recipients (25 female and 26 male recipients) among a total of 263 kidney transplants at the Gazi University Transplantation Center in Ankara. The median age of recipients was 13.4 ± 3.1 years, with age ranging from 4.5 to 17 years. Kidney grafts were obtained from 18 deceased donors (35%) and 33 living donors (65%). Among living donors, 21 were mothers and 12 were fathers. The mean HLA matches among the 51 pediatric transplants was 3.6 ± 2.3.

The etiology of ESRF included reflux nephropathy in 15 of 49 patients (30.6%), lower urinary tract dysfunction in 7 patients (14.3%), glomerulonephritis in 6 patients (12.2%), nephronophthisis in 3 patients (6.1%), amyloidosis in 2 patients (4.1%), nephrolithiasis in 2 patients (4.1%), Henoch-Schoenlein purpura in 2 patients (4.1%), polycystic kidney disease in 1 patient (2.0%), periarteritis nodosa in 1

patient (2.0%), cystinosis in 1 patient (2.0%), and nephritic syndrome in 1 patient (2.0%). In 10 of 51 transplant procedures (19.6%), the cause of ESRF was unknown. Two patients underwent retransplantation because of chronic allograft nephropathy (CAN) and BK nephropathy.

Among 51 pediatric renal transplants, 10 (19.6%) had surgical complications: 6 were early and 4 were late complications. Five of 51 (9.8%) had surgical complications and 1 (1.9%) had an urologic complication, but no vascular complications were observed. Among 5 surgical complications, 3 of 51 (5.8%) had lymphoceles and 2 (3.9%) had bleeding. The smallest infant that we successfully transplanted with good long-term graft survival weighed 4.5 kg at the time of transplant.

All lymphoceles were diagnosed in routine follow-up visits by radiology with ultrasonography, which was confirmed by needle aspiration of the lymphocele content and estimation of the creatinine concentration. One patient with lymphocele complication needed drain placement by interventional radiology; collection did not reoccur, and no further problems were shown. The other 2 lymphoceles resolved spontaneously. Two postsurgical bleeding events were resolved by medical treatment without any surgical approach. One urinary leak detected as an early complication was successfully treated by interventional radiology.

Among the 4 patients with late complications, 2 were renal artery stenosis and 2 were ureter stenosis. Only one renal artery stenosis needed treatment with balloon angioplasty and polytetrafluoroethylene grafting. The other case of renal artery stenosis and the 2 cases of ureter stenosis did not require further intervention because of good kidney graft function.
Of 51 kidney transplant procedures, 27 infections were found in 15 recipients (29.4%). Of the 27 cases of infection, 16 had living donor transplant and 11 had deceased donor transplant. Of 27 cases of infection, 21 occurred within the first-year posttransplant. Cases found during posttransplant follow-up were as follows: BK viremia and/or nephropathy in 12 patients, Epstein-Barr virus in 4 patients, cytomegalovirus in 8 patients (including myocarditis and encephalitis), Zona zoster virus in 1 patient, parvovirus infection in 1 patient, and Brucella virus in 1 patient. In addition, 13 recurrent urinary tract infections occurred in 5 transplant recipients, all of whom had lower urinary dysfunction.

Acute rejection occurred in 21 episodes among 14 of the 51 pediatric transplants (27.5%), with all episodes treated with pulse steroids. Humoral rejection occurred 4 times (7.8%) among 3 patients. Three episodes in 2 of 3 of patients responded favorably to treatment with pulse corticosteroids and plasmapheresis. Unfortunately, 1 patient did not respond to medical treatment.

Of 51 transplant procedures, 28 cases (54.9%) of lost kidney grafts over the 15-year follow-up period. Main reasons for graft loss were CAN in 11 patients, BK virus nephropathy in 6, recurrence of the primary disease in 4, cytomegalovirus in 2, and hyperacute rejection in 1 patient. Two transplant recipients required retransplantation because of CAN and BK nephropathy. Three patients died (disseminated intravascular coagulation, sepsis, sepsis) with functioning graft at median follow-up of 95 months. Twenty-four renal transplant patients (47%) showed normal graft functions at median follow-up of 95 months (98.7 ± 57.7; 58-233 mo). No graft loss or patient deaths occurred because of surgical complications.

