

Postoperative Breakthrough Infection and Re-operation in Patients with Duplicated Collecting Systems: A Comparative Analysis of Surgical Outcomes

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Objective: The purpose of surgical intervention for ureteral duplication is to decrease the risk of infections, preserve renal function and avoid bladder dysfunction. The objective of this study was to determine if there is a difference in outcome between total reconstruction of the urinary tract, an upper tract approach, or a lower tract approach.

Materials and Methods: The outcomes of partial nephrectomy, common sheath re-implantation, total reconstruction and transurethral incision of ureterocele were pooled and compared against each other. Primary outcome criteria included breakthrough infection, voiding dysfunction and need for a second surgery. Procedural dependence of the primary outcomes for each surgery was analyzed using Chi square test. Odds ratio was then computed for each procedure with total reconstruction as the standard. Logistic regression analysis of the odds ratio was done to determine statistical significance.

Results: A total of 128 patients were included in the study. Breakthrough infection was seen in 18.8% of those who underwent partial nephrectomy, 23.8% of those who underwent re-implantation, 19.4% of those who underwent total reconstruction, and 46.4% of those patients who underwent TUI-U. Only 1 patient from the partial nephrectomy group and 1 patient from the total reconstruction group experienced voiding dysfunction. Of the 23 patients who underwent TUI-U, 5 (17.9%) needed a secondary procedure, while 3 from the partial nephrectomy, and none from the re-implantation and total reconstruction groups required re-operations. Analysis showed that breakthrough urinary tract infection is dependent on the type of procedure. Using total reconstruction as the standard, the odds ratio for partial nephrectomy is 0.962, 1.302 for common sheath re-implantation and 3.611 for TUI-U. Logistic regression analysis showed statistical difference in the odds ratio of TUI-U and total reconstruction.

Conclusion: Breakthrough infection is shown to be dependent on the procedure. TUI-U has a 3.6-fold higher chance of breakthrough infection compared to total reconstruction, hence up to 18% of patients who opt for TUI-U should be counseled regarding the need for a secondary operation. The odds of breakthrough infection in common sheath re-implantation and partial nephrectomy is not significantly different from total reconstruction. No evidence was established regarding the dependence of re-operations and voiding dysfunction to the primary procedure.

Key words: breakthrough infection, renal function, bladder dysfunction, ureteral duplication

Introduction

Ureteral duplication is a common condition, described in approximately 1 in 125 people (0.8%) based on autopsy series.¹ The female to male ratio is 1.6:1 and the duplication is unilateral six times more frequently than bilateral.¹ They can be uncomplicated wherein no treatment is necessary or complicated by upper pole malformations such as ureteral ectopia and ureterocele or by lower pole conditions such as vesico-ureteral reflux and ureteropelvic junction obstruction. This anomaly is seen more frequently in patients with urinary tract disease, e.g. 8% of children with urinary tract infections (UTI), and in 15% of patients with renal scarring.⁷ The purpose of surgical intervention for this condition is to decrease the risk of infections, preserve renal function and avoid bladder dysfunction and incontinence; and prevention of infection is key to preserving function and preventing long-term untoward outcomes.

To achieve these goals, different surgical options have been proposed. These include total reconstruction of the urinary tract (Upper pole partial nephrectomy, ureterocele excision, bladder neck reconstruction, common sheath re-implantation), an upper tract approach (Heminephrectomy of the non-functioning renal moiety), and a lower tract approach (common sheath re-implantation, excision of ureterocele). Total reconstruction has been viewed consistently as the most effective way to achieve single-stage cure and prevent long-term bladder dysfunction. Beganovic, et al. (1999) reported on a 17% post-operative reinfection rate in a series of 55 patients who underwent total reconstruction, Lewis, et al. (2008) reported on 54 patients who underwent lower tract reconstruction wherein 24 (44%) had recurrence of UTI in the post-operative period. Hussman, et al. (1995) reported on a series of 87 patients who underwent upper pole heminephrectomy, with 24 (32%) patients having post-operative UTI.⁶ Unfortunately, the ideal procedure for such a condition is still controversial, and uncertainty still exists with what procedure offers the better outcome over the other.

