The Prevalence of Redo-Ureteroneocystostomy and Associated Risk Factors in Pediatric Vesicoureteral Reflux Patients Treated with Ureteroneocystostomy

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Purpose: The aim of the study was to examine the prevalence of redo-ureteroneocystostomy (redo-UNC) in pediatric vesicouretheral reflux (VUR) patients following open UNC and factors associated with redo-UNC.

Material and methods: Data on 122 patients who underwent open UNC for VUR were analyzed in this retrospective case–control study. The patients were divided into a successful initial UNC group (UNC group, control) and an unsuccessful initial UNC group (redo-UNC group, case). The following variables were analyzed: sex, age, dysfunctional voiding, laterality of VUR (unilateral or bilateral), VUR grade, etiology of VUR (primary or secondary), relative renal function on renal scintigraphy, and surgical technique. The use of the following procedures in the initial UNC was recorded: an endoscopic subureteric injection(ESI) and ureteral tapering.

Results: In our clinic, 122 patients (177 ureters), with an average age of 55.7 ± 41.2 months (range, 1–18 years) underwent open UNC for VUR between November 2005 and June 2014. Of these,67 (55%) had unilateral VUR, and 55 (45%) had bilateral VUR. There were 127 (71.8%) cases of grade 4–5 reflux. Postoperatively, hydronephrosis was noted in 19 (15.6%) patents. Ten (8.2%) patients underwent redo-UNC. In eight cases (6.5%), redo-UNC was performed because of ureterovesical (UV) junction obstruction.In the other two cases (1.7%), redo-UNC was due to high-grade reflux. There were no statistically significant differences between the redo-UNC and UNC groups in any of the variables studied.

Conclusion: Redo-UNC was required in 10 (8.2%) of cases after UNC. Age, sex, laterality of VUR, VUR grade, existence of primary or secondary VUR, relative renal function on renal scintigraphy, UNC technique, ESI procedure, and ureteral tapering were not risk factors for redo-UNC in our series.

Keywords: re-ureteroneocystostomy; ureteroneocystostomy; vesicoureteral reflux

INTRODUCTION

Operative and nonoperative options are available for the treatment of vesicoureteral reflux (VUR). Endoscopic VUR treatment has become popular during the last 20 years as an alternative to open procedures. Endoscopic VUR treatment is widely used due to its ease of use, ready availability, and absence of complications in outpatients[1-4]. Conversely, the use of ureteroneocystostomy (UNC) for VUR has shown a declining trend. Although UNC has a high success rate[5-7], redo-operations are required in some cases. According to the literature, VUR persisted in 19.3% of cases with high-grade reflux who underwent UNC, and 0.3–9.1% of these cases required reoperations[6]. There is a paucity of studies on the risk factors for redo-ureteroneocystostomy (redo-UNC). Redo-UNC after failed open correction of VUR can be a challenging procedure because of scar formation at the anastomosis site and decreased vascularity of the ureter[5,7]. The aim of this study was to examine the prevalence of redo-UNC in children treated by UNC for VUR and to identify factors that can predict the success or failure of UNC.

PATIENTS AND METHODS

Study population

Data on 122 children with VUR who underwent open surgery interventions in our clinic between November 2005 and June 2014 were analyzed retrospectively. The study was approved by the hospital's local ethics committee (2013/203).

VUR was diagnosed in patients with various complaints, such as urinary tract infections (UTIs), a neurogenic bladder, voiding dysfunction, and antenatal hydronephrosis. It was also diagnosed by sibling screening. The classification system used by the International Reflux Study Group was used for grading reflux on voiding cystourethrography[8].

