

Nine Year Retrospective Review of Surgical Treatment of Vesicoureteral Reflux: Comparison of Three Approaches

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Abstract

Objective: To analyze our nine-year experience in the surgical management of vesicoureteral reflux (VUR) with open ureteral reimplantation, robotic reimplantation, and endoscopic correction with Deflux.

Methods: We retrospectively reviewed all patients undergoing surgical intervention for primary VUR at our institution between 2001 and 2010. Treatment success was defined as complete resolution of VUR on postoperative voiding cystourethrography. Surgeries were performed by four pediatric urologists. All robotic reimplantations were performed by a single surgeon. Categorical comparisons were made using Pearson's Chi-Square or Fisher's Exact test, and continuous variables were compared using Mann-Whitney U.

Results: One hundred eighty-three patients (287 ureters) were included. Fourteen patients underwent robotic surgery, while the open surgery and Deflux cohorts included 93 and 76 patients, respectively. Due to the significantly smaller sample size of the robotic cohort, statistical comparisons were made only between the open surgery and Deflux cohorts. Postoperative VUR resolution rate was 100% (open), 85% (robotic), and 78.4% (Deflux). Open reimplantation had a significantly higher VUR resolution rate than Deflux ($p < 0.001$). Overall, 13.9% of patients developed contralateral reflux, with no significant differences between the open and Deflux cohorts.

Conclusions: In this study, we found significantly higher success rates with open reimplantation versus Deflux. While robotic reimplantation had high success rates and short hospital stays, the smaller sample size limited statistical comparison of this modality to open surgery or Deflux. We continue to enroll patients into a prospective series of all VUR procedures at our institution, which will result in more robust comparisons.

Keywords: Vesicoureteral reflux; Reimplantation; Robotics; Deflux; Pediatrics

Abbreviations: VUR: Vesicoureteral Reflux; UTI: Urinary Tract Infection; VCUG: Voiding Cystourethrogram; STING: Subureteral Transurethral Injection; HIT: Hydrodistention-Implantation Technique

Introduction

Vesicoureteral reflux (VUR) is present in approximately 1% to 3% of all children and is diagnosed in 30% to 40% of children with a febrile urinary tract infection (UTI) [1,2]. VUR in the presence of UTI increases the risk of pyelonephritis, which may cause renal parenchymal scarring. Renal scarring occurs in up to 15% of children with grade III or IV VUR and may be associated with the development of hypertension and end-stage renal disease [3].

The goals of treatment of VUR include prevention of recurrent febrile UTI and renal injury, as well as minimizing treatment morbidity [4]. Initial management usually includes close surveillance with consideration of continuous antibiotic prophylaxis, especially among children with low-grade VUR in which spontaneous resolution is common [5]. Indications for surgical intervention may include breakthrough UTI, noncompliance with medical management, persistent high-grade VUR, impaired renal growth or function, and parental preference.

Open ureteral reimplantation remains the gold standard of surgical intervention, with success rates from 95% to 99% and low complication rates [6]. Minimally invasive ureteral reimplantation and endoscopic correction of VUR have shown promising results; however, management guidelines are limited by a paucity of randomized, prospective studies comparing the various surgical modalities.

While some centers may favor one treatment modality, we routinely offer and utilize all three approaches. Patients' parents are educated on the risks, benefits, and expected success rates of all three treatment modalities on a case-by-case basis, and the surgical approach is ultimately selected based on parental preferences.

In this study, we sought to analyze our nine-year experience in the surgical management of VUR with open ureteral reimplantation, robotic reimplantation, and endoscopic correction with Deflux.

Methods

After obtaining Institutional Review Board approval, a retrospective review was performed of all patients who underwent surgical intervention for primary VUR between October 2001 and June 2010 at our institution. Patients with additional diagnoses associated with secondary VUR [ureterocele (20), ectopic ureter (3), posterior urethral valve (3), neuropathic bladder (2), and exstrophy (2)] were excluded.

Our primary outcome was resolution of VUR, which we

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defined as absence of VUR on the most recent postoperative voiding cystourethrogram (VCUG). Secondary outcomes included development of contralateral VUR as well as intraoperative and postoperative complications. Patients without postoperative VCUG (39 patients, 63 ureters) were excluded from analysis. We also excluded ureters with resolved VUR prior to treatment (n=5) in patients with a history of bilateral VUR who underwent bilateral intervention.

