Native Ureteropyelostomy versus Ureteroneocystostomy in Ureteral Complications after Renal Transplantation

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ABSTRACT

Background: There is no consensus regarding the standard surgical care after renal transplantation complications, and it mostly depends on the surgical team's judgment.

Objective: Therefore, in this study, we tried to compare the outcomes of native ureteropyelostomy and ureteroneocystostomy in ureteral complications after renal transplantation.

Methods: This case-control study was performed in a referral center for kidney diseases. Patients underwent native ureteropyelostomy and ureteroneocystostomy according to the time passed from renal transplantation surgery. Finally, outcomes between the two groups were compared using SPSS software version 20. A P-value below 0.05 was considered statistically significant.

Results: A total of 1316 kidney transplants were performed in our center during 2010 and 2020. Overall, 16 patients (1.21%) required post-operative reconstructive surgery. The main reasons for reoperation were stenosis in 11 patients (68.8%), leakage in 3, stenosis and leakage in one, and leakage and necrosis in another patient. Seven patients (43.8%) underwent native ureteropyelostomy and 8 (50%) ureteroneocystostomy. There was no significant difference between the two reconstructive surgical techniques in terms of patients' background characteristics, waiting time for transplantation, duration of preoperative dialysis, post-op complications, and rejection or mortality rate. However, there was a significant difference between the two surgical techniques regarding the donor type. However, the trend of serum Cr changes between the two surgical techniques did not show a significant difference (P= 0.329).

Conclusion: Native ureteropyelostomy and ureteroneocystostomy effectively treated post-op ureteral complications with good results. We suggest performing native ureteropyelostomy if more than eight weeks have passed from renal transplantation and if distal ureter blood supply is under question.

KEYWORDS: End-stage reanal disease; Renal transplantation; Native Ureteropyelostomy; Ureteroneocystostomy

INTRODUCTION

End-stage renal disease (ESRD), mainly due to diabetes mellitus (DM) and hypertension, is a major cause of morbidity and mortality, which necessitates long-term hemodialysis or renal transplantation [1-3]. It has been shown that renal transplantation is superior to long-term hemodialysis in many aspects [4]. Despite this, patients might be on the waiting list for quite a long time, or the operation might be associated with some complications. The most common complications include graft rejection, renal artery or vein thrombosis, ureteral stenosis and necrosis, infection, abscess, graft failure, or even sepsis and mortality [5-8].

Surgical techniques for renal transplantation are very diverse. Nevertheless, the organ of choice for performing an anastomosis between the donor kidney and recipient genitourinary system is the host bladder, called the ureteroneocystostomy [9]. The modified Lich-Gregoir technique is usually performed as the standard procedure for ureteroneocystostomy, as it takes less time and is associated with

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fewer complications than similar techniques [10]. Therefore, other techniques, such as ureteroneocystostomy, Native ureteropyelostomy, pyelopyelostomy, etc., have been developed to maintain the continuity of the urinary system [11-13]. In some conditions, including a history of bladder or pelvic surgery and the presence of ileal conduit, patients' bladder or neobladder is the first choice.

Uysal *et al.* [14] reviewed the causes and treatment options after renal transplant complications. In their study, the most common complications were ureteral complications and urinary tract infection (UTI). Ureteral complications were most common with urine leak and obstruction occurring in 2.9% and 3.0% of recipients, respectively. All perioperative complications occurred mainly following cadaveric renal transplant for harvest techniques. They finally performed native ureteropyelostomy and ureteroneocystostomy to manage complications in most patients. Most patients had good outcomes following the secondary surgery, but they concluded that there is still no consensus regarding the most acceptable options after renal transplant failure. Noteworthy, nephrectomy and ureter dissection are performed more carefully during living donor nephrectomy, which might justify the higher rate of complications in cadaveric renal transplant.

Many studies are available in the literature to use different strategies to manage renal transplant complications. However, there are few studies in referral centers with higher experience comparing different surgical or non-surgical modalities to treat post-transplantation ureteral complications. Therefore, in this study, we tried to compare the outcomes of native ureteropyelostomy and ureteroneocystostomy in ureteral complications following renal transplantation.

