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Comparing two ureter reimplantation techniques in kidney transplant recipients

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Summary

We compared the incidence of urological and anastomotic complications for the ureteroureterostomy and Lich–Gregoir techniques in kidney transplant recipients. Between May 2003 and February 2004, 75 kidney transplant recipients from living donors were divided into two similar groups to receive ureteroureterostomy ($n = 41$, 28 male, 13 female) and Lich–Gregoir techniques ($n = 34$, 24 male, 10 female) for ureteral reimplantation. Patients with vesicoureteral reflux (VUR) to the native kidneys were excluded from the study. The urological complications included complicated hematuria, ureteral stenosis, symptomatic VUR, recurrent urinary tract infection (UTI). There was no statistical significance between two groups in terms of gender, age, end-stage renal disease etiology, human leucocyte antigen (HLA) mismatch numbers, type and duration of dialysis, and cold ischemia time. The incidence of urologic and anastomotic complications was 12%. Complications in the Lich–Gregoir group included symptomatic VUR in 8.8% and stent migration in 2.9% of cases. Complications observed in the ureteroureterostomy group were ureteral stricture 7.3% and complicated hematuria in 4.9% of cases. However, symptomatic reflux was not observed in the ureteroureterostomy group. UTI frequency was similar in both groups. Ureteroureterostomy can be safely performed as a primary choice in kidney transplant recipients.

Introduction

The most widely accepted way of reconstructing the continuity of the urinary tract during kidney transplantation is an ureteroneocystostomy (UNC). Regardless of the surgical technique performed for the UNC, the incidence of urological complications tends to be around 2–14%, which the majority develops within the first month of transplant [1–9]. Late complications are predominantly ureteral obstruction and vesicoureteral reflux (VUR) [10]. Although there has been a significant increase in short-term graft survival recently, kidney transplantation has still not reached its goal in terms of long-term graft survival. The late failure of allografts is usually attributed to chronic rejection in most cases [11]. However, it has been reported that histopathologic findings of the chronic rejection and late urologic complications (such as obstructive nephropathy) may overlap in some cases. There are also some reports pointing on the importance of the urological complications on long-term graft survival [12]. To our knowledge, limited number of studies comparing the efficacy of UNC and ureteroureterostomy techniques has been reported in the literature [13]. To investigate the impact of the type of ureteral anastomosis on late functional changes in kidney transplants, we performed a prospective randomized study in which these two techniques of ureteral reconstruction were compared.

Patients and methods

In this prospective, randomized study, 75 (52 male, 23 female) consecutive kidney recipients who received their

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first grafts from living donors, between May 2003 and February 2004, were consented. The patients were divided into two groups in an alternating fashion to receive either Lich–Gregoir or ureteroureterostomy techniques for ureteral reimplantation. Subjects with a history of VUR to the native kidneys were excluded from the study in the first place. The following characteristics for each case were recorded: recipient–donor gender and age, recipient's primary disease, dialysis duration, cold ischemia time, surgical technique, complications, need for reoperation, and treatment of complications.

Renal function was monitored by serum creatinine (Cr), urine output and a Doppler ultrasound (US) to confirm the patency of the vessels, in the early postoperative period. A diethylenetriaminepentaacetic acid (DTPA) renal scan on postoperative first month, and a voiding cystourethrogram (VCUG) on post-transplant third month were performed regularly. Whenever a renal dysfunction occurred, a repeat Doppler US and a DTPA renal scan were carried out to identify the etiology.

For the patients with a positive VCUG, symptomatic VUR was defined as diagnosis of more than two febrile, culture positive urinary tract infections in the first 3 months.

Surgical technique

All donor nephrectomies were open procedures and carried out by two different surgeons. Both types of the ureteral anastomosis in all patients were performed by the same surgeon. Patients who underwent Lich–Gregoir UNC had their graft's ureter shortened to facilitate a non-redundant and tension-free anastomosis. After placing a 5 Fr 16 cm double-J catheter, the ureter-to-mucosa anastomosis was performed using a running 6–0 PDS and the bladder muscle was closed with again interrupted sutures of 6–0 PDS. An 18 Fr Foley catheter was routinely inserted intraoperatively and removed on postoperative fourth day, if no other contraindication occurred.

