

Renal transplantation in patients with an augmentation cystoplasty

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Background: The effects of renal transplantation in patients with augmentation cystoplasty are still controversial. We retrospectively analyzed nine patients who underwent renal transplantation after augmentation cystoplasty.

Methods: A total of nine patients who underwent augmentation cystoplasty prior to renal transplantation between January 1990 and May 2020 were reviewed. Basic information on augmentation cystoplasty, transplant procedures, and long-term outcomes of renal transplantation were analyzed.

Results: The bowel segments utilized for augmentation cystoplasty were the stomach in two patients (one patient needed revision using the ileum), the ileum in four patients, the ileocolic pouch in one patient, the sigmoid in one patient, and the ureter in one patient. All the cystoplasties were performed prior to renal transplantation. The mean follow-up period after transplantation was 161 months (range, 2–341 months). Two patients had an episode of acute rejection each; however, their graft functions were well-maintained. Five patients had recurrent urinary tract infections, and three of these patients progressed to allograft failure. One patient died from bladder cancer with a functioning graft. Five of nine patients showed well-maintained graft function.

Conclusions: Renal transplantation after bladder augmentation surgery is a major operation requiring a high level of surgical skill. Based on our long-term experiences, we recommend diligent postoperative monitoring for urinary tract infections, optimal catheter use, and use of appropriate antibiotic prophylaxis to avoid severe complications.

Keywords: Kidney transplantation; Bladder augmentation; Cystoplasty

INTRODUCTION

About 15% of patients with end-stage renal disease (ESRD) have structural urinary tract abnormalities that may lead to lower urinary tract dysfunction [1,2]. Neurovesical dysfunction is one of the important causes of ESRD, and accounts for 20%–30% of ESRD in pediatric patients [3]. For the last several decades, there has been controversy about the safety of patients with augmentation for lower urinary tract

dysfunction receiving renal transplantation because of the possibility of urinary tract infections (UTI) that can develop in immunosuppressed patients, leading to pyelonephritis and eventually graft loss. With the recent improvements in the management of lower urinary tract dysfunction, the outcomes of renal transplantation in these patients have improved [3].

It is now well known that in patients with bladders having a small volume and poorly compliance, bladder aug-

HIGHLIGHTS

- Renal transplantation after bladder augmentation surgery is a major operation requiring a high level of surgical skill.
- Based on our long-term experiences, we recommended diligent postoperative monitoring for urinary tract infection, optimal catheter use, and use of appropriate antibiotic prophylaxis to avoid severe complications.

mentation surgery can lower bladder pressure, and protect the upper urinary tract and post-transplant allograft function [4]. We also published a case series with good mid-term outcomes [5,6]. However, there have been only a few reports on the long-term outcomes of kidney transplantation in patients with a history of augmentation cystoplasty. We analyzed our single-center experience in patients with renal transplantation after bladder augmentation and their long-term outcomes.

METHODS

This study was approved by the Institutional Review Board of Seoul National University Hospital (IRB No. 2009-102-1157) and was conducted in accordance with the Declaration of Helsinki. The requirement for obtaining informed consent was waived by the Board.

Patients who received renal transplantation and had previously undergone augmentation cystoplasty or urinary diversion between January 1990 and May 2020 were retrospectively analyzed (Table 1). Nine patients were included in this study. Eight patients were male. The mean age at bladder augmentation was 17 years (range, 9–35 years). The average interval from bladder augmentation surgery to transplantation was 71 months (range, 2–240 months). The mean age at transplantation was 23 years (range, 10–51 years). The cause of ESRD was neurogenic bladder with myelomeningocele in six cases, renal tuberculosis in two cases, and bilateral reflux disease in one case. All patients could not self-void and required clean intermittent self-catheterization (CISC). Except for two patients, all patients underwent a primary operation to prevent vesicoureteral reflux, such as nephrostomy or ureteroneocystostomy, before the cystoplasty. However, all patients progressed to ESRD.

Table 1. Basic information of pre-transplantation

Variable	Patient no.								
	1	2	3	4	5	6	7	8	9
Sex	F	F	F	F	F	F	M	F	F
Cause of ESRD	Renal TBc	NB	NB	NB	NB	Renal TBc	Bilateral VUR	NB	NB
	Bilateral PCKD	MMC	MMC	MMC	MMC			MMC	MMC
Pre-cystoplasty intervention	PCN nephrectomy	-	UNC	Ureteroureterostomy	UNC	Nephrostomy	UNC	-	UNC
Cystoplasty									
Age at cystoplasty (yr)	33	13	10	14, 23	19	35	9	9	10
Source of reconstruction	Ileal	Stomach	Ileal	Stomach, ileal	Sigmoid	Ileocolic pouch	Ureter	Ileal	Ileal
Ureter implantation site	Conduit	Stomach	Native bladder	Native bladder	Sigmoid	Native bladder	Native bladder	Native bladder	Native bladder
Appendicovesicostomy (Mitrofanoff)	-	-	-	+	-	-	-	+	-
VUR	-	-	-	-	-	+	+	-	+
Bladder capacity (mL)	NA	300	130	NA	400	400	NA	100	190
Interval to transplant (mo)	2	2	3	143, 34	5	197	34	16	240
Mode of dialysis	HD	HD	PD	HD	HD	HD	-	HD	HD
Duration of dialysis (yr)	0.1	1.2	3.5	11	8	2	-	4	8

