Renal Transplantation in Patients with Lower Urinary Tract Dysfunction: A Single Center Experience from a Developing Country

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Abstract

Objectives: Historically, patients with lower urinary tract dysfunction (LUTD) were considered poor candidates for renal transplantation (RT). We aimed to review our experience with this procedure for its safety and efficacy.

Methods: We reviewed the case records of patients with LUTD who underwent RT at our center. Graft and patient survival were analyzed.

Results: Out of 2053 RTs, 26 (1.2%) patients had LUTD as the primary cause of end-stage renal disease (ESRD). All patients underwent cystourethroscopy prior to transplantation, had abnormal bladders and all underwent bladder augmentation. Only 16 (81.5%) patients had urodynamic (UDN) evaluation prior to transplantation. Pretransplantation augmentation cystoplasty (AC) was performed in 24 (92.3%) patients, and post-RT in two (7.7%). Mitrofanoff channel was made in 25 (96.1%) patients using appendix in 14 (56%) patients and native ureter in 11 (44%). Double-J (DJ) stents were placed in all patients peroperatively. All patients developed 156 episodes of urinary tract infections (UTIs), with an average of 6 UTIs/patient. All patients except three are maintaining their graft function within acceptable limits. We observed 100% patient and graft survival rates in this series.

Conclusions: In conclusion, RT combined with AC is a feasible option for patients with LUTD with good results in the medium term and should be explored in selected patients.

Keywords: Augmentation cystoplasty; Graft outcome; Lower urinary tract dysfunction; Renal transplantation; Urodynamics

Abbreviations: BOO: Bladder Outflow Obstruction; CISC: Clean Intermittent Self Catheterization; DJ: Double J; ESRD: End Stage Renal Disease; LUT: Lower Urinary Tract; LUTD: Lower Urinary Tract Dysfunction; PUV: Posterior Urethral Valves; RT: Renal Transplantation; UTI: Urinary Tract Infection; VUR: Vesicoureteral Reflux

Introduction

Renal transplantation (RT) is considered the treatment of choice for patients with end-stage renal disease (ESRD). There are many causes of ESRD, out of which lower urinary tract dysfunction (LUTD) contributes to approximately 7-20% of cases in children and adults [1,2]. Traditionally, patients with LUTD have been considered poor candidates for RT [3-5]. However, innovative techniques of diagnosis and reconstructive surgery, together with better understanding of the physiological aspects of RTs, excellence in surgical skills, diagnostic tools and the introduction of novel immunosuppressive regimens and antibiotics have led to a better outcome of RTs in LUTD [6-8]. Excellent patient and graft survival rates have been reported in these patient cohorts in different studies. Most of these studies have been reported from centers in the developed world with very few reports from developing countries [5-8]. However, to the best of our knowledge, no such experience with a fair number of patients is available in the literature from Pakistan.

In this study, we analyzed the safety and outcome of RTs in patients with LUTD who underwent bladder augmentation surgery prior to or after RT.

Materials and Methods

From 1985 to 2011, a total of 3448 RTs were performed at our center. Case records of these patients were analyzed retrospectively for identifying RTs in LUTD with bladder augmentation procedures. A total of 26 such cases were identified who were transplanted for LUTD. First transplant for this indication was performed in 2005. Their case files were scrutinized in detail. The specific causes of renal failure for the patients who had LUTD were noted. Pretransplant urodynamic (UDN) findings and any surgical procedures done were recorded. Peroperative and post-transplant complications were also recorded. Written informed consent was obtained from patients or parents prior to performance of surgical procedures. Standard techniques were used for the RT and the augmentation cystoplasty (AC) in all patients. They all were transplanted kidneys from living-related donors. Standard triple immunosuppressive therapy was used in standard dosages, as described in our previous study [9]. Briefly, the immunosuppressive regimen used at our center comprised of a combination of calcineurin inhibitors (CNIs), anti-proliferative agents and steroids. CNIs included cyclosporine in a dose of 6 mg/kg/day tapered to 3 mg/kg/day by the end of 6 months. Tacrolimus was used in high immunological risk groups. Anti-proliferative agents used included azathioprine in a dose of 1.5-2 mg/kg/day for standard risk patients and mycophenolate mofetil (MMF) in high risk patients. Steroids were used in a dose of 0.5 mg/kg/day tapered to 7.5-10 mg/day by the end of three months. Prior to 1991, azathioprine was used in combination with steroids. One patient with 0 haplotype 1 antigen match was induced with

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an antithymocyte globulin (ATG) and six children less than 12 years were induced with interleukin-2 receptor blocker, basiliximab. Renal graft biopsies were performed and interpreted according to Banff 97 classification as described earlier [9]. The patterns of serum creatinine at defined time intervals were analyzed. Episodes of urinary tract infection (UTI) with causative organisms were analyzed. UTI was defined as midstream urine with ≥ 10^5 organisms/ml of a single organism irrespective of symptoms [10,11]. Any rejection episodes and the treatment with antithymocyte globulin (ATG) were also recorded. Peroperative placement of double-J (DJ) stent and clean intermittent self-catheterization (CISC) were also recorded. Graft and patient survival were analyzed at last follow-up. A matched control population of 28 non-LUTD renal transplant recipients were analyzed was graft survival. Graft failure was defined as return to dialysis.