MATERIALS AND METHODS

The present study was a case-control study performed from 2010 to 2020. All patients who underwent renal transplantation at Hasheminejad Hospital affiliated with Iran University of Medical Sciences, Tehran, Iran, and presented with post-operative complications were assessed to enter the study. Hasheminejad Hospital is a large tertiary and referral center for kidney diseases.

Baseline demographic characteristics, complications, and surgical outcomes were recorded. Patients underwent native ureteropyelostomy or ureteroneocystostomy despite post-operative ureteral stenosis or failure.

Surgical Technique

Nephrectomy from a living donor or a cadaver was performed through midline incision intraperitoneally. A flank incision was done for right nephrectomy in obese patients or the presence of abdominal scars. Failure of ureteral anastomosis was detected by clinical suspicious and following paraclinical investigations such as urinary output monitoring, ultrasonography, and renal DTPA (Diethylenetriamine pentaacetate) scan.

If a reoperation was needed within eight weeks from the renal transplantation; a Lich-Gregoir ureteroneocystostomy was considered. However, if more than eight weeks passed, a native ureteropyelostomy was performed. Despite this, the surgical team's judgment was the key factor in deciding between the two options. The key factor to decide was the blood supply condition of the distal ureter.

To perform a ureteroneocystostomy, a 2 cm incision was performed, a detrusor muscle was inserted around the hiatus of the ureter, and a mucosal prolapse was created. Finally, a 1-cm incision perforated the bladder, and the new vesicoureteral anastomosis was made using 5-0 absorbable sutures. Finally, a Double-J was inserted. Ischemic parts of the ureter were resected, and the remaining viable ureter was anastomosed to the bladder dome.

Moreover, for Native ureteropyelostomy, a lower midline incision was made, and the posterior peritoneum was cut after shaving the bowel loops. The native ipsilateral (or contralateral one in case of ipsilateral ureter agenesia

Table 1: Comparison of demographic factors between the two surgical techniques.

Variables		Native ureteropyeloplasty	Ureteroneocystostomy	P-Value
Age (year)		39.85 ± 12.21	34.25 ± 13.43	0.416
BMI (kg/m^2)		24.02 ± 1.33	22.30 ± 2.99	0.186
Gender	Male	5 (71.4 %)	3 (37.5 %)	0.214
	Female	2 (28.6 %)	5 (62.5 %)	
KT waiting time (month)		22.28 ± 16.14	12.62 ± 6.25	0.232
Pre-KT dialysis duration (year)		1.66 ± 1.53	3.25 ± 3.96	0.534
Immunosuppressive therapy	Cyclosporine	3 (42.9 %)	5 (62.5 %)	0.405
	Tacrolimus	4 (57.1 %)	3 (37.5 %)	0.405
Donor type	Cadaver	6 (85.7 %)	2 (25 %)	0.032*
	Live	1 (14.3 %)	6 (75 %)	
ESRD etiology	PN	3 (42.9 %)	4 (50 %)	0.595
	SLE	2 (28.6 %)	0	0.200
	IgA nephropathy	1 (14.3 %)	1 (12.5 %)	0.733
	VUR	0	1 (12.5 %)	0.533
	MGN	1 (14.3 %)	0	0.467

*Significant difference (P<0.05)

Abbreviations: BMI; body mass index, KT; kidney transplantation, ESRD; end-stage renal disease, PN; pyelonephritis, SLE; systemic lupus erythematosus, VUR; vesicoureteral reflux, MGN; membranous glomerulonephritis

or previous damage) ureter of the host kidney was connected to the graft pelvis through an end-to-side anastomosis using 4-0 or 5-0 Vicryl. The proximal end of the host ureter was ligated using Vicryl 2-0. A standard Immunosuppression regimen was given to all patients. Patients were followed regarding the outcomes between the groups.

Ethical Considerations

All the steps of the study were performed according to the Helsinki Declaration. A written informed consent was obtained from all patients. The ethics committee of Iran University of Medical Sciences approved the study protocol. Patients could leave the study at any point without affecting their routine standard care. They were ensured regarding their information confidentiality.

