Surgical Management of Bilateral Vesicoureteral Reflux With Unilateral High-Grade Involvement: Comparative Outcomes of Endoscopic, Open Intravesical, and Hybrid Approaches

Araz Musaev, Can Sicimli, Ataxan Musayev, Hüzeyfe Yusuf Şahin, Michele Gnech, Yakup Tarkan Soygür, and Berk Burgu

OBJECTIVE To determine the optimal surgical approach for patients with high-grade vesicoureteral reflux (VUR) on one side and low-grade VUR on the contralateral side by comparing three strategies: bilateral endoscopic correction, bilateral intravesical cross-trigonal ureteral reimplantation (Cohen technique), and a combined approach involving extravesical reimplantation for the high-grade side and endoscopic correction for the low-grade side.

METHODS Between 2010 and 2023, pediatric patients under the age of eighteen who underwent surgery at our clinic for VUR characterized by high-grade reflux on one side and low-grade reflux on the contralateral side were retrospectively reviewed. Based on the surgical technique, patients were categorized into three groups: Group 1 underwent bilateral endoscopic correction, Group 2 underwent bilateral intravesical reimplantation, and Group 3 underwent the combined approach.

RESULTS A total of 140 patients were included: 40 in Group 1, 53 in Group 2, and 47 in Group 3. The clinical success rates were 40%, 95%, and 94% for Groups 1, 2, and 3, respectively ($P < .001$). The median length of hospital stay was 0, 4, and 1 days, respectively ($P < .001$).

CONCLUSION Bilateral endoscopic correction was found to be an inferior treatment option compared to both bilateral intravesical ureteroneocystostomy (UNC) and the combined approach. Unilateral extravesical UNC combined with endoscopic subureteric injection for the contralateral low-grade VUR appears to offer comparable clinical success to bilateral intravesical UNC, while requiring less postoperative hospitalization, pain, and overall cost. UROLOGY 205: 209–214, 2025.

Vesicoureteral reflux (VUR) is the abnormal retrograde flow of urine from the bladder into the ureter(s) and/or kidney(s).[1] VUR is a common urinary tract anomaly in children, with an estimated prevalence of approximately 1%.[1,2] VUR is associated with an increased risk of febrile urinary tract infections (fUTI) and renal scarring, also referred to as reflux nephropathy.[3] Long-term follow-up studies have demonstrated that 10%-20% of children with reflux nephropathy develop hypertension or progress to end-stage renal disease.[4]

Surgical management of VUR is typically based on reflux severity. Endoscopic correction is generally preferred for low-grade VUR (Grades I-III), while ureteral reimplantation is reserved for high-grade VUR (Grades IV-V), with both approaches demonstrating high success rates.[5–7] To the best of our knowledge, the optimal surgical strategy for patients with high-grade VUR on one side and low-grade VUR on the contralateral side has not yet been established and has not been sufficiently investigated.

Accordingly, in this study, we aimed to determine the optimal surgical option for patients with high-grade VUR on one side and low-grade VUR on the contralateral side by comparing bilateral endoscopic injection of a bulking agent,

Abbreviations: VUR, Vesicoureteral reflux; fUTI, Febrile urinary tract infection; ESRD, End-stage renal disease; RN, Reflux nephropathy; USG, ultrasonography; UNC, ureteroneocystostomy; DMSA, dimercaptosuccinic acid; IQR, interquartile range; SPSS, Statistical Package for the Social Sciences

From the Department of Urology, Division of Pediatric Urology, Ankara University School of Medicine, Ankara, Turkey; and the Fondazione IRCCS Ca' Granda - Ospedale Maggiore Policlinico, Milano, Italy

Address correspondence to: Araz Musaev, M.D., Ankara Universitesi Tıp Fakultesi, İbni-Sina hastanesi, 06230, Altındag, Ankara, Turkey. E-mail: Msyv.araz@gmail.com

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bilateral intravesical cross-trigonal ureteral reimplantation (Cohen technique), and a combined approach involving extravesical reimplantation for the high-grade side and endoscopic correction for the low-grade side.