The study included all pediatric surgical patients with

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Table 1. Comparison results of the the two groups

	Redo-UNC Group (n= 10)		UNC Group (n=112)		
	n	%	n	%	*P*
Sex					
Female	6	60	63	56.2	1.000
Male	4	40	49	43.8	
Diagnosis					
Primary	6	60	77	68.8	0725
Secondary	4	40	35	31.2	
Side					
Unilateral	3	30	64	57.1	0.183
Bilateral	7	70	48	42.9	
Initial intervention					
STING	5	50	49	43.8	0.749
UNC	5	50	63	56.2	
Surgical technique					
Cohen	6	60	51	45.5	0.651
Politano Leadbetter	4	40	47	42	
Lich–Gregoir	0	0	14	12.5	
Tapering					
Applied	2	20	4	3.6	0.076
Not applied	8	80	108	96.4	
VUR grade					
1–2	0	0	9	8	0.325
3	1	11	27	24	
4-5	9	89	76	67	
Scintigraphy					
Good	1	10	28	25	0.493
Average	4	40	47	42	
Poor	5	50	37		
Voiding dysfunction					
Yes	2	20	29	26	0.682
No	8	80	83	74	

primary or secondary reflux etiology. The exclusion criteria were as follows: treatment not completed in our clinic, treatment initiated in another clinic, absent data during file screening, medical treatment without surgical interventions, and endoscopic treatment without open procedures or other initial surgical interventions (e.g., ureteropelvic obstruction, urolithiasis, primary obstructive megaureter, and extrophia vesica).

Preoperative evaluation procedure

In our series, an open surgical intervention was selected as the first choice in patients aged 1 year and older with bilateral/unilateral high-grade reflux or kidney function loss in follow-up detected on scintigraphy. Open surgery was also performed in cases of failure of the endoscopic subureteric injection (ESI) procedure and in patients with recurrent UTIs.

Before UNC, urine culture, urinary system ultrasonography (USG), and renal scintigraphy technetium-99m mercaptoacetyltriglycine 3 (MAG 3) were performed in all patients. Differential kidney function was classified as follows: 40–50%, good; 20–39%, average; and 0–19%, poor[1]. In all patients, lower urinary tract dysfunction were evaluated based on a voiding diary and symptom scoring systems[9]. Patients thought to have voiding dysfunctionunderwent urodynamic testing. Bladder training, constipation treatment, anticholinergic treatment, and biofeedback were prescribed, as appropriate. The treatment was continued for at least 3 months before the surgical intervention.

Surgical technique

In our clinic, the Cohen, Politano–Leadbetter, or Lich–Gregoir techniques were applied as open surgical methods. In the selection of the surgical technique, reflux grade, ureter dilatation, and the surgeon's preference were taken into consideration. For patients undergoing UNC with the Cohen and Politano–Leadbetter techniques, a 6 French ureteral catheter and perivesical Penrose drain were inserted and then removed at the end of the 7th postoperative day. Ureteral tapering was applied in cases of advanced ureteral dilatation, and ureteral catheters were left for 10 days in these patients. A ureteral catheter was not used for patients undergoing UNC with the Lich–Gregoir method. In all cases, an age-appropriate bladder catheter was inserted at the beginning of the operation and removed 24 h later when the ureteral catheter was removed. Circumcision was performed routinely in all boys with VUR to decrease the risk of UTIs.

Redo-UNC technique

Dissection of the bladder from the anterior abdominal wall requires careful attention. Intravesical and extravesical dissection of the ureter and extensive mobilization are required to achieve an adequate submucosal tunnel. The ureter was carefully evaluated, and ischemic segments were excised. The Politano–Leadbetter type re-ureteroneocystostomy was performed in all redo-UNC patients

Outcome assessment

All the patients underwent renal USG in the first month following ureteral reimplantation to detect hydronephrosis and possible obstructions. Mild dilation was expected due to transient edema. Patients with moderate or worsening hydronephrosis underwent monthly USG for 3 months due to the suspicion of an obstruction. Asymptomatic postoperative hydronephrosiswas assessed by comparing the degree of postoperative hydronephrosis to preoperative USG images.

Voiding cystouretrography (VCUG) was performed in the 6th month postsurgery, and scintigraphy and renal function were evaluated again in the first year after the operation. During the postoperative follow-up, patients who reported reflux persistence and in whom hydroureteronephrosis had increased were re-evaluated by urodynamics. Cystoscopy was applied in cases of obstruction for the evaluation of the ureterovesical (UV) junction, and the location of the obstruction was identi-

Table 2. Comparison of data in the two groups.

