



Risk Factors of Febrile Urinary Tract Infection after Ureteral Reimplantation in Infant

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Purpose: Children with febrile urinary tract infection (fUTI) and vesicoureteral reflux (VUR) show significant morbidity. Few studies have examined the incidence of fUTI after ureteral reimplantation for congenital urinary tract anomalies, particularly in infants. Therefore, this study examined the incidence and risk factors of fUTI after ureteral reimplantation in infants.

Materials and Methods: Children under one year of age, who underwent ureteral reimplantation from July 2017 to December 2018, were reviewed retrospectively. The patients' data were analyzed to evaluate the predictors of fUTI after ureteral reimplantation.

Results: Ureteral reimplantation was performed in 16 patients (25 ureters) at a mean of 8.9 ± 2.8 months. The preoperative diagnosis was VUR 14 (87.5%), obstructive megaureter 1 (6.3%), duplicated ureter 1 (6.3%). Postoperative fUTI occurred in five patients (31.3%) during the follow-up period (average 9.6 ± 5.9 months, range 3-18 months). UTI occurred at 40.8 ± 16.6 (17-61) days after surgery. Fourteen ureters were implanted with a ureteral catheter for three days, and 11 ureters were implanted with a double J ureteral stent for six weeks. The children's age, sex, surgical method, renal scar, reflux grade, laterality, persisting VUR, and presence of double J ureteral stent were not predictive factors for postoperative fUTI.

Conclusions: The incidence of fUTI after ureteral reimplantation in infants was 31.3%, and all fUTI occurred within two months after surgery. The risk factors associated with fUTI after ureteral reimplantation could not be predicted.

Keywords: Pyelonephritis; Urinary tract infections; Urologic surgical procedures; Vesico-ureteral reflux

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INTRODUCTION

Children with congenital urinary tract anomalies associated with either reflux or obstruction, such as vesicoureteral reflux (VUR), obstructive megaureter, and ectopic ureter, often require ureteral reimplantation for

definitive management. Recurrent febrile urinary tract infection (fUTI) in very young children causes new renal scarring and, eventually, hypertension or chronic renal insufficiency over time.

VUR is one of the most common urological anomalies in children, affecting approximately 1% of children [1]. VUR can

increase the risk of fUTI and pyelonephritis, which are associated with renal scarring and chronic renal insufficiency [1-4]. Therefore, appropriate management of VUR is required to prevent the significant morbidities and renal scarring caused by VUR. Antibiotic prophylaxis and endoscopic injections are often used as primary treatment options. On the other hand, ureteral reimplantation is an important treatment option with high success rates of 95% to 98% [5,6] and low complication rates, but it is more invasive than other treatment options.

Despite the high success rate of ureteral reimplantation for VUR, postoperative fUTI occurs in 4.6% to 24% of cases [4,7-9]. The causative risk factors of fUTI after ureteral reimplantation in children with VUR reported thus far were a preoperative grade of reflux, the presence of dysfunctional elimination syndrome, the presence of renal scar and preoperative breakthrough infection, female gender, and voiding dysfunction [7,9-13]. Nevertheless, the incidence and risk factors of fUTI after ureteral reimplantation in infants have received little attention.

According to a literature review, there are no reports on the incidence and risk factors of fUTI after surgery in children with an obstructive megaureter and ectopic ureter. On the other hand, fUTI after surgery caused increased hospital utilization and new renal scarring [14,15].

The literature on fUTI after ureteral reimplantation in very young children is sparse. Therefore, this study evaluated previous data to investigate the incidence and risk factors for children younger than one year of age.

MATERIALS AND METHODS

The data for children less than one year of age, who underwent ureteral reimplantation in Pusan National University Children's Hospital from July 2017 to December 2018, were reviewed retrospectively. In each patient, sex (male and female), age, body mass index (BMI), cause of surgery, laterality (both, left, and right), operation method (Cohen and Politano-Leadbetter), and operation duration were evaluated. VUR, megaureter, and duplicated ureter were included as potential causes of ureteral reimplantation surgery.

fUTI after ureteral reimplantation was diagnosed by a fever of more than 38°C and pyuria during the follow-up period. Pyuria was defined as the presence of 6 to 10 white blood cells per high power field in a urine sample.