In the present series, the authors sought to compare the incidence and relative risk of breakthrough urinary tract infection and re-

operation rates in patients who underwent total reconstruction (TR), upper pole partial nephrectomy (UPPN), common sheath re-implantation (CSR) and transurethral incision of ureterocele (TUI-U).

Materials and Methods

Design & Conduct

The present series is a retrospective analysis of patients with a duplicated collecting system, with or without a ureterocele or ectopic ureter. The study included all patients operated on by a single urologist from January 1990 to January 2017. The existence of the duplicated system was discovered by way of a voiding cystourethrogram (VCUG) and an ultrasound done during the initial consultations. All data were transcribed by personnel under the supervision of the study authors. The statistical analyses were performed by an independent statistician employed by the authors. All the authors assume responsibility for the completeness and integrity of the data. They had full access to all parts of the data and drafted the manuscript with their respective inputs.

Patients & Treatments

From January 1990 to January 2017, 228 patients documented of having a duplicated collecting systems were seen during the entire study period. All patients who did not undergo any of the procedures under study or those who were lost to follow-up were excluded from the study. Patient characteristics were pooled and analyzed. A total of 128 eligible patients were included, 23 (17.9%) were males, 105 (82%) were females. 48 (37.5%) patients underwent Partial Nephrectomy (PN), in this group, 9 (18.8%) were males, 41 (81.3%) were females. 37 (77%) presented with recurrent urinary tract infection, 10 (20.8%) with voiding dysfunction, and 5 (10.4%) were diagnosed during a prenatal checkup. Ten patients (20.8%) had a concomitant ureterocele, while 35 (72.9%) had an ectopic ureter. A total of 21 (16.4%) patients underwent common sheath re-implantation, 5 (23.8%) were

males, 16 (76%) were females. 17 (80.9%) presented with recurrent urinary tract infections, 1 (4.7%) with incontinence and 3(28.5%) detected thru during prenatal checkup. Ten (47.6%) were associated with an ectopic ureter, 9 (42.8%) with a ureterocele. In the Total Reconstruction group, 31 (24.2%) were included, 5 (16.1%) were males, 26 (83%) were females. 30 (96.7%) presented with recurrent UTI, none had a voiding dysfunction during initial consult and 1 (3.2%) was detected during a prenatal checkup. Twenty (64%) were associated with an ectopic ureter and 11 (35%) had a ureterocele. Twenty-eight patients underwent TUI-U, 4 (14.2%) were males, 24 (85.7%) were females. 20 (71%) presented with recurrent UTI, none had dysfunctional voiding. Eight (32%) were seen during their prenatal check-up. All had a ureterocele, none had an ectopic ureter. Patient characteristics, imaging study results, operative records and post-operative course were collected and recorded. The follow-up consultations were done during the 1st post-operative week, 1st post-operative month, and at a scheduled date thereafter, depending on the discretion of the principal investigator. During the follow-up consultations, a bedside ultrasound was conducted to assess for the status of the remaining renal moieties. The patient was assessed for evidence of breakthrough infection clinically and by follow-up urinalysis and urine cultures.

End Points

The primary end-points were breakthrough infection and the need for re-operation. Secondary endpoint was the incidence of voiding dysfunction in the postoperative period. Breakthrough infection is defined as the presence of any of the following at any point in the postoperative period: Clinical signs and/or symptoms of urinary tract infection such as fever, chills, dysuria, flank pain; pyuria and/or bacteriuria on urinalysis and/or a positive growth on urine culture and sensitivity. Re-operation is defined as any surgical procedure done after the primary operation. Voiding dysfunction is defined as either incontinence or dribbling in the postoperative period.

Statistical Analysis

The analysis was done by an independent statistician employed by the authors. SPSS Statistics 17.0 was used for the analysis of the data. Pearson chi-square tests were used to determine the existence of a relationship or dependence of the end-points to the procedure done as well as to establish a difference among the operations. ($p < 0.05$). Logistic regression was conducted to omit the influence of age and gender on occurrence of breakthrough infection. With total reconstruction as the standard for comparison, the authors determined the odds ratio of breakthrough infection, second surgery and voiding dysfunction for partial nephrectomy, CSR and TUI-U. Logistic regression analysis was used to determine statistical difference in the ratios.