Statistical Analysis

SPSS software version 20 (SPSS Inc. Chicago, Il, The USA) was used to analyze data. Mean and standard deviation or frequency and percentage were used to express quantitative and qualitative data, respectively. The Kolmogorov-Smirnov test was performed to check the normal distribution of data. Independent t-test and chi-square or their non-parametric counterparts, such as Mann-Whitney and Fisher's exact tests, were used where appropriate. A P-value below 0.05 was considered as statistically significant.

RESULTS

A total of 1316 kidney transplants were performed in our center during 2010 and 2020. Of these, 489 (37.15%) were from a cadaver donor, and 827 (62.85%) were from living donors. In total, 16 patients (1.21%) required reconstructive surgery postoperatively. The mean ± SD age of these patients was 38 ± 13.12 years (minimum and maximum 17 and 62 years). Nine patients (56.3%) were male, and 7 (43.8%) females. The mean and standard deviation of the waiting time until transplantation was 16.37 ± 12.44 months. The most

Table 2: Comparison of Intra- and post-operative outcomes between the two surgical techniques.

Variables		Native ureteropyeloplasty	Ureteroneocystostomy	P-Value
Ischemic time (min)		182.57 ± 72.10	91.63 ± 86.01	0.181
Suturing time (min)		36.29 ± 5.93	43.13 ± 2.58	0.011
Administered packed cell (N)		0.71 ± 0.95	0.25 ± 0.70	0.232
DJ insertion Duration (week)		3.00 ± 0.00	3.00 ± 0.75	1.000
Early complications	UTI	3 (42.9 %)	3 (37.5 %)	0.622
	Acute rejection	2 (28.6 %)	1 (12.5 %)	0.446
	ATN	1 (14.3 %)	1 (12.5 %)	0.733
Late Ureteral complications	Stenosis	6 (85.7 %)	4 (50 %)	0.182
	leakage	1 (14.3 %)	3 (37.5 %)	0.338
	Necrosis	0 (0.0 %)	1 (12.5 %)	0.533
Mortality		2 (28.6 %)	1 (12.5 %)	0.446
Hospital stays (day)		15.14 ± 6.81	16.50 ± 5.65	0.641

Abbreviations: DJ; double-J stent, UTI; urinary tract infection, ATN; acute tubular necrosis

common type of blood type in these patients was O^+ (43.8%), followed by A^+ (31.3%). Fifty percent of the transplants were from a cadaver, 18.8% from a relative living donor, and the rest were from a non-relative living donor. The mortality rate in these 16 patients was 18.8%, one due to endocarditis and the other two due to severe sepsis. The overall incidence of transplant rejection was 25% (4 patients). The main reason for reoperation was stenosis in 11 patients (68.8%). Other reasons were leakage in 3 patients, stenosis and leakage in one, and leakage and necrosis in another.

Seven patients (43.8%) underwent native ureteropyelostomy and 8 (50%) ureteroneocystostomy. One patient underwent ureteroneocystostomy at first, but due to the operation failure, he underwent a native ureteropyelostomy. The mean ± SD follow-up of these patients was 57.63 ± 37.74 months. There was no significant difference between the two reconstructive surgery techniques in terms of patients' background characteristics, waiting time for transplant surgery, duration of preoperative dialysis, type of immunosuppressive treatment, ESRD etiology, graft ischemic time, number of administered packed cells, duration of Double-J catheter, post-op complications, incidence of UTI, acute transplant rejection and ATN (Acute Tubular Necrosis), ureteral stenosis, urinary leakage, ureteral necrosis and finally mortality rate. Despite this, there was a significant difference between the two surgical techniques regarding the donor type, as most patients (75%) who underwent ureteroneocystostomy had received a graft from a living donor. Still, in the native ureteropyelostomy method, most patients had received a cadaver graft (85.7%) (Tables 1 and Table 2).

Furthermore, there was a significant decrease in creatinine levels after surgery in both native ureteropyelostomy (P= 0.001) and ureteroneocystostomy (P= 0.001). However, the trend of changes between the two surgical techniques did not show a significant difference (P= 0.329) (Table 3). Besides, serum creatinine levels six months after surgery were significantly higher in native ureteropyelostomy. Fig. 1 shows the trend of creatinine level changes between the two groups. Table 4 also depicts the detailed characteristics of these sixteen patients.