	Redo-UNC group (n= 10) n(%)	UNC group (n=112) n (%)	P
Sex			
Female	6 (60)	63 (56.2)	1.000
Male	4 (40)	49 (43.8)	
Diagnosis			
Primary	6 (60)	77 (68.8)	.725
Secondary	4 (40)	35 (31.2)	
Side			
Unilateral	3 (30)	64 (57.1)	.183
Bilateral	7 (70)	48 (42.9)	
Initial intervention			
ESI	5 (50)	49 (43.8)	.749
UNC	5 (50)	63 (56.2)	
Surgical technique			
Cohen	6 (60)	51 (45.5)	.651
Politano–Leadbetter	4 (40)	47 (42)	
Lich–Gregoir	0 (0)	14 (12.5)	
Tapering			
Applied	2 (20)	4 (3.6)	.076
Not applied	8 (80)	108 (96.4)	
VUR grade			
1–2	0 (0)	9 (8)	.325
3	1 (11)	27 (24.1)	
4–5	9 (89)	76 (67.9)	
Scintigraphy			
Good	1 (10)	28 (25)	.493
Average	4 (40)	47 (42)	
Poor	5 (50)	37 (33)	
Voiding dysfunction			
Yes	2 (20)	29 (26)	.682
No	8 (80)	83 (74)	

fied by synchronic retrograde pyelography.
A redo procedure was performed in the following cases: an increase in hydronephrosis as a result of an obstruction or renal parenchymal thinning with renal function loss and high-grade reflux on follow-up.

Study design

In this retrospective case–control study, the patients were divided into a successful initial UNC group (UNC group, control) and an unsuccessful initial UNC group (redo-UNC group, case). These two groups were then compared in terms of sex, age of operation, laterality of VUR (unilateral or bilateral), VUR grade, VUR etiology (primary or secondary), dysfunctional voiding, relative renal function on renal scintigraphy, and UNC technique. In addition, the use of the following procedures in the initial UNC was recorded: ESI and ureteral tapering.
The Mann–Whitney *U* test, Fisher's exact test, and X^2 test were used, as appropriate based on data characteristics and distribution. All analyses were performed using the Statistical Package for the Social Sciences, version 22.0 (IBM SPSS, Inc., Chicago, IL, USA). *P*-values of < 0.05 were considered signicant.

RESULTS

In total, 122 VUR patients (girls, n = 69; boys, n = 53 boys; 177 ureters),with an average age of 55.7 ± 41.2 months (range, 1–18 years) underwent UNC between November 2005 and June 2014. The patients' demographic data are outlined in **Table 1**.
VUR persisted in 22 (18%) patients after UNC. VUR resolved spontaneously on follow-up in 13 of 22 (10.6%) patients. The ESI procedure was performed in seven patients with persistent VUR. Two (1.7%) patients with high-grade reflux underwent redo-UNC.
Postoperatively,an increase in hydronephrosis was noted in 19 (15.6%) patients. A double J stent was inserted in four (3.3%) of these patients, and hydronephrosis was resolved in all these cases. Severe voiding dysfunction was noted in another two (1.7%) patients with hydronephrosis. Following bladder exercises and anticholinergic treatment, hydronephrosis was resolved in these patients. Redo-UNC was performed in eight patients (6.5%) because of UV junction obstruction. Hydronephrosis resolved spontaneously in five (4.1%) patients.
In total, 10 (8.2%) of the 122 patients underwent redo-UNC. In this group, the average time to redo-UNC was 16.4 ± 13.2 months (range, 4–48 months) after the initial procedure. Two of these patients had persistent high-grade reflux after the initial UNC. In one of these patients, grade 5 reflux persisted following the initial UNC, and an ESI attempt was made before the redo-UNC was performed. The same patient experienced acute pyelonenephritis and developed new renal scarring after the initial UNC. Following redo-UNC, this patient had no new pyelonephritis, renal scarring, or decreased renal function on follow-up. In addition, the VUR resolved. The other patient was followed up due to recurring UTIs after the initial UNC. The patient also had persistent grade 5 reflux, as seen on VCUG. New scars were apparent on renal scintigraphy, and redo-UNC was performed. High-grade reflux persisted after the redo-UNC in this patient. However, at the 2-year follow-up, no pyelonephritis or new scarring was seen. On pathology, distal ureteral specimens from both patients showed mild lymphoplasmocytic inflammation. These two patients had initially undergone open surgery without any endoscopic procedure.
The remaining eight patients had no VUR on follow-up VCUG 6 months after the initial UNC but UV junction obstruction, with progressive hydroureteronephrosis was present. In all cases, the UV junction obstruction was diagnosed by retrograde pyelography and confirmed by a MAG 3 renal scan. In four patients (3.3%), the distal ends of the ureters were strictured. Tapering of the ureter was performed in two (1.7%) of these patients. The ESI procedure was the initial approach in