Materials and Methods

Patients & Treatments

A total of 128 patients with double collecting systems were included in the study. Forty eight (48) patients underwent partial nephrectomy, 21 underwent common sheath re-implantation, 31 underwent total reconstruction of the urinary tract, and 28 underwent TUI-U. Of the overall population, 23 (17.9%) were males, 105 (82%) were females. Their mean age at the time of the procedure was 3.4 years of age. The mean follow-up period was 138 months (Table 1). Mean age at present of the study population is 15 years. All patients were assessed for breakthrough infection based on their clinical picture and on laboratory results during the follow-up period.

End Points

Overall, 33 (25.8%) of the 128 patients experienced breakthrough infection at least once in the postoperative period. Of the 48 who underwent upper pole partial nephrectomy, 9 (18.8%) experienced recurrence of urinary tract infection after the procedure. In the group who underwent common sheath re-implantation, 5 (23.8%) had a breakthrough infection, while 6

Table 1. Patient characteristics

Patient Characteristics (n=128)	Partial		Total	
	Nephrectomy (PN) (n=48)	CSR (n=21)	Reconstruction (n=31)	TUIU (n=28)
Age (mean in years)	4.78	3.19	3.18	1.28
Gender (Male:Female)	9:39	5:16	5:26	4:24
<i>Presentation</i>				
RUTI (n=x)	36	17	30	19
Incontinence	12	1	0	0
Prenatal	7	3	1	9
<i>Laterality</i>				
Right Side	14	8	12	12
Left Side	34	13	19	16
<i>Hydronephrosis</i>				
<i>Upper Pole</i>				
None	0	0	0	0
Grade I	3	1	0	2
Grade II	8	3	3	3
Grade III	16	11	13	11
Grade IV	21	6	15	12
<i>Lower Pole</i>				
None	46	20	28	27
Grade I	1	1	2	0
Grade II	0	0	0	1
Grade III	1	0	1	0
Grade IV	0	0	0	0
Ureterocele	10	9	11	28
Ectopic Ureter	35	10	20	0
Length of Follow-up (years)	11.7	12.8	12.9	9

(19.4%) of the 31 who underwent total reconstruction had a breakthrough infection (Table 2). The highest rate of breakthrough infection postoperatively was seen in those who underwent TUI-U wherein 13 of the 28 (46.4%) had a breakthrough infection after the operation.

Pearson Chi square analysis of the variables revealed that breakthrough infection was

dependent on the procedure in this series ($p < 0.05$). Logistic regression was conducted to check the influence of age and gender on occurrence of breakthrough. Results showed that both of these variables were removed from the model after three iterations, leaving only the type of procedure as the only variable among those considered that was found to influence occurrence of breakthrough

Table 2. Results

	n=128 (%)	Breakthrough Infection	Second Surgery	Voiding Dysfunction
Partial Nephrectomy	48 (37.5)	9 (18.8)	3 (6.3)	1 (2.1)
Common Sheath Reimplantation	21 (16.4)	5 (23.8)	0 (0)	0 (0)
Total Reconstruction	31 (24.2)	6 (19.4)	0 (0)	1 (3.2)
TUIU	28 (21.8)	13 (46.4)	5 (17.9)	0 (0)

infection. Risk of breakthrough UTI post-operatively was determined for each of the procedures. Using total reconstruction as the baseline standard for comparison, logistic regression analysis of the odds ratio of each procedure showed that only the comparison between total reconstruction and transurethral incision of ureterocele (TUIU) was statistically significant, with a ratio of (TUIU:TR) 3.6:1. The comparison of odds between partial nephrectomy and common sheath re-implantation to total reconstruction was not statistically significant (Table 3).

Need for Second Surgery

In the partial nephrectomy group, 3 (6.3%) of the 48 patients had to undergo a secondary procedure. Of the 3, one patient had a breakthrough infection. Ultrasound revealed a prominent distal ureteral stump measuring 1.3cm; urine culture was positive for pseudomonas aeruginosa. This patient underwent cystoscopy followed by distal ureterectomy with re-implantation of the lower moiety ureter. After 1 month, the stent was pulled out, the patient remained asymptomatic on follow-up. Another patient also underwent distal ureterectomy due to breakthrough UTI, an ultrasound likewise revealed a prominent distal stump. Among the patients who underwent common sheath re-implantation and total reconstruction, no one had to undergo a second operation. Of the 28 patients who underwent transurethral incision of ureterocele, 5 (17.9%) underwent re-operation.