**Statistical Methods**

Statistical analysis was performed by SPSS version 10.0 (SPSS Inc., Chicago, IL, USA). Data were presented as median ± interquartile range (IQR) for continuous variables and numbers (percentages) for categorial variables.

**Results**

Out of 3448 RTs, 2053 were performed during the last seven years of study (2005-2011). Among the later, 26 (1.2%) patients underwent RT with LUTD. All of them had undergone bladder augmentation procedures. The demographic characteristics of these patients and specific causes of renal failure (Table 1). The median age of recipients was 21 (IQR: 15-27) years and of donors, 35 (IQR: 25-48) years. All patients were transplanted kidneys from live related donors. All the patients included in this study underwent cystourethroscopy prior to transplantation, and all showed abnormal bladders (thick walled, trabeculations, small capacity, bladder outlet obstruction (BOO)). Only 16 (61.5%) patients had UDN studies prior to RTs, the findings of which are shown in Table 1. AC with ileal patch was carried out before RTs in 24 (92.3%) patients. In two (7.7%) patients, the procedure was performed after transplantation. Mitrofanoff channel was made in 25 (96.1%) patients using appendix in 14 (56%) patients while native ileum in 11 (44%) patients. The duration between RTs and cystoplasty is shown in Table 1. DJ stents were placed in 22 patient’s preoperatively. Postoperative complications of urinary fistula, ureteric obstruction, anastomotic leakage and lymphocele, one each, were observed in 4 (15.3%) patients.

The pattern of serum creatinine over time for two years and at the last follow-up and the best serum creatinine values are shown in Table 2. The median lowest serum creatinine was 0.9 (0.8 - 0.99) mg/dl and was achieved over a median of 6 (5-8) days. The median serum creatinine at last follow-up was 1.48 (1.21-1.92) mg/dl. Regarding infectious complications, all patients developed UTIs with a total number of 28 UTIs, and an average of 6 UTIs/patient. Asymptomatic UTIs were seen in 23 (88.46%) patients with total episodes of 156, and an average of 6 UTIs/patient. Symptomatic UTIs were induced with interleukin-2 receptor blocker, basiliximab. Renal graft biopsies were performed and interpreted according to Banff 97 classification as described earlier [9]. The patterns of serum creatinine at defined time intervals were analyzed. Episodes of urinary tract infection (UTI) with causative organisms were analyzed. UTI was defined as midstream urine with ≥ 10^5 organisms/ml of a single organism irrespective of symptoms [10,11]. Any rejection episodes and the treatment with antithymocyte globulin (ATG) were also recorded. Peroperative placement of double-J (DJ) stent and clean intermittent self-catheterization (CISC) were also recorded. Graft and patient survival were analyzed at last follow-up. A matched control population of 28 non-LUTD renal transplant recipients were analyzed was graft survival. Graft failure was defined as return to dialysis.

**Discussion**

Patients with congenital or acquired lower urinary tract (LUT) complications, all patients developed UTIs with a total number of 28 UTIs, and an average of 6 UTIs/patient. Asymptomatic UTIs were seen in 23 (88.46%) patients with total episodes of 156, and an average of 6 UTIs/patient. Symptomatic UTIs were induced with interleukin-2 receptor blocker, basiliximab. Renal graft biopsies were performed and interpreted according to Banff 97 classification as described earlier [9]. The patterns of serum creatinine at defined time intervals were analyzed. Episodes of urinary tract infection (UTI) with causative organisms were analyzed. UTI was defined as midstream urine with ≥ 10^5 organisms/ml of a single organism irrespective of symptoms [10,11]. Any rejection episodes and the treatment with antithymocyte globulin (ATG) were also recorded. Peroperative placement of double-J (DJ) stent and clean intermittent self-catheterization (CISC) were also recorded. Graft and patient survival were analyzed at last follow-up. A matched control population of 28 non-LUTD renal transplant recipients were analyzed was graft survival. Graft failure was defined as return to dialysis.

