

The impact of prophylactic ureteral stenting during kidney transplantation on postoperative surgical outcomes

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Background: The aim of this study was to evaluate the safety and feasibility of prophylactic ureteric stenting during kidney transplantation (KT).

Methods: The authors retrospectively reviewed patients who underwent KT between June 2016 and June 2019. The prophylactic ureteral stenting group (double-J [DJ]) and no-stent group (no-DJ) were compared with respect to the clinical data and surgical outcomes.

Results: A total of 42 patients underwent KT; 17 patients were classified into the DJ group and 25 patients into the no-DJ group. Antithymocyte globulin induction and donor-specific antibody positivity were significantly higher in the DJ group. There were no significant differences between the groups in terms of symptomatic urinary tract infection (UTI). The time to postoperative UTI was significantly shorter in the DJ group than in the no-DJ group (33.5±7.8 vs. 105.3±71.6 days, P=0.013). The development of postoperative BK viremia was significantly higher in the no-DJ group (0.0% vs. 16.0%, P=0.035). Urologic complications were significantly higher in the no-DJ group (0.0% vs. 16.0%, P=0.035). In the no-DJ group, urologic complications occurred in four patients: ureteroneocystostomy stenosis in three patients and ureteroneocystostomy leakage in one patient. Percutaneous ureteral interventions were performed for all patients using percutaneous nephrostomy and reno-uretero-vesical stenting. However, there were no postoperative urologic complications in the DJ group.

Conclusions: Prophylactic ureteric stenting during KT may be safe and feasible without significantly increasing the incidence of UTI and BK viremia. Additionally, prophylactic ureteric stenting may reduce urologic complications after KT.

Keywords: Ureter; Stents; Postoperative complication; Kidney transplantation; Urinary tract infection

INTRODUCTION

Urologic complications after kidney transplantation (KT) have gradually decreased in recent years owing to advances in surgical techniques and increased surgical experi-

ence. The incidence of urologic complications after KT has been found to vary between 0.22% and 14.1% [1-3]. The widespread adoption of extravesical anastomosis appears to have lowered the urologic complication rates below 5% while being a technically easier and faster anastomosis

HIGHLIGHTS

- Prophylactic ureteric stenting during kidney transplantation (KT) may be safe and feasible without significant increasing incidence of urinary tract infection and BK viremia.
- Prophylactic ureteric stenting may reduce the urinary complications after KT.

to perform. A previous study suggested that the urologic complication rates could be in the 2%–3% range with routine stent use [3]. However, urological complications are still associated with high morbidity and mortality [4]. Therefore, a number of centers have carried out prophylactic ureteric stenting during KT, with the aim of reducing the risk of urological complications [5].

Ureteral stents have a protective role in reducing urologic complications after KT. The benefits of a stented anastomosis include continuous decompression of the ureter to avoid anastomotic tension, maintenance of the ureter in a more linear alignment to avoid kinking, and protection from ureteral narrowing or postoperative luminal obstruction due to edema or external compression [3,6]. In fact, the use of double-J (DJ) stents with ureteroneocystostomy reduced the rate of major urologic complications to nearly 2% to 5% [2,7]. However, the stents can migrate, cause dysuria, and may increase the risk of developing urinary tract infection (UTI) [8-10]. Moreover, there have also been recent reports that the ureteral stent placement during KT is a risk factor for BK viremia, BK viremia, and BK virus nephropathy [10-13]. Thus, the role of stents in KT remains controversial in both retrospective studies and randomized trials. Thus, the aim of this study was to evaluate the safety and feasibility of prophylactic ureteral stenting during KT.

METHODS

We conducted this study in compliance with the principles of the Declaration of Helsinki. This study was performed after receiving approval from the Institutional Review Board of the National Health Insurance Service Ilsan Hospital (IRB No. NHIMC 2020-03-006). Requirement of informed consent was waived by the board.

We retrospectively reviewed patients who underwent KT between June 2016 and June 2019. Patients who underwent living donor and deceased donor KT were included. The patients were divided into two groups according to ureteral DJ stenting during KT. The prophylactic ureteral stenting group (DJ) and no-stent group (no-DJ) were compared with respect to clinical data and surgical outcomes. Delayed graft function (DGF) was defined as the need for dialysis during the first posttransplant week.

Complications related to the ureteric stent were defined as pain requiring early removal, visible hematuria requiring catheterization with or without irrigation, migration confirmed on ultrasound or radiography, fragmentation, and UTI within 3 months of KT. Symptomatic UTI was defined as simple cystitis and complicated UTI. Simple cystitis was defined as having significant growth of uropathogen in urine culture (>10 WBC/mm³ and $>10^3$ CFU/mL uropathogen) and lower urinary symptoms such as dysuria, frequency, or urgency, but no systemic symptoms such as fever, allograft pain, hemodynamic compromise, or indwelling device [14].