The ureter was also shortened for the patients who underwent for an end-to-side, donor-to-native ureteroureterostomy. After making an incision of approximately 1 cm on the distal native ureter, a 5 Fr ureter catheter was passed distally to the bladder to confirm the patency of the ureter. Then, the donor ureter was spatulated and a 5 Fr 16 cm double-J catheter was inserted. The ureter-to-ureter anastomosis was also completed with a running 6–0 PDS suture. An 18 Fr Foley catheter was routinely inserted intraoperatively and removed on postoperative first day, if no other contraindication occurred.

As it has been suggested not to remove the double-J catheters for the first 7 days to avoid early leaks and stenosis, they were kept for 8 days in both groups [14].

Antibiotics and immunosuppression

A single preoperative dose of second generation cephalosporin was administered routinely.

All patients received sulfamethoxazole/trimethoprim (80 mg/400 mg) daily for the first 9 months for prophylaxis of urinary tract and *Pneumocystis carinii* infection. Immunosuppression consisted of triple immunotherapy including either cyclosporine A or tacrolimus combined with mycophenolate mofetil and prednisone. Antibody induction with basiliximab was used only in patients who received a spousal kidney.

Statistical analysis

SPSS for Windows version 11.5 (SPSS, Chicago, IL, USA) was used; in addition to descriptive analysis, chi-squared and Student's *t*-test were performed, values of $P < 0.05$ were accepted as significant.

This study has been reviewed and approved by local ethical committee.

Results

In this study, the mean follow-up was 16.2 ± 2.7 (range: 12–21) months. Among 75 patients, 52 (69.3%) of them were male, while 23 (30.7%) were female. The mean age of the patients was 34.6 ± 11.9, ranging between 7 and 67 years. End-stage renal disease etiology of the patients were: diabetes mellitus in 4, glomerulonephritis in 22, polycystic kidney disease in 7, hypertension in 11, stone disease in 6, drug toxicity in 1, Familial Mediterranean Fever in 4, and unknown in 20. Among all the patients, 66 of them (88%) needed renal replacement therapy; hemodialysis for 58 and peritoneal dialysis for 8, dialysis duration of these 66 patients ranged between 1 to 180 months (mean = 26.4 months), while 9 (12%) of them were pre-emptive. Mean HLA-mismatch number was 3.1 ± 1.4 (Table 1).

There was no statistical significance between Lich–Gregoir and ureteroureterostomy groups in terms of gender (24 male/10 female vs. 28 male/13 female), age (32.8 ± 14.3 vs. 36.1 ± 9.4 years), dialysis type and duration (26.7 ± 24.6 vs. 26.3 ± 26.1 months), cold ischemia time (70.5 ± 29.1 vs. 76.9 ± 30.2 min), follow-up duration (16.6 ± 2.4 vs. 15.8 ± 2.8 months), and HLA-mismatch numbers (3 ± 1.5 vs. 3.2 ± 1.2), respectively (Table 1). Mean serum Cr levels were similar in both groups throughout the follow-up (1.3 ± 0.6 vs. 1.4 ± 0.5 mg/dl at 12 months).

The incidence of urologic and anastomotic complications in the Lich–Gregoir and ureteroureterostomy groups was 11.7% and 12.2%, respectively (Table 2). VCUGs

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Table 1. Demographic features of the patients.