DISCUSSION

Renal transplantation is now the preferred treatment choice for patients with ESRD. Despite this, post-operative complications due to recipient underlying diseases, grafts, or tech

Table 3: Changing trends of serum creatinine level in the two surgical techniques.

Variables	Native ureteropyeloplasty	Ureteroneocystostomy	P-Value
Pre-surgery Cr (mg/dl)	6.58 ± 2.59	6.42 ± 2.70	0.909
1 month Post-surgery Cr (mg/dl)	2.88 ± 1.65	1.52 ± 0.75	0.057
6 months Post-surgery Cr (mg/dl)	2.41 ± 0.67	1.41 ± 0.50	0.006
12 months Post-surgery Cr (mg/dl)	1.77 ± 0.70	1.25 ± 0.36	0.111
Follow-up time (month)	44.86 ± 41.50	70.00 ± 35.00	0.225

Abbreviations: Cr; creatinine

nical issues need special and prompt attention. The most common complications after renal transplant include UTI, early rejection, ATN, ureteral stenosis, necrosis of the ureter or leakage, renal artery stenosis, renal artery and renal vein thrombosis, etc. [15-17]. Among these, ureteral stenosis, necrosis, or leakage might need reoperation or minimally invasive interventions. Therapeutic approaches in such circumstances include various options such as endourological or percutaneous interventions, reoperations for re-implantation, or even nephrectomy [18-20]. A decision from possibilities for each individual requires high expertise by the surgical team, considering the circumstances precisely because a wrong decision might lead to graft failure, nephrectomy, severe sepsis, and mortality. There is still debate about the best therapeutic surgical intervention, and few studies are available comparing these options prospectively.

The two most widely performed options in the literature to treat ureteral complications such as stenosis, leakage, or necrosis include native ureteropyelostomy and ureteroneocystostomy. However, a comparison between their advantages and disadvantages is less performed.

Uysal *et al.* [14] reported the management of post-operative complications in patients receiving a renal transplant. The rate of reoperation in their study was 6.25%, which is significantly higher than ours. Reoperation options included native ureteropyelostomy, ureteroneocystostomy, and ureteroureterostomy. The most common complication in their research was ureteral stenosis, which is in line with our study. They finally concluded that native ureteropyelostomy and ureteroneocystostomy are the two methods for corrective ureteral surgeries with low complications and good outcomes. The rate of complications was higher in this study, probably because the overall number of transplants in our study (1316 patients) was approximately eight times more than their study population (160 patients). This indicates a higher volume and probably more expertise in our center.

In another investigation by Lehmann *et al.* [21] studying the outcomes of 887 renal transplantation, ureteral complications were reported in 50 patients (5.6%). Patients underwent native ureteropyelostomy (35 patients) or ureterocystostomy (14 patients). Ureteral stenosis occurred more often in secondary surgery (10% compared to 3.6%, P= 0.039). In our study, only one patient needed a third operation. They reported that graft pyelonephritis was significantly lower in patients who underwent native ureteropyelostomy than ureterocystostomy (P= 0.019). They concluded that secondary surgery can effectively treat reflux and recurrent graft pyelonephritis. Despite this, we found no significant difference regarding UTI or ATN between the two surgical techniques. Further studies are still needed to elucidate more details of such restorative surgical options in the future.

Furthermore, Riediger *et al.* [22] reported that 26 of 646 (4%) who underwent renal transplantation needed a reoperation. Most of their patients (62%) underwent ureteropyelostomy by the ipsilateral recipient ureter, which was successful in 14 of 16 patients (87.5%). Consistent with our study, they found no association between underlying renal disease, immunosuppression regimen, etc., with the