The children were categorized into "No UTI" (11 children, 68.8%) and "UTI" (5, 31.3%) groups based on the occurrence of fUTI during the follow-up period. Sex (male and female), age, BMI, cause of surgery, laterality (both, left, and right), operation method (Cohen and Politano-Leadbetter), and operation duration in the two groups were compared. Moreover, the presence of renal scarring, the use of a ureteral stent in the catheter, and VUR grade were compared.

Statistical analyses were performed using IBM SPSS Statistics version 20.0 (IBM Corp., Armonk, NY, USA); p-values were <0.05 considered significant. A student t-test and Pearson's chi-square test were applied to assess the differences between the groups.

RESULTS

Ureteral reimplantation surgeries were performed in 25 ureters of 16 children (male: 11, 68.8%; female: 5, 31.3%). The mean age and BMI of the children were 8.9 ± 2.8 months (3-12 months) and 17.3 ± 4.1 kg/m², respectively. The causes of their condition were VUR (14 children, 87.5%), megaureter (1, 6.3%), and duplicated ureter (1, 6.3%). Ureter reimplantation was performed: bilateral, right, and left in nine (56.3%), one (6.3%), and six (37.5%) children, respectively. The Cohen technique and Politano-Leadbetter technique were performed in seven (43.8%) and nine (56.3%) children, respectively. The mean

Table 1. Patients and procedure characteristics

Variable	Value
Infant	16 (100.0)
Reimplanted ureter	25
Sex	
Male	11 (68.8)
Female	5 (31.3)
Age (mo)	8.9 ± 2.8
BMI (kg/m ²)	17.3 ± 4.1
Cause of condition	
VUR	14 (87.5)
Megaureter	1 (6.3)
Duplicated ureter	1 (6.3)
Laterality	
Bilateral	9 (56.3)
Right	1 (6.3)
Left	6 (37.5)
Operation method	
Cohen	7 (43.8)
Politano-Leadbetter	9 (56.3)
Operation duration (min)	196.7 ± 38.5

Values are presented as number (%), number only, or mean \pm standard deviation. The sum of the percentages does not equal 100% because of rounding.

BMI: body mass index, VUR: vesicoureteral reflux.

Table 2. Comparison in patients and procedure factors between No UTI and UTI groups

Variable	No UTI	UTI	p-value
Number	11 (100.0)	5 (100.0)	
Sex			
Male	8 (72.7)	3 (60.0)	1.000
Female	3 (27.3)	2 (40.0)	
Age (mo)	8.5±2.6	9.6±3.0	0.248
BMI (kg/m ²)	17.5±5.0	16.8±4.8	0.955
Diagnosis			0.542
VUR	10 (90.9)	4 (80.0)	
Megaureter	1 (9.1)	0 (0.0)	
Duplicated ureter	0 (0.0)	1 (20.0)	
Laterality			0.308
Bilateral	5 (45.5)	4 (80.0)	
Right	1 (9.1)	0 (0.0)	
Left	5 (45.5)	1 (20.0)	
Operation method			0.197
Cohen	6 (54.5)	1 (20.0)	
Politano-Leadbetter	5 (45.5)	4 (80.0)	
Operation duration (min)	184.7±28.9	223±53.6	0.111

Values are presented as number (%) or mean±standard deviation. The sum of the percentages does not equal 100% because of rounding. UTI: urinary tract infection, BMI: body mass index, VUR: vesicoureteral reflux.

operation time was 196.7±38.5 minutes (Table 1).

Postoperative fUTI occurred in five patients (31.3%) during the follow-up period (average, 9.6±5.9 months; range, 3–18), and all cases of fUTI occurred at 40.8±16.6 (17–61) days after surgery.