Complicated UTI was defined as having significant growth of uropathogen (>10 WBC/mm³ and $>10^4$ CFU/mL uropathogen) and at least one of the following: fever, chills, malaise, hemodynamic instability, leukocytosis, and either bacteremia (with the same organism as found in the urine) or signs of allograft or native kidney involvement (pain over the allograft or the costovertebral angles). Time to postoperative UTI was defined as the amount of time (in days) until the first occurrence of UTI after KT. Graft loss was defined as an estimated GFR <15 mL/min/1.73 m² and return to dialysis.

Surgical Technique

If there were no contraindications, the allograft was placed in the right iliac fossa. Urethral catheterization was performed on all recipients before the surgery and the Foley catheter was clamped by filling the bladder with 80–100 mL 0.9% NaCl solution with an antibiotic. Presence of immunological risks (e.g., ABO incompatible, positive lymphocyte cross-match, positive donor-specific antibody), deceased donor KT, and bladder volume <50 mL was used as indication of DJ stent insertion in our institution. However, the decision to employ ureteral stenting was based on the operative findings and preference of the surgeon. The ureteric stents used were 5-Fr Polaris Ultra ureteral stent (Boston Scientific, Natick, MA, USA). All ureteroneocystostomies were performed using a Lich-Gregoir (external

ureteroneocystostomy) technique. Before terminating the operation, a drain was placed in the surgical region in all patients. The ureteral stents were kept in place for at least 2 weeks. The ureteral stents were subsequently removed depending on the patient's condition and functional status of the transplant kidney. The ureteral stent was removed using a flexible cystoscope under local anesthesia.

Immunosuppressive Regimen

The patients were administered an immunosuppressive regimen based on routine induction with basiliximab (20 mg on days 0 and 4) or rabbit antithymocyte globulin (ATG; 3–4 doses of 1.5 mg/kg each) for high-risk patients, and

intravenous methylprednisolone (1,000 mg) was administered just before induction. Immunosuppressed status was maintained with tacrolimus, mycophenolate mofetil, and steroids. Mycophenolate mofetil was administered 1 week before KT in cases of ABO-incompatible (ABOi) or positive cross-match. In cases of ABOi, positive cross-match, or high panel-reactive antibodies (PRA; having a PRA >50%), rituximab (200 mg, single dose) was administered within 7 days before the KT. Plasmapheresis was performed until the target antibody titer (IgG titer ≤1:16 in ABOi KT, conversion of a positive cross-match to negative) was achieved. Acute cellular rejection (ACR) was treated using methylprednisolone pulse therapy (500 mg/day,

Table 1. Patient characteristics

Variable	No-DJ (n=25)	DJ (n=17)	P-value
Age (yr)	48.1±12.9	52.2±8.8	0.228
Female sex	8 (32.0)	6 (35.3)	0.824
Body mass index (kg/m ²)	23.0±3.9	23.4±2.9	0.739
Dialysis duration (mo)	37.9±44.6	43.0±44.4	0.735
Cause of ESRD			0.152
Hypertensive	7 (28.0)	2 (11.8)	
Diabetes	7 (28.0)	6 (35.3)	
Glomerulonephritis	7 (28.0)	5 (29.4)	
Polycystic kidney	1 (4.0)	4 (23.5)	
Unknown	3 (12.0)	0	
Pre-emptive	3 (12.0)	2 (11.8)	0.982
Dialysis type			0.549
Hemodialysis	11 (50.0)	6 (40.0)	
Peritoneal dialysis	11 (50.0)	9 (60.0)	
Donor type			0.122
Living	19 (76.0)	16 (94.1)	
Deceased	6 (24.0)	1 (5.9)	
Duration of Foley catheter (day)	9.7±3.6	13.1±7.1	0.085
Mean trough level of tacrolimus			
At 1 month post-KT (ng/mL)	7.9±1.5	8.0±1.4	0.849
At 6 months post-KT (ng/mL)	6.5±1.3	7.4±1.5	0.069
At 12 months post-KT (ng/mL)	6.3±1.2	6.8±1.3	0.239
Mycophenolate mofetil dose (mg/day)	940±219	970±214	0.657
ATG induction	0	5 (29.4)	0.004
Hepatitis B virus carrier	5 (20.0)	1 (5.9)	0.199
ABO incompatible	4 (16.0)	6 (35.3)	0.150
Cross match positivity (flow)	0	2 (11.8)	0.079
Donor specific antibody (+)	1 (4.0)	5 (29.4)	0.021
HLA mismatch >3	6 (24.0)	6 (35.3)	0.426

Values are presented as mean±standard deviation or number (%).