MATERIAL AND METHODS

Patient Selection/Study Population

The medical records of all the pediatric patients under the age of 18 who underwent surgical or endoscopic treatment for symptomatic (fUTIs) primary VUR at our center between 2010 and 2023 were retrospectively reviewed. A protocol defining the inclusion criteria, outcomes, and statistical plan was established prior to data collection and analysis.

Eligibility criteria were defined as follows: patients were included if preoperative voiding cystourethrography (VCUG) demonstrated high-grade VUR on one side and low-grade VUR on the contralateral side. In the preoperative VCUG evaluation, grades 1, 2, and 3 were classified as low-grade VUR, while grades 4 and 5 were classified as high-grade VUR.[8]

Exclusion criteria included the presence of unilateral VUR, secondary VUR, bilateral high-grade VUR, duplex systems associated with VUR, bilateral low-grade VUR, or a history of prior urinary tract or VUR-related surgery.

Study Design

Given the retrospective design of the study, patients were stratified into three groups based on the type of surgical procedure previously performed, with group allocation determined by the intervention received. Group 1 included patients who underwent bilateral endoscopic correction using subureteric injection of dextranomer/hyaluronic acid (Dexell) injection. Group 2 consisted of patients who underwent bilateral intravesical cross-trigonal ureteral reimplantation (Cohen technique). Group 3 included patients who underwent open extravesical ureteral reimplantation (Lich-Gregoir technique) on the side with high-grade VUR and endoscopic subureteric Dexell injection on the side with low-grade VUR performed during the same surgical session. All procedures were conducted by one of two experienced pediatric urologists at our center.

Data Collection

Demographic data, preoperative imaging findings, surgical indications, perioperative complications, length of hospital stay, day of urethral catheter removal, day of pelvic drain removal, day of ureteral stent removal, total treatment cost, treatment success, and complications were collected and compared among the groups.

Outcome Measures

At our center, patients who underwent surgical treatment for VUR were routinely followed up with a urinary tract ultrasound (USG) 1 month after hospital discharge. Subsequent follow-up evaluations were performed at 6 months postoperatively and then annually.

Following surgery, prophylactic antibiotic therapy (either sulfamethoxazole/trimethoprim or nitrofurantoin) was continued until the first-month follow-up visit, at which time the decision to continue or discontinue prophylaxis was made based on clinical evaluation. In patients with intraoperatively placed ureteral stents, prophylactic antibiotics were maintained until stent removal. Postoperative VCUG was performed only in cases of fUTI during follow-up.

Postoperative fUTI episodes were identified through a comprehensive review of inpatient and outpatient medical records, including emergency department visits and routine follow-up notes. A fUTI was defined as the presence of a documented fever > 38 °C accompanied by a positive urine culture, with other potential sources of infection either excluded or evaluated for co-occurrence.

Clinical treatment success was defined as the absence of fUTI and the need for reintervention during a 1-year follow-up period. Considering the challenges associated with long-term imaging-based follow-up in real-world clinical settings and the fact that up to 10% of patients may still experience fUTIs despite the absence of reflux on postoperative VCUG,[9] we focused on clinically meaningful outcomes, such as fUTI occurrence and the requirement for reintervention, which are more reliably documented and directly relevant to patient care.

Although the study is retrospective, the total treatment cost (including surgery procedures, length of hospital stays, and medical supplies) was recalculated based on current institutional pricing (as of May 1, 2025).

For the purposes of this study, the postoperative course was divided into early (≤30 days post-surgery) and late (> 30 days post-surgery) periods.