According to the comparison of the patient and procedure factors between the No UTI and UTI groups, the number of boys and girls were eight (72.7%) and three (27.3%) in the No UTI group, respectively, and three (60.0%) and two (40.0%) in the UTI group, respectively. The mean age in the No UTI and UTI groups was 8.5±2.6 months and 9.6±3.0 months, respectively. The BMI in the No UTI and UTI groups was 17.5±5.0 kg/m² and 16.8±4.8 kg/m², respectively. No significant differences were observed when comparing the two groups (Table 2). The diagnosis included 10 children (90.9%) with VUR and one (9.1%) with a megaureter in the No UTI group and four (80.0%) with VUR and one (20.0%) with a duplicated ureter. Ureter reimplantation was performed in the following cases: five (45.5%) bilaterally, one (9.1%) on the right ureter, and 5 (45.5%) on the left ureter in the No UTI group; and four (80.0%) bilaterally and 1 (20.0%) on the left ureter in the UTI group. In the No UTI group, the Cohen and Politano-Leadbetter techniques were performed in six (54.5%) and five (45.5%) children in the No UTI group, and one (20.0%) and four (80.0%) in the UTI group, respectively. The mean operation durations in the No UTI and UTI groups were 184.7±28.9 minutes and

Table 3. Comparison of renal scar, ureteral stenting, and VUR grade of renal units between No UTI and UTI groups

Variable	No UTI	UTI	p-value
Number of renal units	16 (100.0)	9 (100.0)	
Preoperative renal scar	11 (68.8)	4 (44.4)	0.397
Ureteral stent or catheter			0.115
Double J stent	5 (31.3)	6 (66.7)	
Ureteral catheter	11 (68.8)	3 (33.3)	
VUR grade			0.460
0	1 (6.3)	2 (22.2)	
I	0 (0.0)	0 (0.0)	
II	0 (0.0)	1 (11.1)	
III	2 (12.5)	0 (0.0)	
IV	9 (56.3)	4 (44.4)	
V	4 (25.0)	2 (22.2)	

Values are presented as number (%). The sum of the percentages does not equal 100% because of rounding.

VUR: vesicoureteral reflux, UTI: urinary tract infection.

223±53.6 minutes, respectively. The parameters were similar in the two groups (Table 2).

Preoperative renal scars were observed in 11 (68.8%) renal units in the No UTI group and four (44.4%) in the UTI group. Double J ureteral stents and ureteral catheters were inserted in five (31.3%) and 11 (68.8%) ureters in the No UTI group, respectively, and six (66.7%) and three (33.3%) ureters in the UTI group, respectively. VUR grade 0, III, IV, and V was observed in one (6.3%), two (12.5%), nine (56.3%), and four (25.0%) renal units, respectively, in the No UTI group; VUR grade 0, II, IV, and V were noted in two (22.2%), one (11.1%), four (44.4%), and two (22.2%) renal units, respectively, in the UTI group. Renal scarring, ureteral stenting, catheterization, and VUR grade were similar in the two groups (Table 3).

DISCUSSION

This study examined the incidence and predisposing factors of fUTI after ureteral reimplantation in children less than one year of age. fUTI in children is a significant health burden. Recurrent episodes of pyelonephritis can be associated with permanent renal parenchymal scarring, hypertension, and chronic renal insufficiency. Therefore, the early detection and optimal management of fUTI must evolve to minimize morbidity by preventing recurrent pyelonephritis and renal damage [9].

With cure rates approaching 96%, ureteral reimplantation has long been the gold standard for the surgical treatment of VUR [6]. Endoscopic subureteral injection treatment has become a popular alternative to open surgery and is used as

a primary treatment method. On the other hand, a large meta-analysis revealed endoscopic success rates of 85% after one or more injections [16]. Therefore, open surgery is still applied despite its invasiveness and complications. Shimada et al. reported that the growth of the affected kidneys could not catch up with normal kidneys after successful ureteral reimplantation, but they could grow at a rate parallel to the expected growth curve. Therefore, it is important to perform ureteral reimplantation to prevent kidney damage [17].