DJ, double-J; ESRD, end-stage renal disease; KT, kidney transplant; ATG, antithymocyte globulin; HLA, human leukocyte antigen.

three–four times). The patients with steroid-resistant ACR received rabbit ATG. Antibody-mediated rejection (AMR) was treated with a combination of plasmapheresis and intravenous immunoglobulin with rituximab.

Patient Follow-up and Renal Biopsy

After discharge, patients visited the transplant clinic every week for laboratory assessments during the first post-transplant month. All recipients underwent monthly serum and urine BK polymerase chain reaction measurements, urinalysis, and urine culture. Screening for BK viremia and bacteremia was also performed monthly within the first year. Renal biopsies were performed in cases of acute allograft dysfunction (increased serum creatinine >30% from baseline or proteinuria >1 g/day). All acute rejections were biopsy-proven and classified as AMR or ACR using the Banff criteria [15]. All biopsy specimens were stained for C4d.

Prophylaxis Protocol and Infection Monitoring

Prophylactic intravenous second-generation cephalosporin was administered daily to the recipients for a period of 5 days. All patients received trimethoprim–sulfamethoxazole as *Pneumocystis jirovecii* pneumonia prophylaxis (3 months). Fungal prophylaxis consisted of 4 mL of oral nystatin four times daily for a period of 6 months. No prophylaxis against cytomegalovirus infection was administered to any patient.

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Statistical Analysis

The data are presented as patient numbers (percentages) or as median values (range). Categorical variables were analyzed using the chi-square test or Fisher’s exact test. Continuous variables were analyzed using the Mann-Whitney U-test. P-values <0.05 were considered statistically significant. The statistical procedures were conducted using SPSS ver. 18.0 (SPSS Inc., Chicago, IL, USA).

RESULTS

Patient Characteristics

A total of 42 patients underwent KT from June 2016 to June 2019; 17 patients were classified into the DJ group and 25 patients into the no-DJ group. The median follow-up time was 794.5 days (range, 392–1,479 days). Patient characteristics are shown in Table 1. There were no significant differences between the groups in terms of age, sex, body mass index, dialysis duration, cause of end-stage renal disease, pre-emptive KT, type of dialysis, type of donor, proportion of hepatitis B virus carriers, ABOi,

Table 2. Surgical outcomes by group

Variable	No-DJ (n=25)	DJ (n=17)	P-value
Operative time (min)	365.6±68.8	410.6±73.5	0.054
Cold ischemic time (min)	87.6±72.6	78.5±94.5	0.739
Warm ischemic time (min)	51.2±12.1	66.8±15.9	0.002
Delayed graft function	3 (12.0)	1 (5.9)	0.507
Biopsy proven acute rejection	4 (16.0)	5 (29.4)	0.298
Acute cellular rejection	3 (12.0)	2 (11.8)	0.982
Acute antibody mediated rejection	1 (4.0)	3 (17.6)	0.139
6-Month GFR (mL/min/1.73 m ²)	68.2±22.5	71.4±12.7	0.656
Time to postoperative UTI (day)	105.3±71.6	33.5±7.8	0.013
Time to postoperative BK viremia (day)	77.8±22.1	-	-
Urologic complication	4 (16.0)	0	0.035
Bacteriuria within 1 year	4 (16.0)	4 (23.5)	0.542
Symptomatic UTI	4 (16.0)	2 (11.8)	0.700
Simple cystitis	2 (8.0)	1 (5.9)	0.794
Complicated UTI	2 (8.0)	1 (5.9)	0.794
BK viremia	4 (16.0)	0	0.035

Values are presented as mean±standard deviation or number (%).

DJ, double-J; GFR, glomerular filtration rate; UTI, urinary tract infection.

Table 3. Details of urological complications

Age (yr)	Sex	Donor type	Complication	Treatment	Duration of stenting (day)
38	F	Deceased	Stenosis	PCN+balloon+DJ stenting	92
57	M	Living	Stenosis	PCN+balloon+DJ stenting	50
37	M	Living	Stenosis	PCN+balloon+DJ stenting	129
55	M	Deceased	Leakage	PCN+DJ stenting	181

PCN, percutaneous nephrostomy; DJ, double-J.

cross-match positivity, and human leukocyte antigen mismatch. However, ATG induction and donor-specific antibody positivity were significantly higher in the DJ group. The mean time of DJ stent removal was 44.3 ± 29.1 days after KT in the DJ group. The DJ stent was removed within 6 weeks in 12 patients (70.6%).

