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Urological Complications in 1,223 Kidney Transplantations

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Key Words
Kidney transplantation · Urological complications · Ureteroneocystostomy · Ureteroureterostomy

Abstract
Introduction: Urological complications after kidney transplantation may lead to graft loss. In this study, we retrospectively reviewed urological complications in 1,223 kidney transplantations that were performed at our institution. ***Materials and Methods:*** The occurrence of urological complications such as urine leakage, ureteral obstruction and vesicoureteral reflux (VUR) according to the different way of urinary tract reconstruction, ureteroneocystostomy (U-C) and ureteroureterostomy (U-U), was studied. ***Results:*** Urological complications were encountered in 92 (7.5%) cases, including urine leakage (n = 43, 3.5%), ureteral obstruction (n = 35, 2.9%) and VUR (n = 14, 1.1%). 75 cases (7.9%) were in the U-C group and 17 cases (6.2%) in the U-U group. 91 recipients were successfully treated, and 1 patient lost the graft due to kidney pelvis and ureteral necrosis. There was no recipient loss due to these complications. For recipients with urological complications, the 1- and 3-year survival rates were 90 and 88% for recipients and 87 and 82% for grafts, respectively. ***Conclusions:*** After U-U, the same number of overall incidences of urological complications is observed as after U-C; however, a decrease in the number of incidences of urine leakage is apparent. Therefore, U-U is a good first option with a greater success rate of resolving ureteral stenosis with endourology and no risk of VUR.

The occurrence of urological complications after kidney transplantation may lead to graft loss and increased patient morbidity [1]. In the early days of kidney transplantation, the number of incidences of major urological complications, including urine leakage, ureteral obstruction and vesicoureteral reflux (VUR), was reported to be between 10 and 25% [2, 3]. This number has decreased significantly over the past 40 years due to refinements in surgical techniques and largely improved suture materials. Currently, the rate of urological complications is 2.5–14.1% [4–7]. The most important factor associated with these urological complications is the method used for establishing the continuity of the urinary tract. Nowadays, the most widely accepted method of reconstructing the continuity of the urinary tract during kidney transplantation is extravesical ureteroneocystostomy (U-C) such as the Lich-Gregoir technique. Pyeloureterostomy and

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ureteroureterostomy (U-U) are usually reserved for patients with short or ischemic allograft ureters or for patients with very limited bladder capacity.

Our transplantation team performed 1,223 kidney transplantations between December 1993 and April 2007. Initially, we chose U-C as our first option and U-U was performed only in cases of very difficult bladder or kidneys with shorter ureter, or to correct urological complications such as urine leakage or stenosis. Interestingly, urological complications in these recipients were rarely observed. Therefore, we changed our surgical technique and performed termino-terminal U-U as the first option in anuric recipients. This study aims at comparing the urological complications in kidney transplant patients who had undergone different procedures of establishing the continuity of the urinary tract.

Materials and Methods

A retrospective review of the clinical records of 1,223 kidney transplant patients was performed. We focused our attention on early and late postoperative urological complications after kidney transplantation, including urine leakage, ureteral obstruction and VUR, paying particular attention to the different methods of establishing the continuity of the urinary tract that were used. The incidence, management and outcomes of the major urological complications were recorded. Demographic data, including recipient and donor age, gender, type and duration of dialysis, human leukocyte antigen mismatch, living or cadaver donor were collected.

In all patients, standard procedures were used for harvesting and transplantation of the kidneys. The maintenance immunosuppressive regimen consisted of cyclosporine, azathioprine and low-dose steroids. More recently, some patients received tacrolimus and mycophenolate mofetil. Induction with Okt3, antithymocyte globulin or anti-interleukin-2 (daclizumab) was used in retransplants or in patients with a high panel reactive antibody. Acute rejection episodes were treated with corticosteroids or with immunoglobulins.

The 1,223 patients were divided into two groups according to the method of establishing continuity of the urinary tract. Extravesical U-C (Lich-Gregoir technique) was performed with standard use of an indwelling ureteral stent on the 948 patients in the U-C group. U-U was performed on the 275 patients in the U-U group.

Statistical analysis was performed using SPSS 13.0 software. A χ^2 test was used for analysis of nonparametric data. A p value <0.05 was considered to indicate statistical significance.

Results

There were 1,154 grafts (94.4%) from cadaver donors and 69 (5.6%) from living donors. The study population included 714 (58.4%) male patients and 509 (41.6%) female patients. All patients had a 1-year or more post-transplant follow-up. A demographic comparison of patients in the U-C and the U-U group is shown in table 1.

