

Long-Term Results of Posterolateral Extravesical Ureteroneocystostomy and its Comparison with the Conventional Anterior Extravesical Ureteroneocystostomy Method in the Management of Urologic Complications in Kidney Transplant Patients

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Purpose: Urological complications are common and serious in kidney transplant patients. Correct diagnosis of urological complications and rapid intervention are very important to maintain the transplanted organ. Using endoscopic methods and rapid access to ureteral orifice can be effective in treatment and management of urological complications in transplant patients.

Materials and Methods: In this retrospective cohort study, 934 medical records of kidney transplant patients who underwent surgery through Posterolateral Extravesical Ureteroneocystostomy (PLEVUNC) and anterior extravesical ureteroneocystostomy (AEVUNC) techniques from 2011 to 2018 were evaluated. The outcomes of PLEVUNC and AEVUNC techniques were evaluated in 461 and 473 transplant patients, respectively. The patients were followed up for 60 months. Immediate and delayed complications, urological complications requiring endoscopic intervention, duration of access to ureteral orifice, as well as ureteroscopic and endoscopic outcomes were evaluated.

Results: The mean and \pm SD (standard deviation) age of patients in PLEVUNC and AEVUNC groups were 46.27 ± 2.7 years and 47.3 ± 3.6 years, respectively. Urinary leakage and UTI were the most common immediate (7% and 6.2%) and delayed (5.5% and 5.5%) complications in both groups, respectively. The time to find ureteral orifice in patients requiring endoscopic intervention was significantly shorter in PLEVUNC group 3.5 ± 1.2 compared with the AEVUNC group 10 ± 4.5 ($P < .001$). In 100% of PLEVUNC group and 62.6% of AEVUNC group, ureteral orifice of transplanted kidney was observed ($P < .001$). Ureteroscopy was reported successful in 94.5% and 37.4% of patients in PLEVUNC and AEVUNC groups, respectively.

Conclusion: Easy and safe access to the ureteral orifice and to the upper urinary tract in transplant recipients can be achieved with the PLEVUNC technique. In case of urological complications this method facilitates endoscopy.

Keywords: kidney transplantation; ureteroneocystostomy; urological complications; urologic surgical procedures

INTRODUCTION

The number of chronic renal failure patients needing alternative treatment is increasing annually. The treatments put a great economic and social burden on the health system.⁽¹⁾ There are three treatment methods for patients with End-Stage Renal Disease (ESRD): hemodialysis, peritoneal dialysis and kidney transplantation.⁽²⁾ The most appropriate and effective treatment for patients with ESRD is kidney transplantation.^(3,4) In fact the goal of kidney replacement therapy is to increase the patients' survival rate and quality of life.⁽¹⁾ The incidence of urological renal complications after transplantation has been reported in 3.8% of all recipients.^(5,6) Although there has been a significant improvement in the incidence of such complications in the last decade, urological complications are still common. Anterior Extravesical Ureteroneocystostomy in kidney transplantation has become popular because it is an easy technique to perform⁽⁷⁻¹⁰⁾. Modern endoscopic in-

struments have made it possible to use endoscopic procedures in kidney and urinary tract.^(11,12)

Anterior Extravesical Ureteroneocystostomy (Lich-Gregoire) is usually an easy and fast method for ureteral reimplantation. However, this procedure has been severely criticized due to difficult endoscopic access to the reimplanted ureter and the transplanted kidney. In the AEVUNC method, reimplantation is usually performed on bladder dome in a filled bladder, and the angle between the orifice of the reimplanted ureter and the ureteroscopic device is about 90 degrees. In the last two decades, endourology interventions have been introduced as acceptable methods for the management of urological complications following kidney transplantation.^(13,14)

Previously and traditionally, ureteral obstruction was managed by open surgery, which was associated with significant morbidity and mortality. Nowadays, endourological techniques such as intra-luminal ureteral

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Table 1. Determination and comparison of demographic variables in the two groups.