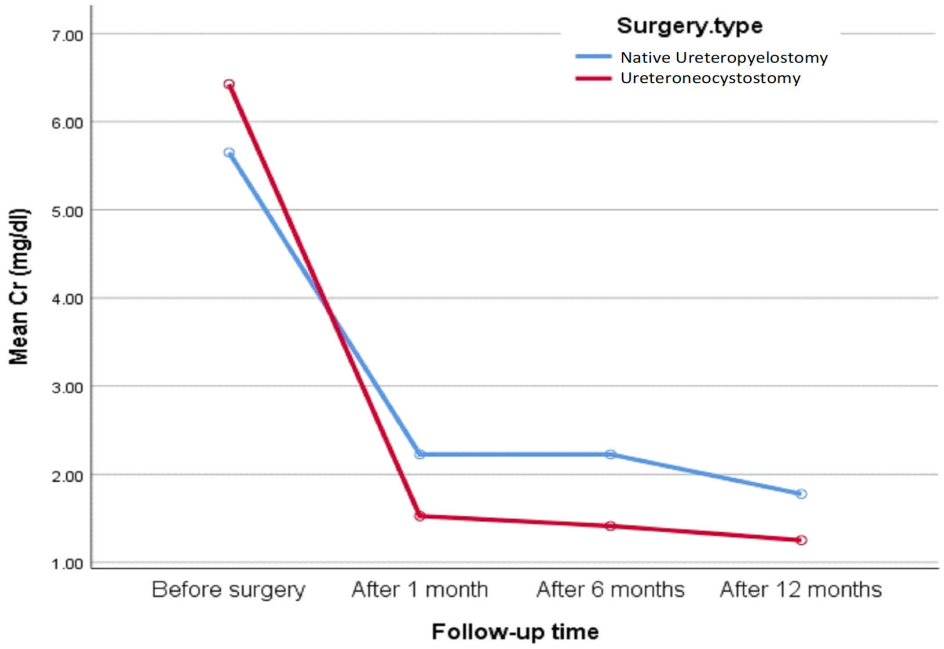

Figure 1: Changing trends of serum creatinine level.

risk of complications. They also reported successful outcomes in four patients after graft-urethrostomy, primary suturing, or fibrin gluing for small ureteral defects. We did not perform any primary repair of the defects because we think that impaired blood supply of the anastomosis increases the risk of failure of such repair. Some investigations claim that inadequate blood supply to the distal ureter, probably due to many dissections in renal transplantation surgery, is the main underlying reason for anastomosis complications [23]. They also reported that creatinine levels decreased after native ureteropyelostomy in 12-month follow-up visits. However, they did not compare different modalities regarding Cr level changes. However, in our study, patients who underwent ureteroneocystostomy had lower Cr levels than native ureteropyelostomy after six months. Still, there was no difference between the two modalities by passing time.

Moreover, there was a significant difference in our study between the two surgical techniques regarding the donor type, as most patients (75%) who underwent ureteroneocystostomy had received a graft from a living donor. Still, in the native ureteropyelostomy method, most patients had received a cadaver graft. The reason for such preference by our surgical team was the possibility of blood supply loss in the cadaver graft ureter during the harvest period. Also, as more time passed, the risk of blood loss to the distal ureter was increased; therefore, a native ureteropyelostomy seemed to be more logical. Loss of blood supply at the distal ureter from cadaver graft has been supported by many investigations [24, 25].

Moreover, a large series by E.H. Streeter et al. [26] assessing the outcomes of 1535 patients showed that the overall rate of urological complications was about 9.2%. The most common ones were ureteral obstruction or leak, which aligns with our trial. They also reported three mortality in their series, the same as our experience. The rate of mortality after renal transplantation has significantly decreased from 20% to less than one percentage in recent studies, which could be largely due to prompt diagnosis and treatment of post-operative complications and enhanced techniques of transplantation [27-29]. Streeter et al. also found no association between the risk of ureteral complications and recipient age, graft type, cold ischemia time, etc. They claimed that the degree of vascular compromise at the anastomosis site could determine the inter

Table 3: Detailed characteristics of the study Individuals.