Table 1. Demographic features of the patients

Characteristics	U-C group (n = 948)	U-U group (n = 275)	p value
Gender, male/female	563/385	151/124	NS
Age at transplantation, years	42.6 ± 11.8	38.5 ± 10.9	NS
Dialysis duration, months	14.7 ± 10.2	13.8 ± 9.3	NS
Hemodialysis/peritoneal dialysis	803/145	241/34	NS
Donor age, years	37.6 ± 8.3	37.8 ± 7.6	NS
Cadaver donor/living donor	897/51	257/18	NS
HLA mismatch	3.2 ± 1.1	3.1 ± 1.4	NS
Tx duration, months	62.6 ± 43.9	67.8 ± 49.1	NS

NS = Not significant; HLA = human leukocyte antigen; Tx = treatment.

Table 2. Complications in the post-transplant period

Complications	All patients	U-C group (n = 948)	U-U group (n = 275)	p value
Urine leakage	43 (3.5)	39 (4.1)	4 (1.5)	<0.05
Ureteral obstruction	35 (2.9)	22 (2.3)	13 (4.7)	<0.05
VUR	14 (1.1)	14 (1.5)	0	<0.05
Total	92 (7.5)	75 (7.9)	17 (6.2)	NS

Figures in parentheses are percentages. NS = Not significant.

Urological complications were observed in 92 (7.5%) recipients. Of these, 43 (3.5%) were urine leakages, 35 (2.9%) ureteral obstruction and 14 (1.1%) VUR. Urological complications in the two groups are compared in table 2. Urological complications occurred in 75 (7.9%) patients of the U-C group and in 17 (6.2%) patients of the U-U group. The difference between the U-C and the U-U group was not statistically significant.

Urine Leakage

43 (3.5%) patients suffered urine leakages of whom 39 patients were in the U-C group. Of these, 5 patients suffered bladder leakage. Conservative treatment with a stent and Foley catheter drainage for 1–2 weeks was successful. 33 patients underwent further examination revealing distal ureteral necrosis requiring either repeat U-C or U-U using the native ureter. One patient underwent transplant

Table 3. Surgical treatment methods for urological complications after transplantation

Complication	U-C group	U-U group
Urine leakage (43)	39	4
Bladder leakage (5)	Foley catheter drainage (5)	
Ureteral leakage (3)		double J (3)
Distal ureteral necrosis (34)	U-C revision (14), U-U (19)	U-U revision (1)
Pelvis and ureteral necrosis (1)	transplant nephrectomy (1)	
Ureteral obstruction (35)	22	13
Early (8)	4	4
Extraluminal (4)	2	2
Hematoma (4)	surgical drainage (2)	surgical drainage (2)
Intraluminal (4)	2	2
Clot (2)	open surgery (1)	replacing double J (1)
Calculi (2)	ESWL (1)	ESWL (1)
Late (27)	18	9
Intraluminal (27)	18	9
Stenosis (19)	U-U (9), nephrostomy (4)	balloon dilation (6)
Calculi (8)	ESWL (3), endourology (2)	endourology (3)
VUR (14)	medicine (8), U-U (6)	

Figures in parentheses are number of cases. ESWL = Extracorporeal shock wave lithotripsy.

nephrectomy due to kidney pelvis and ureteral necrosis. 4 patients were in the U-U group. Conservative treatment was successful in 3 patients. 1 patient needed a second U-U due to distal ureteral necrosis (table 3).

Ureteral Obstruction

We identified ureteral obstruction in 35 (2.9%) patients. Of these, 8 patients suffered early obstruction, including hematoma in the iliac fossa in 4 patients, ureteral blood clot in 2 patients and calculi in 2 patients. They were successfully treated with surgical drainage, replacement of the ureteral stent or extracorporeal shock wave lithotripsy. 27 patients suffered late obstruction, including U-C in 13 patients, U-U in 6 patients and calculi in 8 patients. The overall number of incidences of ureteral obstruction was significantly different between the U-C and the U-U group ($p < 0.05$). Stenosis was successfully treated with endourology, either by balloon dilation or percutaneous nephrostomy, and open surgery either by repeat U-C or U-U. The calculi were treated with either endourology or extracorporeal shock wave lithotripsy (table 3).

Vesicoureteral Reflux

14 (1.1%) patients suffered symptomatic VUR and recurrent pyelonephritis, all in the U-C group. A voiding cystourethrogram performed to evaluate the cause of the pyelonephritis revealed reflux. 8 patients received only medical treatment and 6 patients were reoperated with conversion to U-U (table 3).

All recipients with urological complications regained normal graft function except for one who underwent transplant nephrectomy due to kidney pelvis and ureteral necrosis. This is not considered a recipient loss secondary to the complications in the present study. For recipients with urological complications, the 1- and 3-year survival rates were 90 and 88% for recipients and 87 and 82% for grafts, respectively.