**Table 1:** Demographic and clinicopathological findings in 26 patients with abnormal lower urinary tracts who were transplanted kidneys at our centre.

| Causes of renal failure                  |
|-----------------------------------------|
| Neurogenic bladder                      |
| Posterior urethral valves               |
| Vesciculo-urethral reflux               |
| Bladder outlet obstruction              |
| Genito-urinary tuberculosis             |

**Table 2:** Serum creatinine values in mg/dl

| Serum creatinine values in mg/dl | Median (IQR) | Range |
|----------------------------------|--------------|-------|
| Best serum creatinine           | 0.9 (0.8-0.99) | 0.28 - 2.44 |
| Normalization of serum creatinine in days | 6 (5-8) | 4 - 23 |
| Serum creatinine at 4 weeks     | 1.0 (0.89-1.28) | 0.35 - 3.86 |
| at 3 months                      | 1.19 (0.91-1.48) | 0.38 - 4.36 |
| at 6 months                      | 1.1 (0.94-1.56) | 0.45 - 6.57 |
| at 12 months                     | 1.2 (1.11-1.53) | 0.50 - 3.10 |
| at 24 months                     | 1.6 (1.07-1.9) | 0.56 - 2.5 |
| at last follow-up                | 1.48 (1.21-1.92) | 0.70-6.51 |
| Duration of follow-up in years   | 3.09 (2.04-3.5) | 0.42-10.23 |

**Discussion**

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disease frequently develop ESRD requiring renal replacement therapy. Abnormal LUTs of these patients should be managed surgically or sometimes conservatively to preserve normal renal functions. However, patients developing ESRD are scheduled for RTs and augmented procedures to make the reservoir more optimal to sustain the precious renal graft function [3,4].

We herein report our experience with 26 patients who underwent RT for ESRD secondary to LUTD, out of which 24 (92.3%) patients had AC before RTs. The advantages of pretransplantation AC include avoidance of the interaction of the augmentation surgery with immunosuppressive drugs and the facilitation of antireflux mechanisms [5]. Contrary to this, Mc Inerney et al. advocate the policy to perform cystoplasty after RT to avoid dry reservoir, interference with its vascular pedicle at the time of ureteric implantation and to allow renal functions to stabilize [6].

The timing of cystoplasty before RT varies in the literature from 10-12 weeks to 5 years [5,7]. We strongly advocate pretransplantation AC at our center. In this series, we performed 24 AC before RT and the time period between AC and RT was >6 months in the majority of cases (62.5%) (Table 1). The main reason for this somewhat extended time interval was lack of interest for organ donation on the part of the family. In this part of the world there is no deceased donor programme and there are multiple social issues which hinder kidney donation among families.

To achieve the most optimal results in RT especially in LUTD patients, pretransplant LUT UDN studies should be performed with cystoscopy so that any correctable or palliative surgical procedure could be offered to these patients. We performed UDN in 16 patients before RT. The majority of these patients (56.2%) had low capacity and high pressure urinary bladders and 4 patients had low capacity and low pressure bladders (Table 1). All these patients were managed with pre-RT AC. Later, the majority of these patients had LUT UDN in post-RT phase, which showed an adequate volume and pressure in the LUT, which was in concordance with an earlier study [8]. This low pressure and adequate volume of LUT provides an environment for the allograft to function in an optimal manner.

Table 3: Urinary tract infection (UTI) episodes in all 26 patients and the causative organisms.

| Total episodes of UTIs | Mean UTIs/patient | Median (interquartile range) | Range of UTIs/patient |
|------------------------|------------------|-----------------------------|----------------------|
| 156                    | 6                | 5(3-8)                      | 1-19                 |

Micro-organisms causing UTI:

- E. Coli: 74 (47.3)
- Klebsiella: 35 (22.4)
- Pseudomonas: 17 (10.9)
- Morganella: 10 (6.4)
- Acinetobacter: 8 (5.1)
- Enterococcus: 8 (5.1)
- Others: 7 (4.4)

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In conclusion, our results show that AC is a safe and feasible procedure in patients with LUTD and RTs can be done in these patients under a multidisciplinary care with excellent patient and graft survival in the medium term.

References

1. Ali-El-Dein B, Abol-Enein H, El-Husseini A, Osman Y, Shehab El-Din AB, et al. (2004) Renal transplantation in children with abnormal lower urinary tract. Transplant Proc 36: 2968-2973.
2. Koo HP, Bunchman TE, Flynn JT, Punch JD, Schwartz AG, et al. (1999) Renal Transplantation in children with severe lower urinary tract dysfunction. J Urol 161:240-245.
Kelly WD, Merkel FK, Markland C (1966) Ileal urinary diversion in conjunction with renal homotransplantation. Lancet 1:222-226.

Marshall FF, Smolev JK, Spees EK, Jeffs RD, Burdick JF (1982) The urological evaluation and management of patients with congenital lower urinary tract anomalies prior to renal transplantation. J Urol 127: 1078-1081.