Statistical Analysis

Statistical analysis was performed using the Statistical Package for the Social Sciences version 30. Categorical variables were expressed as frequencies and percentages, while continuous variables were reported as means and standard deviations. The normality of the continuous variables was assessed using both visual methods (histograms) and analytical tests (Shapiro-Wilk test, Kolmogorov-Smirnov test, and evaluation of skewness and kurtosis values). For comparisons of continuous variables among the three groups, the Kruskal–Wallis H test was used for non-normally distributed data, whereas one-way analysis of variance was applied for normally distributed data. The Chi-square test, Fisher's exact test, and Yates' continuity correction were performed for comparisons of categorical variables. A P value of less than .05 was considered statistically significant, and a 95% confidence interval was adopted for all analyses.

RESULTS

A total of 140 patients met the inclusion criteria and were enrolled in the study: Group 1 (n = 40, 28.6%),

Table 1. Demographics and preoperative imaging characteristics.

	Group 1 (n = 40)	Group 2 (n = 53)	Group 3 (n = 47)	P value
Age, months median (IQR*)	36 (25-43)	36 (26-47)	35 (20-46)	.8†
Gender, n				.9‡
Male	18	26	22	
Female	22	27	25	
Number of Documented fUTI Episodes Before Surgery, n (IQR)	4 (3-6.5)	5 (3.5-7)	4 (3-7)	.2‡
Preoperative imaging, %				
USG	100	100	100	
VCUG	100	100	100	
DMSA	100	100	100	
Renal Scar on DMSA, %	62	55	69	.4‡
Bilateral renal scars on DMSA, %	19	16	17	.9‡
Unilateral renal scars in high-grade side, %	34	28	39	.5‡
Unilateral renal scars in low-grade side, %	9	11	13	.8‡
Split renal function on DMSA, median % (IQR)				
High-grade side	37 (32-41)	39 (35-43)	38 (33-43)	.4‡
Low-grade side	63 (58-68)	61 (56-65)	62 (56-66)	.4‡

DMSA, dimercaptosuccinic acid; fUTI, febrile urinary tract infection; USG, ultrasonography; VCUG, voiding cystourethrography.
* IQR: Interquartile range.
† Kruskal–Wallis H test was used.
‡ Chi-square test was used.

Group 2 (n = 53, 37.9%), and Group 3 (n = 47, 33.6%). The demographic characteristics and preoperative imaging findings of the patients are presented in Table 1. All patients had preoperative USG, VCUG, and dimercaptosuccinic acid (DMSA) scintigraphy results available. There were no statistically significant differences among the groups in terms of demographic data or preoperative imaging findings. Indications for surgery included fUTI under antibiotic prophylaxis, persistent high-grade reflux, recurrent fUTI off prophylaxis, renal scarring, and caregivers' preference. No intraoperative complications were encountered in any of the 3 groups.

The mean length of hospital stay was 0, 4, and 1 days for Groups 1, 2, and 3, respectively (P < .001) Table 2.

In Group 1, fUTIs occurred in two patients during the early postoperative period. Imaging studies demonstrated increased dilatation on the side of preoperative high-grade reflux; however, no reflux was observed on cystogram and PIC cystography. Double-J stents were placed in both patients, leading to a marked regression of hydroureteronephrosis (HUN) on follow-up ultrasonography 1 month later, after which the stents were removed. Due to an increase in HUN during subsequent follow-up, both patients underwent successful unilateral extravesical dismembered ureteroneocystostomy (UNC).

The success rate in Group 1 was 40% (n = 16), which was significantly lower than the success rates observed in Groups 2 (95%) and 3 (94%) (P < .001), Figure 1. In Group 1, for patients in whom treatment was unsuccessful, VCUG revealed persistent high-grade VUR on the affected side in 17 patients, all of whom subsequently underwent extravesical Lich-Gregoir reimplantation. In an additional 5 patients, low-grade contralateral VUR was detected and managed with a repeat Dexell injection. No fUTI was observed in these patients during follow-up.