ESRD, end-stage renal disease; TBc, tuberculosis; PCKD, polycystic kidney disease; NB, neurogenic bladder; MMC, meningocele; VUR, vesicoureteral reflux; PCN, percutaneous nephrostomy; UNC, ureteroneocystostomy; NA, not applicable; HD, hemodialysis; PD, peritoneal dialysis.

Table 2. Transplant outcomes

Variable	1	2	3	4	5	6	7	8	9
Patient no.									
Transplantation									
Age at transplantation (yr)	33	13	10	26	20	51	11	10	30
Donor type	LD	LD	LD	DD	LD	DD	LD	LD	LD
Donor age (yr)	60	41	42	16	49	65	38	42	57
HLA mismatch	3	3	2	0	1	5	3	2	3
Immunosuppression	CsA, Pd, (+MMF)	CsA, Pd, (-AZA)	TAC, Pd, MMF	TAC, Pd, MMF	TAC, Pd, MMF	TAC, Pd, MMF	TAC, Pd, MMF	TAC, Pd, MMF	TAC, Pd, MMF
Outcome									
Follow-up (mo)	341	259	185	175	148	148	126	49	2
Serum creatinine (mg/dL)	5.64	0.78	6.78	0.72	0.95	1.38	1.36	5.39	1.06
Acute rejection	No	No	No	No	No	Yes	No	Yes	No
Admission for febrile UTI	3	3	3	4	0	0	0	5	0
Pathogens (>10 ⁵ CFU in urine)	<i>Escherichia coli</i> , <i>Pseudomonas aeruginosa</i>	<i>Klebsiella pneumoniae</i>	<i>E. coli</i> , <i>E. aerogenes</i>	<i>K. pneumoniae</i> , <i>Enterococcus Faecalis</i>	None	None	None	<i>E. coli</i> , <i>K. pneumoniae</i> , <i>Proteus penneri</i>	None
Graft failure	Yes	No	Yes	No	No	No	No	Yes	No
Graft survival time (mo)	302	259	107	175	148	148	126	35	2

Borderline change on protocol biopsy without renal dysfunction.

LD, living donor; DD, deceased donor; HLA, human leukocyte antigen; CsA, cyclosporine A; Pd, prednisolone; MMF, mycophenolate mofetil; AZA, azathioprine; TAC, tacrolimus; UTI, urinary tract infection; CFU, colony-forming unit.

RESULTS

Cystoplasty

Urological surgery for urinary bladder dysfunction was performed before renal transplantation. Four patients underwent cystoplasty using the ileum, two patient using the stomach, and the others using the ileocolic pouch and ureter. One patient underwent revision cystoplasty using the ileum because of the formation of a ureterovaginal fistula 8 years after the first operation using stomach. Vesico-ureteral reflux progressed in three patients. The bladder capacity increased to 100–400 mL after cystoplasty (Table 1).

Renal Transplantation

Renal transplantation was performed 71.3 ± 95.2 months after cystoplasty. Eight patients received dialysis prior to transplantation for 4.7 ± 3.9 years. Only one patient underwent pre-emptive transplantation. The baseline characteristics are summarized in Table 2. The mean age at renal transplantation was 23 years. Renal transplantation from living donors was performed in seven patients and from deceased donors in two patients. The mean number of HLA mismatches was 2.8, with types A, B, and DR. The immunosuppression regimen was cyclosporine-based in two patients, and a triple immunosuppressive regimen consisting of tacrolimus, mycophenolate mofetil or mycophenolic acid, and steroid in seven patients. During transplantation, ureter implantation was performed into the native bladder in six patients, the ileal conduit in one patient, and the bowel used for cystoplasty in two patients.

Complications and Clinical Prognosis

The transplant-related outcomes are summarized in Table 2. The mean follow-up period was 161 months (range, 2–341 months). Five of the nine patients had recurrent UTI that presented with fever and chills, required admission and treatment with intravenous antibiotics. The minimum number of times of admissions was >3 . Urine culture tests were performed for all hospitalized UTI patients. The causative bacteria varied, including *Escherichia coli*, *Klebsiella pneumoniae*, *Pseudomonas aeruginosa*, and *Enterococcus faecalis*.