three of the four patients with stricture. During the initial UNC, the ureter was passed through the intestine in one patient, and ureteral stricture was noted in this patient on follow up. Redo-UNC and small bowel serosal repair were performed in this patient. High-grade (grade 4) reflux was present on VCUG 6 months after redo-UNC in one of the patients with UV junction stricture. However, at the 4-year follow-up, neither pyelonephritis nor new scarring in the kidney was present. The other three patients (2.5%) had no complications following redo-UNC. All four patients showed chronic inflammation, with eosinophil leukocytes highly represented in resected specimens from the distal ends of the ureters.

Angle-related UV junction obstructions were determined in four (3.8%) patients. Tapering was not performed in any of these patients, and the patients had no further complications during the follow-up after re-UNC. As with the stricture group, all four patients had signs of chronic inflammation at the distal ends of the ureters.

The comparison of the redo-UNC and UNC groups revealed no significant differences in the variables studied between the two groups. **Table 2** summarizes the results of the statistical comparison between the two groups.

DISCUSSION

Due to the widespread use of endoscopic VUR treatment during the last 20 years, the number of open surgical procedures for VUR has declined. Although UNC has a high success rate(5-7), for various reasons, some cases require redo-UNC. In our series, the redo-UNC rate was 8.2%. Previous research reported a redo-UNC rate after UNC of between 0.3 and 9.1%(6). There was no difference in the average age of the patients in the two groups (51.20 ± 51.97 months in redo-UNC, n=10; 56.19 ± 40.41 months in UNC, n=112; *P* = .431), with normal age distributions in both groups and similar medians (42 and 48 months, respectively). In the redo-UNC group, 6 (60%) were girls, and 63 (56.2%) were girls in the UNC group (*P* = 1.000). The age and sex distribution of the patients in the redo-UNC and UNC groups were similar. Renal function and laterality in VUR were the same in both groups. There were no between-group differences in the ratios of bilateral versus unilateral VUR and VUR grades (P = .325) or renal function (*P* = .493).

The ESI procedure was performed in 5 (50%) of the redo-UNC patients before the initial UNC, whereas it was performed in 49 (43.8%) of UNC patients. The number of patients (UNC and redo-UNC) initially treated endoscopically was similar. Initial endoscopic treatments did not increase the risk of redo-UNC.

Undiagnosed or untreated bladder problems are the primary cause of many unsuccessful reimplantations in VUR patients[10-12]. In many patients, postoperative persistent reflux regresses following treatment of voiding dysfunction[13]. Voiding dysfunction was present in 29 (26%) of the UNC group and 2 (20%) of the redo-UNC group (*P* = .682). In our study, voiding dysfunction did not affect the development of complications requiring redo-UNC, and voiding dysfunction did not differ between the groups.

Complications associated with antireflux surgical procedures may appear shortly after the surgery or some time post surgery. In our clinic, in all VUR patients, urinary system ultrasound is performed in the first postoperative month, and VCUG is performed after 6 months, regardless of symptoms. In many clinics, VCUG is not routinely performed after UNC, and some authors have argued that routine VCUG is not necessary[14,15].