Characteristics	All patients ($n = 75$)	Lich–Gregoir ($n = 34$)	Ureteroureterostomy ($n = 41$)	*P*
Gender (M/F)	52/23	24/10	28/13	NS
Age at transplantation, year (range)	34.7 ± 11.9 (7–67)	32.9 ± 14.3 (7–67)	36.2 ± 9.4 (16–59)	NS
Dialysis duration, month (range)	26.4 ± 24.3 (1–180)	26.7 ± 24.6 (1–124)	26.3 ± 26.1 (1–180)	NS
Type of dialysis (HD*/PD**/pre-emptive)		27/3/4	31/5/5	NS
Cold ischemia time, minute (range)	73.8 ± 29.2 (44–200)	70.5 ± 29.1 (44–190)	76.9 ± 30.2 (45–200)	NS
Tx duration, month (range)	16.3 ± 2.7 (12–21)	16.7 ± 2.4 (12–21)	15.9 ± 2.9 (12–21)	NS
Human leucocyte antigen-mismatch (HLA-MM), mean n ± SD	3.1 ± 1.4	3 ± 1.5	3.2 ± 1.3	NS
Donor age, year (range)	46.2 ± 11.2 (20–72)	45.5 ± 11.5 (20–65)	46.8 ± 11 (30–72)	NS
Creatinine level at 12th month mg/dl	1.4 ± 0.5	1.3 ± 0.6	1.4 ± 0.5	NS

*,hemodialysis.
**,peritoneal dialysis.

Table 2. Complications in the post-transplant period.

Complications	All patients ($n = 75$)	Lich–Gregoir ($n = 34$)	Ureteroureterostomy ($n = 41$)	*P*
(Vesicoureteral reflux	3 (4%)	3 (8.8%)	–	NS
Stent migration	1 (1.3%)	1 (2.9%)	–	NS
Ureteral stricture	3 (4%)	–	3 (7.3%)	NS
Hematuria	2 (2.6%)	–	2 (4.9%)	NS
Total	9 (12%)	11.7%	12.2%	
Urinary tract infection frequency (mean)	0.9 (1–8)	1 ± 0.2	0.8 ± 0.2	NS

performed at the end of the third month revealed VUR in 18 (24%) cases, all in the Lich-Gregoir group. Grade I VUR was observed in six (8%), grade II in six (8%), grade III in five (6.6%) cases, while grade IV VUR was seen in only one (1.3%) case. Symptomatic reflux was observed in only three (8.8%) cases, in which two of them had grade II and one had grade IV VUR. Also, stent migration occurred in one patient (2.9%) in the Lich–Gregoir group. While the VUR cases were corrected by a modified STING operation (subureteral transurethral injection; using dextranomer polysaccharide micro spheres crosslinked in sodium hyaluronan; Deflux; Ixion Biotechnology, Inc, Alachua, FL, USA), the stent migration case required major open surgery after failed attempts of endoscopic surgical procedures. Complications observed in the ureteroureterostomy group were ureteral stricture ($n = 3$) 7.3% and complicated hematuria (defined as hematuria leading to clot retention) in ($n = 2$) 4.9% of cases. All stricture cases required a major operation (conversions to UNC in two and pyeloureterostomy in one) and the hematuria cases were managed conservatively. UTI frequency was similar in Lich–Gregoir and ureteroureterostomy groups (1 ± 0.2 vs. 0.8 ± 0.2). There was no difference in double-J stent removal times between Lich–Gregoir and ureteroureterostomy groups (8.6 ± 1.8 vs. 8.2 ± 3.9 days respectively); however, Foley catheters were removed significantly earlier in the ureterostomy group (2.2 ± 0.9 vs. 4.6 ± 0.9 days) ($P = 0.0001$). In both groups, no ureteral necrosis and ureteral leak occurred. There were no deaths and graft loss as a consequence of these complications.

Discussion

Urological complications following renal transplantation cause significant morbidity and may result in failure of the allograft. Preserving the vascularity of the donor ureter during the donor nephrectomy [15] and the type of the surgical technique used are the major factors influencing the success of the vesicoureteral anastomosis. The complication rates have been reported between 2% to 14% in adult kidney transplant recipients by mainly using ureterovesical anastomosis [1–9]. There are many studies comparing different techniques of ureterovesical anastomosis in kidney transplant recipients; however, only very limited numbers of them have been carried out to compare the long-term effects of the ureteroureterostomy [13].