In Group 2, fUTI was observed in 3 patients (5%) during the late postoperative period. VCUG showed recurrent reflux on the high-grade side. Both patients underwent successful UNC using the Leadbetter-Politano technique.

In Group 3, 3 patients (6%) developed late postoperative fUTIs. VCUG did not reveal VUR in these patients. However, ultrasonography demonstrated marked HUN on the side that had preoperative low-grade reflux. Double-J stents were placed in all three patients, and follow-up ultrasonography performed 1 month later showed a significant reduction in HUN. Consequently, the stents were removed. Nevertheless, due to recurrence of HUN during follow-up, all 3 patients subsequently underwent successful extravesical dismembered UNC.

DISCUSSION

The subureteric bulking agent injection, initially described by Barry O'Donnell and Prem Puri, has become a widely accepted, minimally invasive, outpatient procedure for the treatment of VUR.[10] Among various bulking agents developed for VUR treatment, dextranomer/hyaluronic acid has achieved widespread clinical use due to its favorable properties, including biodegradability, nonallergenic and non-immunogenic profile, lack of malignant transformation risk, minimal theoretical risk of particle migration, and worldwide regulatory approval. A meta-analysis reported that the success rate of subureteric injection therapy is inversely proportional to the severity of reflux, with outcomes of 78.5% for Grades I and II, 72% for Grade III, 63% for Grade IV, and 51% for Grade V.[6]

Various intra- and extravesical techniques have also been described for the surgical treatment of VUR. These approaches generally demonstrate excellent safety profiles, with low complication rates and success rates

Table 2. Clinical outcomes.

	Group 1 (n = 40)	Group 2 (n = 53)	Group 3 (n = 47)	P value
Circumcision before surgery (boys), %	78	84	68	.3[a]
Circumcision on the same day (boys), %	22	16	32	.3[a]
Length of hospitalization, median (IQR)	0	4 (4-5)	1 (1-2)	< .001[b]
Foley catheter placement, %	4	100	100	< .001[a]
Total treatment cost, TL (USD)**, mean	9,280 (232)	19,400 (485)	14,500 (364)	< .001[c]
Day of Foley catheter removal, median (IQR)	1	3 (3-4)	1 (1-2)	< .001[b]
Ureteral stent placement, %	-	69	-	
Pelvic drain placement, %	-	69	4	< .001[a]
Follow-up, median month (IQR)	23 (17-27)	22 (18-25)	22 (17-27)	.5[b]
F-UTI in follow-up, % (n)	56 (22)	5 (3)	6 (3)	< .001[a]
Reintervention in the early postoperative period, % (n)	4 (2)	0 (0)	0 (0)	
Reintervention in the Postoperative Period (Early and Late), % (n)	60 (24)	5(3)	6(3)	< .001[a]
Postoperative VCUG Findings in Patients with fUTI				
Persistent VUR on the preoperative high-grade VUR side, % (n)	77 (17)	100 (3)	0	
Persistent VUR on the preoperative low-grade VUR side, % (n)	23 (5)	0(0)	0	
Persistent VUR on both sides, % (n)	0(0)	0(0)	0	

*IQR: Interquartile range.
fUTI, Febrile urinary tract infection; VUR, Vesicoureteral reflux.
** TL: Turkish Lira, USD: US dollars.
[a] Chi-square test was used.
[b] Kruskal–Wallis H test was used.
[c] One-way ANOVA.