Ureteric reimplantation is effective in preventing UTI. Matsumoto et al. reported that the frequency of fUTI decreased dramatically from 0.23538 preoperatively to 0.00894 and 0.00081 per patient per month at 6 and 12 months after surgery, respectively. On the other hand, some children continued to develop UTI, even after the successful correction of VUR [18].

Many short- and long-term studies have explored fUTI after ureteral reimplantation surgery. A literature review showed that despite the high success rate of ureteral reimplantation for VUR, fUTI occurs at rates of 4.6% to 24% postoperatively [4,7-9]. In a large multicenter prospective trial performed by the International Reflux Study in Children, 5- and 10-year follow-ups revealed 10% and 14% incidences of fUTI after ureteral reimplantation, respectively [8,14]. In their large series, Whittam et al. [9] revealed an fUTI rate of 4.6% after an average follow-up period of 15 months. In contrast, Mariyappa et al. [19] reported an fUTI rate of 4.9% after a mean follow-up period of 42 months. In addition, the risk of post-reimplant UTI continued into adult life. Beetz et al. [7] reported an fUTI rate of 16% after a follow-up of 20 years. The fUTI rate after ureteral reimplantation in the present study was 31.3%, which is higher than that reported elsewhere. This difference was attributed to the small number of children and the much younger mean age (8.9 months old) than in the other studies.

One explanation of fUTI after ureteral reimplantation is that scarring of the bladder after open surgery produces irregularities that may facilitate bacterial adherence. Alternatively, scarring of the bladder may form areas of decreased vascularity, which may limit the innate host defense mechanisms. Bladder coordination and emptying may also be altered after reimplantation and predispose patients to UTI [4]. Younger children have smaller bladders than older children; hence, they are structurally and functionally immature compared to older children's bladders. Therefore, fUTI can

occur in children younger than one year of age.

Despite the small number of children and renal units in this study, there were no significant factors associated with fUTI after ureteral reimplantation in very young children.

Other studies suggested possible risk factors. Nelson et al. [13] reported that female, previous breakthrough infection, high-grade reflux, and preoperative renal scarring were risk factors for post-reimplant UTI. A Swedish reflux study found that girls with high-grade VUR had a significantly higher rate of recurrent fUTI than boys [20]. Mariyappa et al. [19] presented female, pre-reimplant fUTI, high-grade VUR, and bowel bladder dysfunction as the risk factors for post-reimplant UTI.

In an epidemiological study of UTI in children, UTI is more common in boys less than six months of age than in girls of the same age, but UTI is more common in girls less than one year of age [20,21]. The incidences may be influenced by anatomical and immunological factors. In this study, the patients were all under one year old, which differs from other studies.

This study had several limitations. The most important were the small number of children and the short follow-up duration after surgery. A prospective study with a long term follow-up of more children will be required to reinforce the conclusions of this study.

Although more children with a double J stent had UTI than those with a ureteral catheter, the difference was not significant. The effects of a ureteral stent and catheter should be evaluated in future studies.

CONCLUSIONS

The incidence of fUTI after ureteral reimplantation in children less than one year of age was 31.3% of 16 children, and all fUTI occurred within two months after surgery. No significant risk factors predicting fUTI after ureteral reimplantation could be found. Therefore, a larger-scaled multicenter study will be needed to predict the risk factors for fUTI after ureteral reimplantation in very young children.

CONFLICT OF INTEREST

No potential conflict of interest relevant to this article was reported.

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AUTHOR CONTRIBUTIONS

S.L. participated in data collection and wrote the manuscript. S.L., J.M.C., and S.D.L participated in the study design and performed the statistical analysis. J.M.C and S.D.L. participated in the study design and coordination and helped to draft the manuscript. All authors read and approved the final manuscript.

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