Variable a	PLEVUNC (N= 461)	AEVUNC (N=473)	P-value
Gender, N			
Male	316 (68.5)	319 (67.4)	.71
Female	145 (31.5)	154 (32.6)	
Age (year); mean \pm SD, (range)	47.3 \pm 3.6 (17-62)	46.2 \pm 2.7 (19-59)	.12
Duration of dialysis before transplantation (year)	3.5 \pm 0.8 (1-9)	2.5 \pm 0.6 (1-8)	< 0.001
Duration of transplant surgery (minutes)	125 \pm 21 (110-140)	120 \pm 17 (107-139)	< 0.001
Preoperative creatinine	8.2 \pm 1.2 (6.5-11)	8.3 \pm 1.1 (7-11)	.18
Preoperative BUN	90.4 \pm 14.1 (80-115)	95.7 \pm 16.2 (80-120)	< 0.001

Abbreviations: PLEVUNC, Posterolateral Extravesical Ureteroneocystostomy; AEVUNC, anterior extravesical ureteroneocystostomy; SD, standard deviation

^aContinuous variables were compared by independent samples *t*-test

balloon dilatation and ureterotomy are associated with a high success rate.⁽¹⁾ Catheterization and passage of endourological equipment as well as subsequent endourological procedures in AEVUNC technique are difficult, time consuming, and sometimes impossible.⁽⁴⁾ Inability to manage complications with endoscopic procedures can lead to open surgery.^(4,6) The need for an alternative method of ureteroneocystostomy has become apparent because it results in better access to ureter and facilitates endourological interventions.^(1,5,6) Based on this, Therefore, it is claimed that by performing the alternative method of ureteroneocystostomy, the ureter orifice is more accessible and endoscopic interventions are more possible. This study was an attempt to compare and evaluate the long-term outcomes of PLEVUNC and AEVUNC ureteral reimplantation techniques to facilitate the endoscopic management of urologic complications in kidney transplant patients. Also we compared the abovementioned reimplantation techniques in terms of access to orifice of reimplanted ureter.

MATERIALS AND METHODS

Study Population

In this retrospective cohort study, medical records of 934 kidney transplant patients who underwent ureteral reimplantation with AVUNC and PLVUNC techniques were evaluated. All the patients were referred to Shahid Modarres Hospital, affiliated to Shahid Beheshti University of Medical Sciences, from 2011 to 2018. According to clinical conditions, the patients were assigned to one of the AVUNC and PLVUNC surgical techniques groups by the surgeon. The number of patients in PLEVUNC and AEVUNC groups were 461 and 473, respectively. Demographic characteristics of all 934 patients were recorded in a checklist. All donors were live unrelated. Immunosuppressive treatment protocols included induction with globulin antithymocytes

and maintenance therapy with prednisolone, tacrolimus or cyclosporine, and mycophenolate mofetil.

Procedures

The basic technical principles of the PLEVUNC that we have utilized are described briefly: The bladder was filled with saline solution and a 1-cm full-thickness incision was done in the posterolateral wall of the bladder to expose bladder mucosa while applying medial retraction on anterior bladder wall. An ellipse of mucosa was excised from the distal apex. At the distal segment of the ureter, a 1-cm lateral ureteral spatulation is performed and the edges were trimmed. Stent (7-Fr silastic urologic J-J stent) was left in the ureter and apical stitch was placed in spatulated ureter and passed inside out through most caudal portion of mucosal opening. The anastomosis of the mucosa of the bladder to the spatulated lower ureter was made using interrupted 4-0 Vicryl sutures. Detrusor muscle was subsequently closed over the anastomosis using 4-0 Vicryl in interrupted fashion to create the antireflux mechanism. A distal fullthickness anchoring suture was used to keep the ureter from sliding cephalad in a submucosal tunnel.⁽¹³⁾ After surgery, all patients were visited every month in the first year and then every 6 months for 5 years (60 months). They underwent physical and biochemical examination. At each visit, patients were evaluated by careful ultrasound and tests for urinary tract infections or signs of transplant rejection attacks and obstructive complications.

Evaluations

When a urological complication was suspected, various interventions such as IVP, DTPATC99M and CT scan were used. For all patients with persistent leakage in the surgical field, fluid analysis was performed. Hydronephrosis on ultrasound, obstructive uropathy on DTPA scanning, and increased creatinine were considered as ureteral obstruction. A month after the surgery, all pa-

Table 2. Causes of renal failure in the two study groups.