Overall graft and patient survival rates at 1, 5, 10, and 15 years for pediatric patients at our transplantation center were 100%, 85%, 78%, and 35% and 100%, 98%, 95%, and 95%, respectively. The same rates for deceased donor transplants were 100%, 95%, 55%, and 28% and 100%, 98%, 95%, and 95%, respectively. For living donor transplants, the rates were 100%, 80%, 78%, and 36% and 100%, 98%, 98%, and 98%, respectively.

Discussion

Up to 1980, renal transplant procedures in adult patients had better results than results for pediatric patients. But nowadays, improvements in surgical techniques, intensive care conditions and immunosuppressive medications led to great achievements in pediatric renal transplantation similar to those shown in adult patients. Hospitalization and treatment concordance of pediatric patients, psychosocial effects of transplant, unwanted effects of immunosuppression drugs, and surgical technical difficulties because of small body size are all factors that make transplant procedures more sophisticated compared with procedures in adults.[2,5] However, improvements in surgical techniques, intensive care conditions, and immunosuppressive medications

have resulted in great achievements in pediatric renal transplant similar to achievements shown in adult patients. In addition, until now, peritoneal dialysis has been accepted as the initial treatment alternative. However, if appropriate conditions are provided, renal transplant could eventually take the place of dialysis in newborns and infant patients with ESRF.

The best transplantation time for pediatric patients is the preemptive time when dialysis has not yet started. Recent studies have shown that preemptive transplant results are superior to patients who are on dialysis.[6] In our group, 12 of 51 (23.5%) had preemptive transplant procedures; we hope that this number will increase in the future.

Arterial stenosis is regarded as the most common vascular complication in pediatric kidney transplants. Arterial stenosis can stem from various factors such as improper suture techniques, trauma to the renal artery, arterial kinking, vascular-type rejection, and atherosclerosis in the arteries of either the donor or recipient.[7] This condition can lead to hypertension and allograft dysfunction and occurs in 5% to 15% of pediatric kidney transplants.[8] Clinicians should suspect arterial stenosis when a patient exhibits new-onset hypertension or a substantial rise in blood pressure compared with previous levels, often alongside proteinuria and/or increased plasma creatinine. The prevalence of transplant renal artery stenosis has increased with the advent of advanced noninvasive diagnostic techniques.[8,9] Management typically involves surgical revision or percutaneous transluminal angioplasty with balloon dilation or the placement of an endovascular stent.

In our series, none of the arterial stenosis were located at the anastomosis site. One patient presented with hypertension, and another showed no clinical signs of stenosis. One patient did not require intervention because the patient had maintained good graft function. However, the patient with hypertension required balloon dilation and stent placement performed by interventional radiology, after which no further treatment was necessary.

Urological complications can pose great risks to both graft and patient survival. Issues such as urinary leakage and obstruction have been shown to carry a considerable mortality rate. However, in our study, no patient deaths were attributed to urological complications. Our results showed a urinary leak rate of 1.9% and stenosis rate of 3.9%, which are favorable when compared with previously published rates of 2.5% to 25%.[10-13] Decreased blood supply to the donor ureter and surgical techniques are the main causes of urologic complications, but other problems such as immunosuppressive drugs, rejection, and BK virus infection are also important, especially as causes of late obstruction. Although low-dose steroid protocols and meticulous operative technique tend to reduce incidence of urological complications, poor ureteral vascularization owing to increased use of expanded criteria donors, namely, older individuals, can increase this rate. As observed in our department, the technique of ureteral anastomosis does not seem to influence the incidence of complications. We have mainly adopted the extravesical Lich-Gregoir technique to the "Haberal corner saving" technique with an antireflux mechanism. Furthermore, our experience has shown that use of double J stent increases anastomoses safety in ureterocystostomy anastomosis. Unless facing a reverse situation, we remove this catheter at 4 weeks posttransplant.[2] Our findings regarding urologic problems were comparable to those in the published literature.[11,12]