Pearson Chi square analysis was unable to establish dependence or relationship of the procedure to the occurrence of a secondary operation. This is in part due to too few "positive" experiences to make the proper inference. Likewise, logistic regression analysis of the odds of re-operation for each procedure also failed to show any evidence of statistical relationship due to few events (Table 2).

Voiding Dysfunction

Voiding dysfunction was scarcely noted in the postoperative period. Only 1 patient from the hemi-nephrectomy group, and 1 patient in the total reconstruction group experienced occasional urinary incontinence and overactive bladder. Due to very few "positive" experiences, Pearson chi square analysis was unable to show any evidence of relationship between the procedure and the occurrence of voiding dysfunction post-operatively. Determination and comparison of the odds of postoperative voiding dysfunction via logistic regression analysis was unable to precisely show any relationship due to very few occurrences.

Discussion

Duplicated collecting system is the most common congenital anomaly of the upper urinary tract seen in 0.8% of the general population. This entity is associated with the presence of vesico-ureteral reflux in 25-50%, as well as with ureterocele in 10-20%. The natural history of an untreated duplex ureteral system mandates that

Table 3. Procedures risk of breakthrough UTI

	Breakthrough Infection			Second Surgery			Voiding Dysfunction		
	PD	Odds Ratio	Significance	PD	Odds Ratio	Significance	PD	Odds Ratio	Significance
TR	Yes	1.0	-	No	Nil	-	Nil	-	-
PN	Yes	0.962	NS	No	Nil	-	Nil	-	-
CSR	Yes	1.302	NS	No	Nil	-	Nil	-	-
TUIU	Yes	3.611	S	No	Nil	-	Nil	-	-

TR - Total Reconstruction, PN - Partial Nephrectomy, CSR - Common Sheath Reimplantation, TUIU - Transurethral Incision of Ureterocele; PD - Procedure Dependence; S - Significant, NS - Not Significant; Nil - unable to compute due to few "positives".

any therapeutic approach to this condition be aimed at preventing urinary tract infection, decompressing the dilated upper tracts, preserving renal function and maintaining continence. Upper pole nephrectomy is an approach recommended for duplicated systems without VUR with a cure rate of 85%, with a mean follow-up of 72.3 months. When VUR is present, secondary surgery is necessary in 84%. Common sheath re-implantation involves dissection of the two ureters as a unit, after which they are re-implanted sub-mucosally. This approach is suitable for duplex systems with a concomitant vesico-ureteral reflux. Studies have shown that this procedure is effective in decompressing the upper tracts in 92.3%, reoperation was seen 17.9% of patients and differential renal function was decreased by >5% in 13.9%. Although direct comparisons have yet to be established, this approach is deemed as an acceptable surgical option with comparable results. On the other hand, total reconstruction defined as a combination of ureterocelectomy, ureteral re-implantation with or without partial nephrectomy has a reported success rate of as much as 90%, with a secondary operation rate ranging from 0% to 32%. The simplest means to decompress the obstructed upper pole or single system ureterocele is via trans-urethral incision. Reported success rates range from 78% to 97%. Despite publications, no single method is currently regarded as the definitive treatment. To date, no randomized controlled trials have shown superiority of one over the other. Experts have advocated an individualized approach. Hence, it would be highly beneficial for the management status quo if this endeavor were to establish a significant difference in the outcome among these 4 surgical approaches.

In duplicated systems, the anatomical and functional divisions of the renal moieties vary greatly. The lower moiety is usually associated with massive VUR and rarely with obstruction, while the upper renal moiety is usually associated with obstruction secondary to an ectopic ureter, with or without a ureterocele.¹⁰ The existing VUR and/or obstructive uropathy secondary to the ectopic ureterocele predisposes the patient to recurrent urinary tract infections. Endoscopic decompressive techniques such as transurethral