Variables	PLEVUNC (N= 461)	AEVUNC (N=473)	P-value
Nephrotic syndrome	10 (2.17)	9 (1.90)	.95
Pyelonephritis	27 (5.86)	33 (6.98)	
V.U.R	6 (1.30)	3 (1.06)	
Glomerulonephritis	45 (9.76)	41 (8.67)	
Hypertension	133 (25.88)	136 (28.76)	
Diabetes mellitus	100 (21.70)	108 (22.83)	
Polycystic kidney	37 (8.03)	32 (6.77)	
kidney stone	29 (6.29)	31 (6.55)	
Amyloidosis	1 (0.22)	0 (0)	
Lupus	3 (0.65)	2 (0.42)	
Unknown	70 (15.18)	78 (16.4)	

Abbreviations: PLEVUNC, Posterolateral Extravesical Ureteroneocystostomy; AEVUNC, anterior extravesical ureteroneocystostomy

Table 3. Immediate and delayed complications in the two study groups.

	Variables	PLEVUNC (N= 461)	AEVUNC (N=473)	P-value
Immediate complications	Urinary Leakage	32 (7)	29 (6.2)	.92
	Urosepsis	0 (0)	1 (0.2)	
	Significant hematuria	2 (0.4)	2 (0.4)	
	Ureteral necrosis	0 (0)	0 (0)	
	Hydronephrosis after stent removal	17 (3.7)	19 (4)	
	Hematoma around the transplanted kidney	4 (0.8)	5 (1)	
	No Complication	406 (88)	417 (88.2)	
Delayed complications	lymphocele	4 (0.8)	5 (1)	.61
	Vesicoureteral reflux	2 (0.4)	8 (1.7)	
	Urinary fistula	0 (0)	0 (0)	
	UVJ Obstruction	9 (2)	11 (2.3)	
	Urinary system stones	9 (2)	8 (1.7)	
	UTI	25 (5.5)	26 (5.5)	
	Miss JJ stent	2 (0.4)	3 (0.6)	
	No Complication	410 (88.9)	412 (87.2)	

Abbreviations: PLEVUNC, Posterolateral Extravesical Ureteroneocystostomy; AEVUNC, anterior extravesical ureteroneocystostomy

tients underwent cystoscopy and the ureteral orifice was observed.

In patients who needed endourological surgery intervention due to complications, we initially attempted to access to the urinary system with endoscopic devices. Transplant results in the two groups were compared in terms of ureteral and non-ureteral urological complications. In both groups, a total of 145 patients required endoscopic intervention. Patients in the two groups were also compared based on successful ureteroscopy and manipulation Normal ureteroscopy was defined as success in reaching the pelvis of transplanted kidney. Main outcomes of this study were time to find ureteral orifice, ureteral orifice of transplanted kidney, and rate of successful ureteroscopy. Moreover, immediate and delayed complications and urological complications were primary and secondary outcomes. In order to comply with research ethics, all patients participating in the study were informed of the study.

Ethical considerations

This study was approved by the ethics committee of Shahid Beheshti University of Medical Sciences and registered with the code IR.SBMU.MSP.REC.1399.221.

Statistical Analysis

Categorical variables are expressed as frequency (percentage) and continuous variables are reported as Mean ± SD. T-test was used for comparison of continuous data. Categorical data was compared by using Chi-square test and Fisher exact test. All statistical analysis was performed by STATA software version 16. *P* < .05 was considered as statistically significant.

RESULTS

The results of this study showed that in PLEVUNC group, 316 patients were male (68.5%) and 145 were female (31.5%) while in AEVUNC group, 319 patients were male (67.4%) and 154 were female (32.6%). The mean ± SD age in duration PLEVUNC group was 47.3 ± 3.6 and in AEVUNC group was 46.2 ± 2.7. There was no significant difference between the two groups of the patients in terms of sex and preoperative creatinine (*P* > .05) (Table 1). The mean ± SD of transplant surgery in PLEVUNC group was 125 ± 21 minutes and in AEVUNC group was 120 ± 17 minutes.

There was no significant difference between the two groups in terms of causes of renal failure (*P* = .95). The most common causes of renal failure in two groups were hypertension (25.88% and 28.76%) and diabetes mellitus (21.70% and 22.83%) (Table 2).