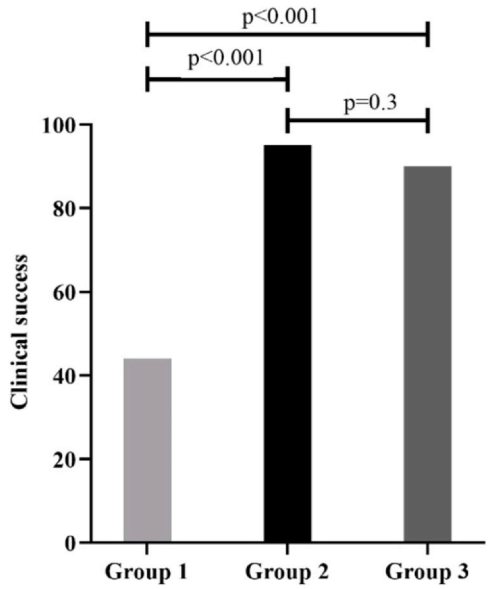

Figure 1. Treatment success rates among surgical group.

ranging from 92% to 98%.[5] Cross-trigonal ureteral reimplantation, as described by Cohen, remains the most widely preferred and dependable open surgical technique. However, a recognized limitation of this technique is the potential difficulty in accessing the ureters endoscopically in later years, should further intervention be necessary.[11] First described in 1964, the Lich-Gregoir procedure provides an extravesical approach for antireflux surgery, avoiding bladder entry and thereby maintaining the anatomical and vascular integrity between the bladder and the affected ureter. Importantly, it preserves the native position of the ureteral orifice.[12] Nevertheless, when applied bilaterally, it has been associated with an increased risk of transient postoperative urinary retention due to potential injury to the subtrigonal nerve plexus.[13]

Previous studies have demonstrated that intravesical cross-trigonal UNC (Cohen technique) is associated with a longer and more painful hospital stay, increased incidence of gross hematuria, and prolonged operative time compared to the extravesical UNC (Lich-Gregoir technique).[14,15] In our study, hospitalization durations varied among the three surgical groups and were primarily influenced by perioperative management practices within our institution. Patients in Group 1 were typically discharged on the same or the following day due to the minimally invasive nature of the procedure. In Group 3, patients were generally discharged the day after surgery. However, patients in Group 2 were discharged on postoperative day 4 on average, depending on the timing of urethral catheter and pelvic drain removal. Notably, this perioperative protocol and the associated length of stay are consistent with previous reports in the literature regarding bilateral intravesical ureteral reimplantation (Cohen) procedures.[16–18]

In our study, the clinical success rate of bilateral subureteric injection (Group 1) was 40%, confirming the limitations of this approach in cases involving high-grade VUR. This is consistent with published data demonstrating the limited efficacy of endoscopic treatment in severe reflux.[6] Additionally, the absence of a learning curve effect (since the procedures were performed by experienced surgeons) suggests that the failure rate is attributable to inherent limitations of the technique rather than operator variability.

Based on the current literature and our findings, a combination of endoscopic subureteric injection, known for its high success rate in low-grade cases, and effective

extravesical antireflux surgery for the high-grade side may be considered a rational and effective treatment strategy.[18,19] This hybrid technique leverages the minimally invasive advantage of endoscopy on the less affected side while ensuring definitive correction on the high-grade side.

According to our data, the success rate of bilateral subureteric injection in this patient group was lower compared to both bilateral intravesical reimplantation and combined surgery. When Groups 2 and 3 were compared, the success rate of combined surgery was found to be similar to that of bilateral intravesical UNC, with no statistically significant difference between them (Fig. 1).

Various studies have reported conflicting findings regarding the cost-effectiveness of endoscopic injection compared to reimplantation surgery. While some suggest that endoscopic treatment is less costly, others highlight its higher overall expense.[20–22] Importantly, none of these studies have included a cost analysis of combined surgical approaches. Although cost structures may vary across healthcare systems and institutions, our results suggest that the combined surgical approach is associated with lower overall costs compared to bilateral intravesical UNC.

Furthermore, performing the combined procedure without the use of ureteral stents offers additional benefits over bilateral intravesical UNC. It eliminates the cost of the stents and the need for a second surgical intervention for stent removal. This not only reduces the financial burden on the healthcare system but also spares the patient from undergoing an additional surgical procedure for stent removal and contributes to a shorter hospital stay. These findings suggest that the combined approach represents a practical, patient-centered alternative with comparable efficacy and lower morbidity.