Riedmiller H, Gerharz EW, Köhl U, Weingärtner K (2000) Continent urinary diversion in preparation for renal transplantation: a staged approach. Transplantation 70: 1713-1717.

McInerney PD, Picramenos D, Koffman CG, Mundy AR (1995) Is cystoplasty a safe alternative to urinary diversion in patients requiring renal transplantation? Eur Urol 27: 117-120.

Marechal JM, Sanseverino R, Gelet A, Martín X, Salas M, et al. (1990) Continent cutaneous ileostomy (Kock pouch) prior to renal transplantation. Br J Urol 65: 317-321.

Nahas WC, Lucon M, Mazzucchi E, Antonopoulos IM, Plovesan AC, et al. (2004) Clinical and urodynamic evaluation after ureterocystoplasty and kidney transplantation. J Urol 171: 1428-1431.

Kazi JI, Mubarak M (2012) Biopsy findings in renal allograft dysfunction in a live related renal transplant program. J Transplant Tech Res 2:108.

Elkhilli IM, Kekli AB, Zaak AS, Salem EL (2010) Urinary tract infection in renal transplant recipients. Arab J Nephrol Transplant 3:53-55.

Iqbal T, Naqvi R, Akhter SF (2010) Frequency of urinary tract infection in renal transplant recipients and effect on graft function. J Pak Med Assoc 60: 826-829.

Rivera-Sanchez R, Delgado-Ochoa D, Flores-Paz RR, Garcia-Jiménez EE, Espinosa-Hernández R, et al. (2010) Prospective study of urinary tract infection surveillance after kidney transplantation. BMC Infect Dis 10: 245.

Golebiewska J, Debeka SA, Komarnicka J, Samet A, Rutkowski B (2011) Urinary tract infections in renal transplant recipients. Transplant Proc 43:2985-2990.

Rice JC, Peng T, Kuo YF, Pandyala S, Simmons L, et al. (2006) Renal allograft injury is associated with urinary tract infection caused by Escherichia coli bearing adherence factors. Am J Transplant 6: 2375-2378.

Fayek SA, Keenan J, Harirlian A, Cooper M, Barth RN, et al. (2012) Ureteral stents are associated with reduced risk of ureteral complications after kidney transplantation: a large single-center experience. Transplantation 93:304-308.

Ranganathan M, Akker M, Ilham MA, Chavez R, Kumar N, et al. (2009) Infective complications associated with ureteral stents in renal transplant recipients. Transplant Proc 41: 162-164.

Flood HD, Malhotra SJ, O’Connell HE, Ritchey MJ, Bloom DA, et al. (1995) Long-term results and complications using augmentation cystoplasty in reconstructive urology. Neurourol Urodyn 14:297-309.

Gill IS, Hayes JM, Hodge EE, Novick AC (1992) Clean intermittent catheterization and urinary diversion in the management of renal transplant recipients with lower urinary tract dysfunction. J Urol148: 1397-1400.

Akoh JA, Choon TC, Akyol MA, Kyle K, Briggs JD (1999) Outcome of renal transplantation in patients with lower urinary tract abnormality. J R Coll Surg Edinb 44: 78-81.

Mitra S, Alangaden GJ (2011) Recurrent urinary tract infections in kidney transplant recipients. Curr Infect Dis Rep 13:579-1587.

Moradi M, Abbasi M, Moradi A, Boskabadi A, Jalali A (2005) Effect of antibiotic therapy on asymptomatic bacteriuria in kidney transplant recipients. Urol J 2: 32-35.

Pereira DA, Barroso U Jr, Machado P, Pestana JO, Rosito TE, et al. (2008) Effects of urinary tract infection in patients with bladder augmentation and kidney transplantation. J Urol 180: 2607-2610.

Blanco M, Medina J, Pamplona M, Miranda N, Gonzalez E, et al. (2009) Outcome of renal transplantation in adult patients with augmented bladders. Transplant Proc 41: 2382-2384.

Bilginer Y, Akki FT, Topaloglu R, Tekgul S, Demirkaya E, et al. (2008) Renal transplantation in children with lower urinary tract dysfunction of different origin: a single-center experience. Transplant Proc 40: 85-86.

Otukesh H, Sharifian M, Simfroosh N, Basiri A, Hoseini R, et al. (2005) Outcome of renal transplantation in children with lower urinary tract abnormality. Transplant Proc 37: 3071-3074.

Taghizadeh AK, Desai D, Ledermann SE, Shroff R, Marks SD, et al. (2007) Renal transplantation or bladder augmentation first? A comparison of complications and outcomes in children. BJU Int 100: 1365-1370.