In more than 88.9% of patients in PLEVUNC group and 87.2% patients in AEVUNC groups, no immediate and delayed complications were reported. There was no significant difference between the two groups in terms of immediate and delayed complications (*P* > .05). The most common delayed complication was UTI (5.5% in both groups). Vesicoureteral reflux as a urinary complication in AEVUNC method was four times more than PLEVUNC (1.7% Vs 0.4 %). In both PLEVUNC and AEVUNC groups, urinary leakage was the most common immediate complication (7% and 6.2%, respectively) (Table 3).

The most common urological complication requiring endoscopic intervention in the two study groups was urinary leakage.

The PLEVUNC group had a urological complication

Table 4. Urological complications requiring endoscopic intervention in the two study groups

Variables	PLEVUNC (N=461)	AEVUNC (N= 473)	P-value
Urinary Leakage	32 (6.9)	29 (6.1)	.99
Hydronephrosis after stent removal	17 (3.7)	19 (4)	
lymphocele	4 (0.8)	5 (1)	.61
Delayed UVJ Obstruction	9 (1.9)	11 (2.3)	
Urinary system stones	9 (1.9)	8 (1.7)	.61
Miss JJ stent	2 (0.4)	3 (0.6)	
No Urologic Complications	388 (84.2)	398 (84.1)	

Abbreviations: PLEVUNC, Posterolateral Extravesical Ureteroneocystostomy; AEVUNC, anterior extravesical ureteroneocystostomy

Table 5. Data regarding ureteroscopy.

Variables ^a	PLEVUNC (N= 461)	AEVUNC (N=473)	P-value
Mean time to find ureteral orifice (min)	3.5 ± 1.2 (2.5-6)	10 ± 4.5 (7-11)	< 0.001
Finding of Ureteral orifice of transplanted kidney	73 (100)	47 (62.5)	< 0.001
Successful ureteroscopy	69 (94.5)	28 (37.5)	< 0.001

Abbreviations: PLEVUNC, Posterolateral Extravesical Ureteroneocystostomy; AEVUNC, anterior extravesical ureteroneocystostomy

^a Continuous variables were compared by independent samples *t*-test

requiring endoscopic intervention rate of 15.8%, which did not significantly differ from those in AEVUNC group (15.9%) ($P = .99$). Urinary leakage was encountered in 32 (6.9%) patients in PLEVUNC group and 29 (6.1%) in AEVUNC group (**Table 4**).

The results showed that the time to find ureteral orifice in patients requiring endoscopic intervention was significantly shorter in PLEVUNC group compared with that of the AEVUNC group (3.5 ± 1.2 minutes vs. 10 ± 4.5 minutes) ($P < .001$) (**Table 5**). In 73 (100%) of PLEVUNC group and 47 (62.6%) of AEVUNC group, ureteral orifice of transplanted kidney was observed ($P < .001$). The results showed that the success rate of ureteroscopy in PLEVUNC group was significantly higher than that of the AEVUNC group. The success rate of ureteroscopy in PLEVUNC and AEVUNC groups were 69 (94.5%) and 28 (37.4%), respectively ($P < .001$) (**Table 5**).

The results of this study showed that 407 patients (88.2%) in PLEVUNC group and 420 patients (88.8%) in AEVUNC group did not have chronic graft nephropathy. The mean creatinine one year after the surgery was 1.34 in the PLEVUNC group and 1.37 in the AEVUNC group, there was no significant difference between the two groups ($P = .19$).

DISCUSSION

One of the major concerns in ureteroneocystostomy is endurological access to the ureter after transplantation. In this study, the success rate and ease of access to the ureter and endoscopic interventions in two methods PLEVUNC and AEVUNC were evaluated. The most common causes of renal failure in two groups were hypertension (25.88% and 28.76%) and diabetes mellitus (21.70% and 22.83%), respectively. In more than 88% of the patients, no immediate and delayed complications were reported. In both PLEVUNC and AEVUNC groups, urinary leakage was the most common immediate complication (7% and 6.2%, respectively).