We excluded all patients treated by urologists who are not currently practicing in our group (232 patients, 369 ureters), so that our results would most accurately reflect the success rates that patients currently treated at our institution could expect. Among patients included in this analysis, surgical intervention was performed by four pediatric urologists. All robotic reimplantations were performed by a single surgeon. Only the initial surgical intervention performed for VUR at our institution was included in this analysis.

Analysis was performed using SPSS 17.0. (IBM Corporation, Armonk, NY) Categorical comparisons were made using Pearson's Chi-Square or Fisher's Exact test with Bonferroni adjustment as appropriate, and continuous variables were compared using Mann-Whitney U. All statistical tests were two-tailed, with a p-value <0.05 considered significant.

Results

Between October 2001 and June 2010, 484 patients (758 ureters) were treated for VUR at our institution. After excluding patients with secondary VUR, patients without postoperative VCUG, and patients who were treated by urologists who are not currently practicing in our group, 183 patients (287 ureters) were included in this study. Patient

characteristics and indications for surgical intervention are displayed in Tables 1 and 2, respectively.

One patient underwent both open reimplantation and contralateral Deflux injection and was included in the open surgery cohort. Of the total study population, ten patients had missing data on indication for surgical intervention.

This study reflects our institution's early experience with robotic reimplantation. Therefore, there were 14 patients in the robotic group, while the open surgery and Deflux cohorts included 93 and 76 patients, respectively. Due to the significantly smaller sample size of the robotic cohort, we were unable to compare outcomes of the robotic cohort to the other treatment groups. We included the results of robotic reimplantation at our institution, but all statistical comparisons were made only between the open surgery and Deflux cohorts.

There were no significant differences in gender, age at diagnosis, or age at surgery between patients undergoing open surgery or Deflux injection. Sixty-four percent of patients had preoperative VUR grades III-V. Patients treated with open surgery had significantly higher grades of VUR preoperatively than those who underwent Deflux (p<0.001). Among patients undergoing robotic reimplantation, 70% had preoperative VUR grades III-IV.

The most common indications for surgical intervention in the overall study population included failure of VUR resolution, recurrent UTI, and decreased renal function or scarring. A significant difference was found among indications for intervention between the open surgery and Deflux cohorts (p<0.001). Univariate comparisons of indications for surgery, with a Bonferroni-adjusted p-value of p<0.007,

Variable (% , n)	Open	Deflux	p-value	Robotic	Total
Patients	50.8% (93)	41.5% (76)		7.7% (14)	100% (183)
Ureters	53.7% (154)	39.3% (113)		7.0% (20)	100% (287)
Laterality					
Unilateral	33% (31)	53% (40)		57% (8)	43% (79)
Bilateral	67% (62)	47% (36)		43% (6)	57% (104)
Gender			p=0.366 [†]		
Female	80% (74)	74% (56)		93% (13)	78% (143)
Male	20% (19)	26% (20)		7% (1)	22% (40)
Age [median in months, (25 th , 75 th percentile)]					
At diagnosis	43 (9-76)	59 (15-87)	p=0.167 [‡]	39 (5-61)	51 (9-78)
At surgery	71 (36-94)	86 (39-105)	p=0.160 [‡]	77 (47-113)	73 (39-101)
Preoperative VUR grade (by ureter)					
			p<0.001 [§]		
I	5% (8)	7% (8)		5% (1)	6% (17)
II	21% (31)	44% (49)		25% (5)	30% (85)
III	36% (54)	38% (42)		55% (11)	38% (107)
IV	27% (41)	8% (9)		15% (3)	19% (53)
V	11% (17)	3 (3%)		0	7% (20)

[†]Pearson's Chi-Square; [‡]Mann-Whitney U; [§]Fisher's Exact test.

Table 1: Patient characteristics.

Indication (% , n)	Open	Deflux	Robotic	Total
Failure of VUR resolution	45.9% (39)	56.6% (43)	45.9% (39)	49.7% (86)
Recurrent UTI	14% (13)	14.5% (11)	14.3% (2)	15.0% (26)
Decreased renal function/scarring	18.3% (17)	2.6% (2)	28.6% (4)	13.3% (23)
Noncompliance	7.5% (7)	7.9% (6)	14.3% (2)	8.7% (15)
Worsening VUR	8.2% (7)	9.2% (7)	8.2% (7)	8.1% (14)
Parental preference	--	9.2% (7)	--	4.0% (7)
Other	2.2% (2)	--	--	1.2% (2)

p<0.001 (Fisher's Exact test).