Number	Age (year)	Gender	Donor type	Underlying Disease	Early urinary complications	Late urinary complications	Operative procedure	IS	Biopsy pathology
1	46	M	Cadaver	PN	ATN	Ureteral stenosis	NUPS+DJ	Tac/ MMF/ Cort	
2	33	F	Living	SLE	UTI & Acute rejection	Ureteral stenosis	NUPS+DJ	Cycl/ MMF/ Cort	Rejection
3	31	M	Cadaver	Not specified	Acute rejection	Ureteral stenosis	NUPS+DJ	Cycl/ MMF/ Cort	
4	47	M	Cadaver	Not specified	No	Urinary leak	UNCS+DJ	Tac/ MMF/ Cort	
5	55	M	Living	PN	UTI	Ureteral stenosis & urinary leak	UNCS & NUPS+DJ	Cycl/ MMF/ Cort	
6	25	M	Living	IgA nephropathy	UTI	Ureteral stenosis	UNCS+DJ	Cycl/ MMF/ Cort	
7	20	F	Living	PN	Acute rejection	Ureteral necrosis & urinary leak	UNCS+DJ	Cycl/ MMF/ Cort	
8	38	M	Cadaver	PN	UTI	Ureteral stenosis	NUPS+DJ	Tac/ MMF/ Cort	Rejection
9	50	M	Living	PN	No	——	UNCS+DJ	Cycl/ MMF/ Cort	
10	25	M	Cadaver	SLE & MGN	No	Ureteral stenosis	NUPS+DJ	Cycl/ MMF/ Cort	
11	50	F	Cadaver	PN	ATN	Urinary leak	UNCS+DJ	Tac/ MMF/ Cort	
12	17	F	Living	VUR	UTI	Ureteral stenosis	UNCS+DJ	Tac/ MMF/ Cort	
13	35	F	Living	PN	UTI	Ureteral stenosis	UNCS+DJ	Cycl/ MMF/ Cort	Rejection
14	30	F	Living	SLE	No	Ureteral stenosis	UNCS+DJ	Cycl/ MMF/ Cort	
15	62	M	Cadaver	IgA nephropathy	No	Urinary leak	NUPS+DJ	Tac/ MMF/ Cort	
16	44	F	Cadaver	PN	UTI	Ureteral stenosis	NUPS+DJ	Tac/ MMF/ Cort	Rejection

Abbreviations: IS; immunosuppression, M; male, F; female, PN; pyelonephritis, SLE; systemic lupus erythematous, MGN; membranous glomerulonephritis, VUR; vesicoureteral reflux, ATN; acute tubular necrosis, UTI; urinary tract infection, NUPS; native ureteropyelostomy, UNCS; ureteroneocystostomy, DJ; double-J stent, Tac; tacrolimus, Cycl; cyclosporine, MMF; mycophenolate sodium, Cort; corticosteroids

vention according to the surgeon's judgment. Small defects with less blood supply compromise were managed using over-suturing and nephrostomy to re-anastomosis, as well as the Boari flap. We believe that the surgical team experience is especially highlighted here to help you decide between a variety of options. However, we suggest performing a more definite procedure such as re-anastomosis or native ureteropyelostomy in case of any doubt, especially in lower volume centers for renal transplantation. Because long-term outcomes after native ureteropyelostomy have been promising in many studies such as ours, the risk of a tertiary explorative laparotomy might not be acceptable for such ESRD patients. Hence, the secondary corrective operation should not leave any doubt behind as much as possible.

We had some limitations. We did not perform other options (e.g., Taguchi, Bari) and only used two surgical methods to treat postop ureteral complications. Therefore, generalization of results to other techniques is not possible. However, we had many strong points. Our study population was large enough, and many factors that were thought to be involved in developing complications were assessed. The novelty of our study was that this was among very few studies comparing two methods of native ureteropyelostomy and ureteroneocystostomy in a referral center with a high level of experience. Also, we reported a detailed comparison regarding postop Cr changing trends after the two techniques. Finally, we suggest performing meta-analyses and systematic reviews to gather information from large studies to elucidate more aspects of restorative surgeries after renal transplantation. Also, the effect of different immunosuppression regimens has been studied less, which is suggested to be considered in further trials.

In conclusion, native ureteropyelostomy and ureteroneocystostomy effectively treat post-op ureteral complications with good results. We suggest performing native ureteropyelostomy if more than eight weeks have passed from renal transplantation and if distal ureter blood supply is under question.

CONFLICTS OF INTEREST: None declared.

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