There was no significant difference between the two groups in terms of immediate and delayed complications ($P > .05$). The most common delayed complication was UTI (5.5% in both groups). Vesicoureteral reflux as a urinary complication in AEVUNC method was four times more than that of PLEVUNC (1.7% Vs 0.4 %). In the PLEVUNC method, the angle created by the spatula helps to prevent vesicoureteral reflux. The inner part of the ureter is surrounded by the muscles of the posterior bladder wall, which inverts the ureteral mucosa inside the bladder lumen.⁽¹³⁾ In a study by Sanei et al., which evaluated urological complications in two Full-Thickness Single Layer Anastomosis and Lich-Gregoir methods, vesicoureteral reflux was reported as 7.4% in the Lich-Gregoir group⁽¹⁴⁾ which was higher than the results of our study. In a study by Balaban et al. they concluded that endoscopic treatment of sympto-

matic VUR in transplanted kidney is a safe and feasible procedure.⁽¹⁵⁾

There were no urological complications, requiring endoscopic intervention, in 84% of the patients in both groups. There was also no significant difference between the two groups in terms of urological complications requiring endoscopic intervention ($P > .05$). In our study urinary leakage was the most common urological complication. In the previous studies, urinary leakage has been reported as one of the most common urological complication after transplantation.^(12,14,18)

In endoscopy procedure, easy and safe access to reimplanted ureter and renal pelvis is important. The results of our study showed that the time to find ureteral orifice in patients requiring endoscopic intervention was significantly shorter in PLEVUNC group compared with that of AEVUNC group (3.5 minutes vs. 10 minutes), ($P < .001$). PLEVUNC provides approximate anatomical location for the ureteral orifice, as well as approximate normal anatomical alignment for the ureter. In this method, ureteral reimplantation is performed in the posterior side of the bladder, which is closer to the anatomical location of the ureteral orifice, as a result endoscopic procedures and finding the new ureteral orifice is easier.⁽¹³⁾ Reoperation on transplanted kidneys is associated with a significant increase in morbidity and mortality. The mortality rate for patients who underwent open correction of ureteral stenosis has been reported as 8%.⁽¹⁹⁾ Currently, the first treatment for ureteral obstruction in a transplanted kidney is endoscopy.⁽²⁰⁾ The first option for treatment of ureteral obstruction, which occurs in 2% to 10% of renal transplant patients postoperatively is interventional radiological methods. If all of these methods are unsuccessful, surgical treatment should be applied.⁽²¹⁾

In our study in 100% (73 patients) of PLEVUNC group and 37.4% (28 patients) of AEVUNC group, ureteral orifice of transplanted kidney was observed during the procedure ($P < .001$). Ureteroscopy success rate was 94.5% (69 patients) in PLEVUNC group and 37.4% (28 patients) in AEVUNC group and the difference between two groups was statistically significant ($P < .001$).

There are limited studies related to our study topic. In the previous study by Dadkhah et al, done with a fewer patients, conducted with the aim of easier access to the upper urinary tract in transplanted kidney with the help of endoscopic devices, the results of renal transplantation comparing two techniques of AEVUNC and PLEVUNC were evaluated. They also compared ureteral and nonureteral complications at 36- to 51-month follow-up. The results showed that access to ureteral orifice and endoscopic interventions were easier in PLEVUNC than AEVUNC methods and the general complications of PLEVUNC technique were not significantly different from that of the AEVUNC, which is the usual method.⁽¹³⁾ Krajewski et al. concluded in

their study that most urological complications could be successfully treated with endourological procedures and kidney function improved in most patients.⁽¹⁶⁾ In the study by Ooms et al., 50 patients who had ureter stricture following kidney transplantation were treated with antegrade balloon dilatation which was technically successful in 86%.⁽¹⁷⁾ Endoscopic treatment of ureteral stenosis after kidney transplantation is recommended to prevent complications of open surgical treatment.⁽¹⁸⁾ The present study was performed with a higher statistical population and longer follow-up of patients. It confirmed the success and ease of access of endourology interventions in reimplanted patients with PLEVUNC technique. Limitation of this study is, the study was performed as a retrospective group and it could have been done as a clinical trial. The study was also conducted at a center.

CONCLUSIONS

The study showed that ureteroneocystostomy by PLEVUNC method provides easy and safe access to the ureteral orifice and upper urinary tract in kidney transplant recipients.

This method facilitates endoscopic intervention in case of urological complications. Therefore, it is recommended to use PLEVUNC method instead of AEVUNC method in kidney transplantation.

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CONFLICT ON INTEREST

The authors declare that there is no conflict of interest.

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