Comparison of Surgical Outcomes after KT by Group

There were no significant differences between the groups in terms of symptomatic UTI (Table 2). The time to postoperative UTI was significantly shorter in the DJ group than in the no-DJ group (33.5 ± 7.8 vs. 105.3 ± 71.6 days, $P=0.013$). The development of postoperative BK viremia was significantly higher in the no-DJ group (0.0% vs. 16.0%, $P=0.035$). Urologic complications were significantly higher in the no-DJ group (0.0% vs. 16.0%, $P=0.035$). In the no-DJ group, urologic complications occurred in four patients: ureteroneocystostomy stenosis in three patients and ureteroneocystostomy leakage in one patient. Percutaneous ureteral interventions were performed in all patients using percutaneous nephrostomy and reno-uretero-vesical stenting (Table 3). There was no graft loss related to urologic complications.

DISCUSSION

The current study found that the surgical outcomes of the DJ group were not significantly different from those of the no-DJ group. Urologic complications were observed only in the no-DJ group, and the incidence rates for UTI were not significantly different between the two groups. Additionally, the development of BK viremia was significantly higher in the no-DJ group. These results suggest that prophylactic ureteral stenting during KT may be feasible and does not lead to an increase in UTI incidence and BK viremia.

UTI is the most common infection after KT and is

responsible for 47% of all infectious posttransplant complications [16]. Moreover, the presence of a foreign body in an immunosuppressed patient has the potential to increase the risk of UTI. Thus, previous studies have recommended the early removal of ureteral stents for the prevention of UTI [17,18]. However, the optimal timing for stent removal is currently unknown. Several previous studies have suggested that stent removal at 1–6 weeks is beneficial [19]. Moreover, Visser et al. [20] recommended that ureteral stents should be removed within 3 weeks to reduce the incidence of infective complications. However, early removal of the stent may cause urological complications. In the current study, the mean time for DJ stent removal was 44.3 ± 29.1 days after KT. Moreover, compared with previous studies, the stent indwelling time was slightly longer. These results may be due to the inclusion of patients with DGF and those requiring a transplant kidney biopsy. Patients with DGF or those requiring transplant kidney biopsy may have delayed stent removal for the exclusion of post-renal acute kidney injury. Therefore, a prospective randomized controlled study is needed to confirm the optimal timing of stent removal.

Studies in animal models have demonstrated biological reactions to stent insertion in the form of epithelial destruction, with erosions and ulcerations of the transitional epithelium [21]. Thus, mechanical trauma associated with stent placement may injure the uroepithelium, allowing latent BK virus to enter replicative phases [22]. These changes were noted after intubation of the animal ureters for 6 weeks [23,24], suggesting a duration-dependent association between placement of ureteral stents and the development of BK viremia. Although the mean time of DJ stent removal was slightly longer than 6 weeks in the current study, 70.6% of patients with DJ stents were removed within 6 weeks. Therefore, removal of the DJ stent within 6 weeks may reduce the development of BK viremia in the DJ stent group.

Urologic complications are generally believed to be of

ischemic origin [25]. Deceased donor kidneys are more prone to ischemic insult secondary to long cold ischemia time and donor characteristics. In addition, deceased donor kidneys are potentially subjected to rougher tissue handling during procurement compared with living donor kidneys. Fayek et al. [9] demonstrated that the rate of urologic complications between the stent group and no stent group with deceased donor transplants was similar even though higher DGF rates were observed in the stent group. In addition, routine stenting is recommended in deceased donor transplants because of its protective effects for urologic complications. Similarly, in our study, the number of patients who are at high risk for urologic complications such as ATG induction and donor-specific antibody positivity was significantly higher in the DJ group than in the no-DJ group. Furthermore, the proportion of ABOi KT was higher in the DJ group. However, there were no postoperative urologic complications in the DJ group. Therefore, prophylactic ureteral stents in high-risk recipients would protect the anastomosis from ischemia-related complications (Supplementary Tables 1-3).

The limitations of this study include its single-center study population and retrospective study design. In addition, the decision for stent placement was based on the preference of the surgeon; therefore, the stent placement was not random and contributed to bias in patient selection. We did not study the peak BK viremia level and incidence of biopsy-proven BK virus nephropathy or graft survival. Finally, the small size of the cohort with a mix of living donors and deceased donor transplants is also a limitation of the current study.

In summary, prophylactic ureteral stenting during KT may be safe and feasible without significantly increasing the incidence of UTI and BK viremia. Additionally, prophylactic ureteral stenting may reduce urological complications after KT. However, the selective insertion of a stent may be recommended in patients with a high risk of urological complications rather than being performed as routine prophylactic stenting. Furthermore, a prospective randomized controlled study is required to confirm the duration of placement of ureteral stents after KT.

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Conflict of Interest

No potential conflict of interest relevant to this article was

reported.

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Supplementary Materials

Supplementary materials can be found via <https://doi.org/10.4285/kjt.20.0050>.

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