Discussion

The occurrence of urological complications following kidney transplantation causes significant patient morbidity and may result in failure of the allograft. The overall rate of incidences of urological complications in our study was 7.5%, comparable with other major centers [4–7]. Vascular integrity of the donor ureter, the anastomotic technique employed and avoidance of technical mishaps such as kinks and twisting of the ureter are major factors impacting the success of ureterovesical anastomosis [8]. Most transplant centers prefer U-C as the initial approach for ureteral reimplantation for kidney transplant recipients. By using an extravesical rather than intravesical tech-

nique, complication rates have been reduced. U-U and pyeloureterostomy are usually carried out as secondary procedures following a failed reimplantation. The reason for not using these as a primary procedure is to save the native ureter if a further correction of a urological complication is necessary [9]. To our knowledge, only a limited number of studies comparing the efficacy of U-C and U-U techniques have been reported in the literature [10].

The rate of incidences of urine leakage in the different transplant centers ranged from 1.2 to 8.9% [11, 12]. Urine leakage arises frequently due to technical problems, during procurement or transplant surgery. Ureteral necrosis due to ischemia is the most frequent cause and can be occasioned during organ retrieval or implantation when extensive ureteral dissection leads to blood supply damage. Ureteral necrosis was also the most frequent cause of leakage in our study, occurring in 76.7% (33/43). Several other risk factors for the development of urine leakage have been mentioned: recipient's age, number of renal arteries, site of arterial anastomosis, occurrence of acute rejection episodes, bladder problems and immunosuppresive regimen [13]. In our study, leaks were more frequent among cadaver donor recipients and significantly more common among patients diabetic at the time of transplantation. Extravesical U-C has proved to be easier and to have a low incidence of complications. U-U and pyeloureterostomy may be better than ureterovesical anastomosis, but they leave far fewer options if problems occur. Therefore, U-U and pyeloureterostomy are usually reserved for patients with short or ischemic allograft ureter or for patients with very limited bladder capacity.

At our center, we used the Lich-Gregoir technique in 948 recipients. A stent was routinely used. We observed a urine leakage rate of 3.5%. The U-U method was adopted in 275 patients. Here, we observed a leakage rate of only 1.5%. One important reason for the observed lower urine leakage rate when using the U-U technique compared with the Lich-Gregoir technique may be the utilization of a shorter ureter. Of course, improvements in donor nephrectomy techniques in recent years may also be a cause for the relatively low urinary leakage rate in the U-U group. The use of ureteral stents in renal transplantation is still controversial. Recently, it was reported that routine use of the double J stent prevented ureteral complications after kidney transplantation [7, 14, 15]. However, other surgeons have reported that routine ureteral stenting is unnecessary for patients with a low risk of urological complications [6]. It must be kept in mind that refinement of surgical techniques and the introduction of new immunosuppressive protocols have also decreased the incidence of urological complications [8].

Ureteral obstruction is one of the major urological complications after transplantation. In the literature, the rate of incidences was reported to range from 3 to 12.4% [4, 12]. In our study, the rate of ureteral obstruction was 2.9%. 22 (2.3%) patients developed ureteral obstruction in the U-C group and 13 (4.7%) in the U-U group. Our study showed that ureteral obstruction might result from intraluminal factors such as calculi or a blood clot, or extraluminal factors such as pressure exerted by blood and also stenosis at the anastomosis line. At the early stage after surgery, the main cause of obstruction was hematoma (50%), which needed surgical drainage. At the late stage, stenosis became the main cause of ureteral obstruction (70.1%). Ureteral stenosis was significantly more common in the U-U compared with the U-C group, which might be associated with surgical skills. We used to perform surgery frequently, because endourology was rarely successful after U-C and percutaneous procedures also had only limited success. In contrast, stenosis dilatation after U-U is an easy option with endourology, often resulting in permanent cure. The small calculi detected early after transplantation may not be found before transplantation or remnant stones after management. The calculi detected late after transplantation probably resulted from metabolic disturbances due to the long-term use of cyclosporine. These calculi are also easily treated with endourology after U-U.

One of the major causes of symptomatic urinary system infection and morbidity after transplantation is VUR. In our study, 14 patients developed symptomatic VUR (1.1%). All of them were in the U-C group. The true rate of incidences of VUR is unknown, since voiding cystourethrogram tests are not routinely performed on all transplant patients; only recipients with recurrent pyelonephritis were evaluated by this method. In the literature, VUR is reported to occur at a rate of 2–79% [16]. The major causes of VUR are related to the surgical reimplantation technique and the quality of the bladder wall. Initially, antibiotic prophylaxis was used on these patients. However, most patients prefer surgical intervention to avoid chronic antibiotic use. We used U-U or pyeloureterostomy for the treatment of patients with VUR with no graft or patient loss after surgery.

In conclusion, U-U is easier to perform and can decrease the incidence of urine leakage after kidney transplantation. It is a good first option with a greater success rate of resolving ureteral stenosis with endourology and no risk of VUR.

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