incision of ureterocele is by far the easiest way to achieve decompression of the obstructing ureterocele.⁶ The advocated technique involves making an incision or puncture in the intravesical position of the ureterocele, just above the level of the bladder wall to create a valve mechanism that prevents VUR in the opened moiety. This approach completely prevented de novo VUR while achieving successful decompression in 82% of cases. In general, the larger the incision, the better the decompression but the higher risk for VUR. In the series of 20 patients who underwent endoscopic decompression by Castagnetti, et al. (2004), 75% had persistent VUR post operatively. Likewise, Chertin, et al. (2005) had similar rates in his series with 61% of cases having persistent VUR. Furthermore, studies have shown that endoscopic decompression such as TUI-U is associated with postoperative breakthrough infection rates as high as 47%. Partial nephrectomy is performed for the non-functioning upper pole moiety in a duplicated system, especially if with a concomitant ectopic insertion of the distal ureter or ureterocele. Studies have advocated removal of the involved moiety if renal function is <10%. Studies by Hussman et.al., have shown that an upper tract approach is significantly better in achieving decompression than endoscopic procedures, being the definitive procedure in 80% of cases.⁶ The downside to this procedure is that the remaining distal ureteral stump may act as a diverticulum, predisposing the patient to breakthrough urinary tract infections.¹³ In the study by Sakellaris, et al. (2011), with a median follow-up of 8.3 years, 16% had breakthrough UTI and 9% had to undergo a second surgery. Controversy still exists regarding the management of the remaining ureteral stump. Although it is obvious that removal of the stump would remove the risk of infection due reflux of urine into the stump, some studies have advocated a more conservative approach. Kim, et al. (2001) studied the natural history of ureteral stumps in children post upper tract surgery and found that spontaneous disappearance or reduction in size of the distal stump occurred frequently. This happens during the first 6 months postoperatively. His study demonstrates that an expectant approach to the stump is a good alternative after the

primary surgery in these patients. When vesicoureteral reflux accompanies a duplicated system, common sheath re-implantation becomes a more suitable option to correct such anomaly. In a study by Matsumoto, et al. (2005), the frequency of febrile UTI was dramatically reduced from 0.23538 pre-operatively to 0.00894 and 0.00081 per patient per month at 6 and 12 months after surgery, respectively.¹⁶ CSR has a success rate of 92.3%, with a re-operation rate of 17.9% as demonstrated in the series by Lee, et al. (2015).

In this study, the authors aimed to compare the outcomes of hemi-nephrectomy, common sheath re-implantation, total urinary reconstruction and transurethral incision of ureterocele (TUI-U) in the management of duplex systems. They sought to determine whether there is a significant difference in the incidence breakthrough urinary tract infections, the need for a secondary operation, and the incidence of voiding dysfunction, as well as the difference in the odds of postoperative breakthrough infection and re-operation. The incidence of breakthrough infection for partial nephrectomy, common sheath re-implantation, total reconstruction and TUI-U is 18.8%, 23.8%, 19.4% and 46.4% respectively. Although statistically, no difference was seen among the 4 procedures when it comes to recurrence of infection, the above values, if taken crudely, show that the ability of the procedure to decompress and relieve the obstructed upper moiety influences the incidence of postoperative breakthrough infection. To successfully decompress the hydronephrotic renal moiety via either re-implantation, total reconstruction or excision of the moiety itself has shown to relate to a lower incidence of breakthrough infection as opposed to simply incising the obstructing ureterocele (18.8 vs 23.8 vs 19.4 vs 46.4). The need for a second surgery is seen in 3 patients who underwent partial nephrectomy (6.3%), and in 5 of those who underwent TUI-U (17.9%). All 3 patients from the partial nephrectomy group experienced febrile breakthrough infection and on work-up, ultrasound revealed a prominent distal ureteral stump. All three (3) patients underwent distal ureterectomy for excision of the distal stump. Postoperatively, these patients remained asymptomatic.

Conclusion

In this series of 128 patients with duplicated collecting system, the analysis showed that breakthrough infection is dependent on the procedure. Logistic regression analysis of the odds ratio demonstrates statistical significance in the comparison of TUI-U to total reconstruction, with an odds ratio of 3.6:1. Hence, an individual is 3.6 times more likely to experience a breakthrough infection as compared to an individual who underwent total reconstruction. Furthermore, for those who decide on TUI-U, it is important to counsel the patient on the possible long-term outcomes of the procedure, since 18% of them will require a second operation.

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