Among these patients with recurrent UTIs, three patients progressed to graft failure. One patient underwent allograft removal because of recurrent perigraft abscesses. After allograft removal, the biopsy showed the presence of adenocarcinoma of small bowel origin in the ileal conduit. She received two courses of chemotherapy;

however, she died of pneumonia. Two other patients progressed to allograft failure and restarted hemodialysis. One patient sustained a functioning kidney graft; however, he died due to metastasized bladder cancer. Two patients had an episode of acute rejection; however, they recovered successfully with steroid pulse therapy. Six out of nine patients maintained graft function with mean post-transplant serum creatinine levels of 1.0 mL/dL (range, 0.72–1.36 mL/dL) at the last follow-up.

DISCUSSION

The issue of renal transplantation after bladder augmentation surgery has been controversial. Some reports have shown that these patients have increased occurrences of post-transplant complications such as urinary leakage, ureteral stenosis, recurrent UTI, and urinary calculi [7-9]. These complications have been thought to affect the progression of allograft failure.

However, in a recent study, there were no significant differences in urological complication rates after renal transplantation between patients who received bladder augmentation surgery and patients who had not received bladder augmentation surgery [10-14]. The location of ureter implantation during renal transplantation is an important issue. According to some reports, ureteral stenosis could progress more frequently when the allograft ureter was not implanted in the native bladder [15,16]. In our study, the ureter was implanted into the native bladder in six out of nine patients, and there were no differences in ureteral stenosis according to the ureteral implantation site. In patients who undergo kidney transplantation after bladder augmentation surgery, the conventional technique recommends that the transplanted ureter be implanted into the native bladder portion [17,18]. Ureter implantation into the gastrointestinal segment of the enterocystoplasty is a lesser known technique with few reported outcomes. Tan and Tiong [19] reported that implanting the donor ureter into the gastrointestinal segment of the enterocystoplasty appears to be a safe option. In our study, we implanted the ureter into sites where anti-reflux methods could be performed. The ureter implantation was performed into the ileal conduit, stomach, and sigmoid colon in each of the three patients, respectively, and into the native bladder in six patients. Graft function was not associated with the ureter implantation site. Therefore, how the

ureter is implanted is a much more important issue than where the ureter is implanted with respect to the patient's clinical results.

Recurrent UTIs are known to deteriorate allograft function, and some reports have suggested that post-renal transplant patients with recurrent UTIs tend to have worse graft function. However, their allograft survival rate does not differ from that of the general transplant population [10,20-22]. In our study, however, there were five patients who had recurrent UTIs, and three of them progressed to allograft failure. All patients had recurrent episodes of UTI and were hospitalized for related infections. Therefore, the long-term transplant outcome may depend on the presence of recurrent UTIs. Rigamonti et al. [2] emphasized the use of prophylactic antibiotics on a long-term basis to help reduce infection rates. Their standard practice was to provide long-term antibiotics in all patients with bladder dysfunction following transplantation, for at least 6 months. Therefore, it is necessary to carefully monitor for urinary infection, use antibiotic prophylaxis, and aggressively treat UTIs in these patients. Providing thorough education about pre- and post-transplant CISC is also important.

Several studies have demonstrated that there are no significant differences in graft survival between patients who underwent bladder augmentation surgery and those who did not [10,15,16,23]. Basiri et al. [15] found significant differences in allograft failure between the bladder augmentation group and the control group ($P=0.03$); however, these differences were due to a higher incidence of acute and chronic rejection in the augmented group than in the control group (41% vs. 33% and 50% vs. 29%, respectively) [15]. Proper immunosuppression, in addition to regular surveillance for urinary tract infection, is important in kidney transplant recipients with a history of bladder augmentation.

This study has several limitations. First, this was a small sample-sized study based on a single-center experience. Second, this was a retrospective, simple case review. Further multicenter studies should be conducted to draw firm conclusions on long-term outcomes of renal transplantations in patients with bladder augmentation cystoplasty. In conclusion, renal transplantation after bladder augmentation cystoplasty in ESRD patients with lower urinary tract dysfunction is considered relatively safe. Ureter implantation with an anti-reflux mechanism is an important surgical technique in these patients. Recurrent UTIs could be the major contributing factor toward graft failure. Therefore, CISC, continuous education on the concept of

thorough hygiene, and close monitoring of UTIs should be strengthened.

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Conflict of Interest

Sangil Min is an editorial board member of the journal but did not involve in the peer reviewer selection, evaluation, or decision process of this article. No other potential conflicts of interest relevant to this article were reported.

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