Table 2: Indications for surgical intervention.

demonstrated that decreased renal function/scarring was the indication for intervention in a significantly higher proportion of patients undergoing open reimplantation versus Deflux injection ($p < 0.001$), and parental preference for treatment of VUR was the indication for intervention in a higher proportion of patients undergoing Deflux versus open surgery ($p = 0.004$). All other comparisons were not significant.

Surgical outcomes are displayed in Table 3 and Figure 1. Median follow-up for the total population was 16 months (range 7-31 months). Patients had significantly longer follow-up after open surgery compared to patients who underwent Deflux injection ($p < 0.001$). Median length of stay after open reimplantation was 4 days (range 1-9 days) versus 1 day after robotic surgery (range 1-2 days).

Postoperative VUR resolution rates per ureter were 100% after open reimplantation, 85% after robotic surgery, and 78.4% after Deflux. Downgrading of VUR occurred in 5% of patients after robotic surgery and 8% after Deflux. Open surgery had a significantly higher success rate than Deflux ($p < 0.001$). Deflux techniques included suburethral transurethral injection (STING), hydrodistention-implantation technique (HIT), and double HIT. However, Deflux techniques and volumes were often unavailable or inconsistently reported. Therefore, these parameters could not be reliably factored into this analysis.

No intraoperative complications occurred in any of the cohorts. Overall, 13.9% of patients developed contralateral reflux, with

Variable (% , n)	Open	Deflux	p-value	Robotic	Total
Follow up (median in months, range)	27 (11-61)	15 (4-18)	$p < 0.001^+$	15 (4-20)	16 (7-31)
Post-op VUR grade (by ureter)			$p < 0.001^+$		
0	100% (151)	78.4% (87)		85% (17)	90% (255)
I	0	4.5% (5)		5% (1)	2% (6)
II	0	7.2% (8)		5% (1)	3% (9)
III	0	8.1% (9)		5% (1)	4% (10)
IV	0	1.8% (2)		0	1% (2)
V	0	0		0	0
Development of contralateral VUR			$p = 0.275^s$		
Yes	13% (4)	13% (5)		25% (2)	13.9% (11)
No	87% (27)	87% (35)		75% (6)	86.1% (68)

⁺Mann-Whitney U; ⁺Pearson's Chi-Square; ^sFisher's Exact test

Table 3: Surgical outcomes.

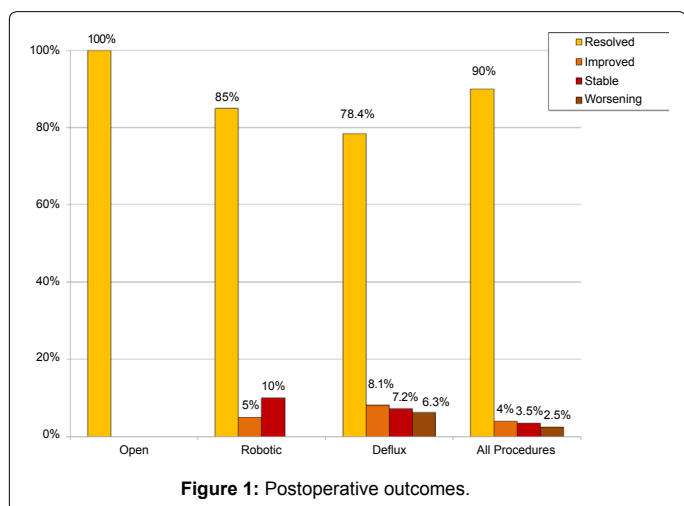


Figure 1: Postoperative outcomes.

no significant differences between the open surgery and Deflux treatment groups. Comprehensive follow-up data was unavailable for many patients, making it difficult to comment definitively on other postoperative complications. After open surgery, 12 afebrile and 7 febrile UTI's were documented, and after Deflux, 1 afebrile and 4 febrile UTI's occurred. (All Clavien grade II complications) No postoperative UTI's or other complications were identified after robotic surgery.