Recently most transplant centers prefer UNC as the initial approach for the ureteral reimplantation for the kidney transplant recipients. By using the extravesical rather than the intravesical technique, less complication rates have been achieved. This decrease was related to limited bladder dissection and the need for a shorter ureteral

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segment from the donor [5,9,16–18]. Also, newer immunosuppressive regimens including cyclosporine and tacrolimus have led to form steroid-free regimens, which has improved the incidences of urologic complications [1]. Waltke *et al.* found a higher incidence of ureteric obstruction with their 'end-to-side' technique compared with Leadbetter–Politano (LP) method [19]. Pleass *et al.* also stated that there was no difference in the incidence of major complications between the extravesical and LP methods when they were not stented; however, stenting improved the results of LP technique but had no effect on the outcomes of the extravesical technique [9]. In a study comparing two different extravesical UNC procedures, Taguchi and Lich–Gregoir techniques had shown similar urologic complication rates; however, Taguchi technique had a less symptomatic reflux rate by being more simple and time consuming [20].

Ureteroureterostomy and pyeloureterostomy have been usually carried out for as a secondary procedure after a failed reimplantation. The reason behind not using them as a primary procedure was to save the ureter if a further correction of an urological complication would be necessary [21–24]. When ureteroureterostomy or pyeloureteral anastomosis used as the primary technique for the ureteral reimplantation in adults, a complication rate of 1.9% to 12.6% has been reported [25–29]. It is indicated that this approach is helpful especially when an ureter length more than 6–7 cm is required for bladder reimplantation [30]. In a pediatric population, Lapointe *et al.* reported an overall complication rate of 8.4% in which the urinary leakage and ureteral obstruction were the most commons by using 'end-to-end' ureteroureterostomy, which is comparable with UNC. The need for performing the vascular anastomosis on the larger vessels necessitates a longer length of ureter in children and besides minimal risk of developing VUR makes ureteroureterostomy an attractive choice for the pediatric kidney transplant population [31].

In our study, patients with a history of VUR to the native kidneys were excluded in the first place. The rationale behind this decision was the idea that comparisons should be made only between groups that include patients who cannot have VUR by definition and can be considered all suitable for either procedure.

In a large series of kidney recipients, patients who had their ureters reconstructed by ureteroureterostomy instead of UNC did not have a significant change in the number of urologic complications, but experienced a significant decrease in the number of postoperative UTIs [13]. The reason why we did not observe difference in the number of postoperative UTIs in our series might be related to the limited number of subjects included.

In a rat isotransplant model, Kouwenhoven *et al.* compared ureteroureterostomy with 1-stitch UNC and showed that the latter technique caused a significant late graft dysfunction starting at week 36 becoming more prominent with interstitial fibrosis by week 52 [32]. Although it is not reliable to compare 1-stitch UNC in rats with Lich–Gregoir technique in humans, it is known to be the only study comparing UNC with ureteroureterostomy in a prospective randomized way. In our prospective randomized study, the allograft function was found to be similar in both groups throughout the follow-up period.

Our incidence of urologic and anastomotic complications by using both Lich–Gregoir and ureteroureterostomy techniques is 12%, which is comparable with the literature [1–7,33]. Routine use of VCUG in the follow-up period might help us to diagnose VUR with a higher incidence than expected [34]. Of interest, absence of VUR cases observed in the ureteroureterostomy group may be related to preservation of the original antireflux mechanism, which appears to be an advantage in maintaining long-term allograft function. Also, early removal of the Foley catheters in the ureteroureterostomy group may have an impact on the lower incidence of urinary tract infection. On the other hand, the need of major operation for the ureteral strictures in the ureteroureterostomy group may seem worrisome; however, this situation depends on the surgeon's experience, besides our low incidence is encouraging. Having no ureteral necrosis and ureteral leak in our series of patients had led us to conclude that both donor nephrectomies and recipient operations were successful for maintaining the vasculature of the ureter.

Thus, on the basis of our results, we conclude that ureteroureterostomy can be safely performed as a primary choice for ureteral reconstruction in kidney transplant recipients without VUR to the native kidneys.

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