Chronic allograft nephropathy (CAN) remains the most common cause of graft loss, as reflected in the literature.[13] In our study group, CAN was the leading cause of graft loss, accounting for 21.5% of cases. Despite substantial advancements in immunosuppression, CAN continues to be the primary reason for graft failure in renal transplant and is responsible for about 40% of renal graft losses. The exact etiology of CAN is not fully understood but appears to be a progressive, time-dependent condition.[13] Factors contributing to CAN are divided into immune and nonimmune categories. Immune factors involve cellular or antibody-mediated responses, leading to acute or chronic rejection.[7] Nonimmune factors include ischemia-reperfusion injury, patient comorbidities (such as hypertension, hyperlipidemia, proteinuria, hyperfiltration, and infections), and CNI nephrotoxicity.[7] There seems to be a synergistic relationship between these risk factors.

In our study group, the mean onset of CAN was at 61.2 ± 44.4 months (median of 55 months; range, 8-163 months). The primary contributing factors in our cohort appeared to be less intensive immunosuppression in the early posttransplant period, particularly in low-risk patients and those who

received organs from living related donors without induction therapy. In addition, lower CNI levels at 1 year post-transplant, often because of patient noncompliance, were a substantial risk factor. These findings suggest that immune-mediated mechanisms play a crucial role in CAN pathogenesis. Inadequate early immunosup-pression may lead to subclinical immune activation, ultimately contributing to chronic allograft dysfunc-tion. Further studies are needed to elucidate the immunological basis of CAN and develop strategies to optimize long-term graft survival.

BK virus infection has been recently added to the transplant field as a major hurtle. The principal treatment for BK virus nephropathy is reduction in immunosuppression. Various strategies, including reduction or discontinuation of the CNI and/or adjuvant agent and changing from mycophenolate mofetil to azathioprine, sirolimus, or leflunomide or from tacrolimus to cyclosporine, have been used.[14] In our clinic, we first decreased immunosuppression and then provided cidofovir for medical treatment of BK virus infection. Two of 6 patients did not respond to medical treatment. Two of 6 had serum and urine BK polymerase chain reaction results that became negative but had intermediated graft function without hemodialysis (glomerular filtration rate of 28 mL/min and 19 mL/min and serum creatinine level of 2.5 mg/dL and 3 mg/dL, respectively) after medical treatment. Two patients were cured of BK infection.

Our results showed overall graft survival over 15 years of 35%. Exiguity of graft loss because of immunological reasons and low infection and nonlymphoproliferative disorder rates versus that shown in the literature showed the efficiency of our immunosuppressive treatment and postoperative follow-up strategy. These results support the idea that the experiences of surgical and anesthesia team and conditions of the intensive care units and wards are proportional with long-term success of pediatric transplant despite difficulties such as small body sizes, small vascular diameter, and surgical manipulations in children.

Despite the favorable outcomes observed in our study, our study had several limitations. First was the relatively small sample size and single-center nature of our analysis, which may limit the generalizability of our findings. Second, the retrospective study design and potential selection bias could influence our results. Variability in immunosuppressive regimens and differences in patient adherence may also contribute to inconsistencies in outcomes. Long-term follow-up beyond 15 years is necessary to assess late complications and overall graft survival more comprehensively. Future multicenter studies with larger cohorts and standardized protocols are needed to validate our findings and optimize pediatric renal transplant strategies.

Conclusions

Our 15-year experience in pediatric renal transplant aligned with outcomes reported in other established series. Our results confirmed that the procedure is both safe and effective, with high patient and graft survival rates and no incidence of graft loss due to surgical complications. These favorable outcomes are attributed to advanced surgical techniques, meticulous perioperative management, and a multidisciplinary team approach. These factors result in pediatric renal transplant at our center being performed at a level comparable to leading transplant centers worldwide.

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