The limitations of our study include its retrospective nature, which inherently precludes the evaluation of certain postoperative parameters, such as bladder dysfunction or voiding symptoms. Moreover, the small number of treatment failures in Group 3 limited our ability to conduct regression analysis to identify predictive factors for unsuccessful outcomes.

In addition, although the baseline characteristics appeared comparable among the groups, the choice of surgical approach was not randomized and may have been influenced by surgeon preference, experience, or intraoperative judgment, potentially introducing selection bias.

Although the absence of fUTI and the need for reintervention are commonly used clinical indicators of clinical success, they do not fully substitute for postoperative VCUG, which remains the gold standard for evaluating surgical (radiological) success. Relying solely on clinical success may result in underdetection of persistent VUR and ongoing renal damage, potentially leading to significant long-term consequences.

According to the literature, it is stated that parenchymal defects observed on DMSA scans may originate from both congenital renal dysplasia and acquired renal scarring.[23] Particularly in male children and in cases of high-grade VUR, a significant proportion of the lesions observed on DMSA may be of congenital dysplastic origin.[24] At the same time, children with high-grade VUR or a history of recurrent fUTIs are at increased risk of developing acquired renal scars.[4] The high rate of renal scarring observed in our study may reflect a combination of these two etiologies (Table 1). Considering the limitations of DMSA in distinguishing between congenital and acquired lesions, it is possible that some of the defects observed in our study may be attributable to congenital dysplasia. This underscores the complexity of the pathophysiology of renal damage in children with VUR.

It should be noted that the decision to place an indwelling ureteral stent during Cohen reimplantation was not standardized and depended on intraoperative findings and surgeon preference. This reflects the ongoing debate regarding routine stenting in ureteral reimplantation and represents a potential limitation of our study. Nevertheless, this variation mirrors real-world surgical practice and highlights the individualized nature of perioperative management. Importantly, the proportion of patients who did not receive an indwelling stent (31%) is consistent with previous reports in the literature.[18,25]

Future prospective studies or multicentric analyses could help validate the generalizability of the hybrid approach and clarify whether specific patient or anatomical characteristics may predict optimal candidacy for this strategy.

CONCLUSION

Bilateral endoscopic correction demonstrated inferior outcomes compared to other surgical strategies in the management of asymmetrical bilateral VUR, as evidenced by persistent high-grade VUR on follow-up VCUG.

By contrast, unilateral extravesical UNC combined with contralateral endoscopic subureteric injection for the low-grade VUR achieved a clinical success rate comparable to that of bilateral intravesical UNC, while offering the advantage of shorter postoperative hospitalization, reduced morbidity, and lower overall cost. Additionally, the hybrid approach obviates the need for ureteral stent placement and subsequent removal, further minimizing patient burden and resource use.

Ethical Declaration

This study was conducted in accordance with the ethical standards provided in the 1964 Declaration of Helsinki and its subsequent amendments and was approved by the local ethics committee.

Disclosures

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CRediT Authorship Contribution Statement

Araz Musaev: Writing – original draft, Visualization, Supervision, Project administration, Methodology, Formal analysis, Data curation, Conceptualization. **Can Sicimli:** Resources, Formal analysis. **Ataxan Musayev:** Data curation. **Hüzeyfe Yusuf Şahin:** Data curation. **Michele Gnech:** Writing – review & editing, Methodology. **Yakup Tarkan Soygür:** Supervision, Methodology. **Berk Burgu:** Writing – review & editing, Validation, Supervision, Methodology, Conceptualization.

Declaration of Competing Interest

The authors have no conflict of interest to declare.

Declaration of Generative AI and AI-Assisted Technologies in the Writing Process

The authors did not use generative AI or AI-assisted technologies in the development of this manuscript.

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