Discussion

Open ureteral reimplantation remains the gold standard of surgical intervention for VUR, with success rates of 95% to 99% [6]. The durability of these positive outcomes has also been demonstrated, with no late recurrences of VUR in a recent retrospective review [7]. However, open reimplantation can be associated with considerable morbidity including postoperative pain, hematuria, and irritative bladder symptoms, often requiring epidural analgesia [8].

Minimally invasive ureteral reimplantation and endoscopic correction of VUR have shown promising results with decreased morbidity; however, outcomes data regarding these newer surgical techniques is still evolving. In a meta-analysis of peer-reviewed articles regarding endoscopic treatment of VUR published through 2003, Elder et al. reported that the success rates after one injection were 78.5% for VUR grades I and II, 72% for grade III, 63% for grade IV, and 51% for grade V [9]. Higher success rates have been achieved with modification of injection technique. Using the double hydrodistention-implantation technique (double HIT), Kalisvaart et al. reported a durable success rate of 93% based on VCUG performed on 30 patients at a mean of one year after injection [10]. Reported success rates of robotic ureteral reimplantation have ranged from 81% to 99.3% [11-14]. The differing success rates among various series of robotic reimplantation may be partially attributed to the initial learning curve with the technique [13] as well as smaller sample sizes in some studies [15].

Studies comparing the various surgical approaches for VUR are lacking, and management guidelines are limited by a paucity of randomized, prospective studies comparing the various surgical modalities.

There have been several previous studies comparing two of the three surgical modalities for treatment of VUR. In 2007, Oberson et al. retrospectively reported their results with endoscopic suburethral collagen injection compared to open cross-trigonal reimplantation, with a mean follow-up of 50 months [16]. Ninety-two refluxing ureters were treated with endoscopic injection, and 123 underwent open reimplantation. The VUR resolution rate was 96% after open reimplantation compared to 64% after a single collagen injection.

Two recent studies compared results from open versus robotic ureteral reimplantation. Marchini et al. retrospectively reviewed their results of robotic reimplantation (19 intravesical, 20 extravesical) compared to a case matched cohort of patients who underwent open reimplantation (22 intravesical, 17 extravesical) [15]. Overall success rates were similar for all surgical techniques (92%-100%). Although robotic reimplantation was associated with longer operative times, patients undergoing robotic intravesical reimplantation benefited from shorter hospital stay, shorter duration of urinary catheter drainage, and fewer bladder spasms compared to the open intravesical cohort. These parameters were not significantly different among patients undergoing open versus robotic extravesical reimplantation.

Smith et al. retrospectively reviewed their results from 25 patients who underwent robotic extravesical ureteral reimplantation compared

to a matched cohort of 25 patients treated with open reimplantation [17]. No significant difference was found in success rates for robotic (97%) versus open surgery (100%). Although mean operative time was 12% longer for robotic surgery, these patients benefited from shorter length of stay and decreased pain medication usage.

To our knowledge, our study is the first to include all three surgical modalities for VUR treatment. We found significantly higher success rates with open reimplantation versus Deflux. We recognize the significant limitations of a retrospective review spanning a nine-year period. Four pediatric urologists performed these operations, and each surgeon was at a different stage in his/her career. Their experience may factor into overall success rates. The collection of data prior to the use of electronic medical records represents an additional challenge. We struggled to obtain reliable data regarding the presence of bladder/bowel dysfunction. In addition, Deflux injection volumes and techniques were often unavailable or inconsistently reported. Therefore, we did not include these parameters in our analysis, although it has been previously demonstrated that they can impact postoperative outcomes [18,19]. Furthermore, the significantly smaller sample size of the robotic cohort compared to the other treatment groups limited our ability to appropriately compare their success rates. Despite these limitations, our study provides a basis for the comparison of the various treatment modalities, and we have been enrolling patients into a prospective registry of all VUR procedures at our institution since 2010.

In conclusion, we found significantly higher success rates with open reimplantation versus Deflux in the treatment of primary VUR. While robotic surgery had high success rates and short hospital stays, the smaller sample size limited statistical comparison of this modality to open surgery or Deflux injection. We continue to enroll patients into a prospective series of all VUR procedures at our institution, which will result in more robust comparisons. Continued analysis of surgical outcomes is important for parental education and a shared decision-making process.

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