Although relatively rate, an obstruction following UNC is a major complication[16-18]. Ureteral obstructions are the most serious types of surgical complications of reimplantation. Such complications can be caused by kinking due to excessive angulation or devascularization of the distal ureter. The diagnosis is readily made on ultrasound, with severe hydroureteronephrosis confirmed by delayed function and excretion on renal scintigraphy. In severe cases, drainage of the system, either by retrograde insertion of a double J stent or a percutaneous nephrostomy tube may be necessary. Following treatment (i.e., placement of a stent or percutaneous nephrostomy tube), many cases resolve and do not require additional surgery. In our series, percutaneous nephrostomy was not preferred. We followed up four patients in a double J stent was placed without reoperation. After UNC ureteral dilatation and mild grade hydronephrosis is relatively common. Most cases of mild-grade hydronephrosis resolve spontaneously. In this series,spontaneous resolution of hydronephrosis occurred in five (4.1%) patients. If dilatation persists for 3 months after UNC or the grade increases overtime, redo-UNC should be considered. If renal scar formation occurs, accompanied by UTIs, the patient should undergo comprehensive radiologic evaluations[19]. A permanent ureteral obstruction may be a late complication after UNC. This type of complication, which arises in 2–4.2% of VUR cases, requires redo-UNC(20-23). In the current study, the rate of permanent ureteral obstructions was about 6.5% of patients. Half of these obstructions comprised a stricture of the UV junction, and the remaining were angle-related obstructions. As compared with reports in the literature[6], the UV obstruction rate in our series was rather high.

Performing UNC is technically more difficult in cases of secondary VUR, and a ureteral obstruction can develop post-UNC[12,24,25]. Briefly, in the redo-UNC group, 60% (6/10) had primary VUR, whereas 68.8% (77/112) had primary VUR in the UNC group (*P* = .725). However, in the present study, we found no statistically significant differences in complications post UNC that led to redo-UNC in patients with primary versus secondary VUR.

Failure of antireflux procedures in primary low-grade reflux is extremely rare. Most failures are due to high-grade reflux or an inadequate ratio of tunnel length to ureteral diameter[5-7,21] . In our study, the rate of grade 4 and 5 reflux was 72% in the UNC group and 89% in the redo-UNC group, but this difference was not significant. Persistent VUR appeared to be the most common postoperative complication in all series, with an incidence of 4–5.6%[6,26,27]. In our study, reflux after UNC persisted in 22 patients, and redo-UNC was performed in two of 22 patients because of renal function loss and frequent UTI comorbidity. In seven patients, VUR resolved following the ESI procedure. On follow-up, spontaneous resolution of persistent VUR after UNC was noted in 13 patients.

In our study, ureteral tapering was performed in 6 (4.9%) patients, and re-UNC was required in only 2

of these patients as a result of stricture growth, with no significant (P = .651) differences between the groups. In six (4.9%) of the reoperated patients, the initial UNC technique used was Cohen, and the Politano–Leadbetter technique was employed in the other four (3.2%) patients. Previous studies that compared ureteral obstructions following the use of different UNC methods reported that obstructions were rarer with the Cohen method than with the Politano–Leadbetter technique[21,28]. The present study find no association between the incidence of ureteral obstructions and type of technique used. Neither the UNC techniques applied nor rates of ureteral tapering differed between the groups.

Redo ureteral reimplantation in VUR cases is technically more challenging than primary implantation and requires careful attention to detail and meticulous surgical techniques. Dis-section of the ureter and extensive mobilization is required to achieve an adequate submucosal tunnel. Careful dissection of the ureter is best accomplished by a combination of extra vesical and intravesical mobilization, as needed. The ureter should be carefully evaluated, and ischemic segments should be excised. Free bleeding from the divided distal end should be observed, in addition to peristaltic activity, to check for normal musculature and blood supply. It is preferable to create a new hiatus and submucosal tunnel. In cases where the ureter is short, a psoas hitch can be used to facilitate the creation of the antireflux mechanism. In our series, all the patients were reoperated using the Politano–Leadbetter technique, and no other procedures were required in these patients. The Politano–Leadbetter procedure was performed extraperitoneally to reduce potential complications, such as small bowel injury.

The main limitations of the present study were the small sample size, heterogeneity of the patients, and low power of the study.

CONCLUSIONS

Ten (8.2%) of the 122 VUR cases required redo-UNC: two (1.7%) patients with persistent VUR and eight (6.5%) patients with an increase in hydronephrosis after the initial UNC. Age, sex, laterality of VUR, VUR grade, existence of primary or secondary VUR, relative renal function on renal scintigraphy, UNC technique, ESI procedure, and ureteral tapering were not risk factors for redo-UNC after open VUR repair in our series.

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