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COMPARISON OF ENDOSCOPIC AND CONSERVATIVE MANAGEMENT IN PEDIATRIC VESICOURETERAL REFLUX: A RETROSPECTIVE STUDY

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Abstract

Background: Vesicoureteral reflux (VUR) is a prevalent congenital urinary tract anomaly in children, often associated with recurrent urinary tract infections (UTIs), renal scarring, and long-term complications such as hypertension and chronic kidney disease. The optimal management of primary VUR—particularly in intermediate grades—remains debated, with both conservative and endoscopic treatments widely used.

Objective: To compare clinical and functional outcomes of endoscopic injection therapy versus conservative management in pediatric patients with primary VUR, focusing on reflux resolution, UTI recurrence, renal scarring, and renal function.

Methods: This retrospective study included 70 pediatric patients with primary VUR treated at a tertiary center between 2015 and 2018. Thirty-five patients underwent endoscopic subureteric injection with dextranomer/hyaluronic acid copolymer, and 35 received conservative management with antibiotic prophylaxis. Comparative analysis assessed changes in VUR grade, recurrence of UTIs, renal scarring (via technetium-99m dimercaptosuccinic acid [DMSA] scintigraphy), renal function by kidney side, and serum creatinine levels.

Results: Endoscopic treatment achieved complete reflux resolution in 74.3% of cases. A significant reduction in reflux grade and improvement in right kidney function were observed in the intervention group ($p < 0.001$). The conservative group showed higher rates of recurrent febrile UTIs and no significant improvement in renal function. Renal scarring was present in both groups but slightly less frequent following endoscopic therapy. Post-treatment left kidney function was significantly higher in the conservative group ($p = 0.020$), likely reflecting baseline differences.

Conclusions: Endoscopic injection therapy is a safe and effective treatment for moderate-to-high-grade VUR in children, associated with superior reflux resolution and better infection control compared to conservative management. Conservative therapy remains appropriate for select low-grade cases but may confer higher risk for recurrent infections and limited renal recovery. Individualized treatment selection is essential to optimize pediatric VUR outcomes.

Keywords: vesicoureteral reflux, endoscopic therapy, urinary tract infection, renal scarring, pediatric urology, reflux resolution

Introduction

Vesicoureteral reflux (VUR) is a common congenital anomaly of the urinary tract in children, characterized by the retrograde flow of urine from the bladder into the ureters and kidneys. It is frequently associated with recurrent urinary tract infections (UTIs), febrile episodes, renal scarring, and long-term complications such as hypertension and chronic kidney disease when inadequately managed [1,2].

Diagnosis of VUR typically involves voiding cystourethrogram (VCUG), the gold standard for assessing the presence and grade of reflux. Renal parenchymal damage and scarring are commonly evaluated using technetium-99m dimercaptosuccinic acid (DMSA) scintigraphy, which also provides information on differential renal function [3,4].

Management of primary VUR remains the subject of ongoing debate, especially in children with intermediate-grade (II–IV) reflux. Conservative therapy with continuous antibiotic prophylaxis has traditionally aimed to prevent UTIs and facilitate spontaneous resolution of reflux [5,6]. However, concerns about antimicrobial resistance, breakthrough infections, and long-term patient adherence have raised questions about its overall efficacy [3,7,8].

Endoscopic injection therapy using bulking agents such as dextranomer/hyaluronic acid copolymer (Deflux) has emerged as a minimally invasive alternative. Numerous studies have reported reflux resolution rates exceeding 70%, particularly in children with moderate-grade VUR, although outcomes vary by injection technique and reflux severity [2,9,10]. Despite its growing adoption, endoscopic management continues to face scrutiny regarding long-term effectiveness, procedural failure, and cost-effectiveness, particularly in high-grade or recurrent cases [5,13,14].

A recent network meta-analysis highlighted the heterogeneity in outcomes across treatment strategies, emphasizing the need for individualized therapeutic decision-making [1]. In this context, further comparative studies are warranted to clarify the clinical utility of each modality.

This retrospective study aimed to compare the clinical and functional outcomes of endoscopic injection therapy versus conservative management in pediatric patients with primary VUR. The analysis focused on key indicators including reflux resolution, recurrence of UTIs, renal scarring, and differential renal function.

Materials and Methods

This retrospective study included 70 pediatric patients with a confirmed diagnosis of primary vesicoureteral reflux (VUR), treated at the University Pediatric Surgery Clinic in Skopje between 2015 and 2018. The dataset was initially compiled as part of the doctoral research of Dr. Shaban Memeti.

Patients were divided into two equal groups of 35. The intervention group underwent endoscopic subureteric injection with dextranomer/hyaluronic acid copolymer (Deflux), while the control group was managed conservatively with antibiotic prophylaxis and clinical follow-up.

Inclusion criteria were: (1) primary VUR confirmed by voiding cystourethrogram (VCUG), (2) available clinical and imaging follow-up, and (3) no prior surgical treatment. Patients with secondary reflux due to anatomical or neurogenic causes were excluded.

Data collected from medical records included sex, reflux grade and laterality, UTI frequency and recurrence, fever status, presence of renal scarring (based on DMSA scans), post-treatment reflux resolution (in the intervention group), differential renal function, and serum creatinine levels.

Comparative analyses between the two groups focused on reflux grade reduction, UTI recurrence, renal scarring, renal function by kidney side, and creatinine levels. Non-parametric tests were used for statistical comparisons, and a p-value < 0.05 was considered statistically significant.

Ethical approval was obtained for the original data collection as part of the doctoral research protocol. The present analysis uses anonymized data for secondary publication purposes.

Results

Table 1. Distribution of patients by sex in both groups

Sex	IG (n=35)	%	CG (n=35)	%
Male	10	28.6%	10	28.6%
Female	25	71.4%	25	71.4%
Total	35	100%	35	100%

Sex distribution was identical in both groups, with 28.6% of patients being male and 71.4% female (Table 1).

Table 2. Combined distribution of VUR side and grade in both groups.

Category	IG Count	IG %	CG Count	CG %
Left	11	31.4%	11	31.4%
Right	10	28.6%	9	25.7%
Bilateral	14	40.0%	15	42.9%
Grade 1	1	2.9%	0	0.0%
Grade 2	3	8.5%	10	28.6%
Grade 3	24	68.6%	19	54.3%
Grade 4	6	17.1%	5	14.3%
Grade 5	1	2.9%	1	2.8%

At baseline, bilateral reflux was the most common anatomical presentation in both groups, affecting 40.0% of patients in the intervention group (IG) and 42.9% in the control group (CG). Left-sided reflux was present in 31.4% of IG and CG patients, while right-sided reflux occurred in 28.6% of IG and 25.7% of CG patients. Grade 3 was the most frequent reflux severity, observed in 68.6% of IG and 54.3% of CG patients. Grades 1 and 2 were recorded in 11.4% of IG and 28.6% of CG, while Grades 4 and 5 were seen in 20.0% of IG and 17.1% of CG (Table 2).

Table 3. Distribution of reflux grades in the intervention group after treatment.

VUR Grade After Treatment	IG (n=35)	%
Grade 0 (Resolved)	26	74.3%
Grade 1	3	8.6%
Grade 2	1	2.9%
Grade 3	4	11.3%
Grade 4	1	2.9%
Grade 5	0	0.0%
Total	35	100%

As presented in Table 3, 74.3% of patients in the intervention group achieved Grade 0 reflux following treatment. Residual reflux grades were observed in 8.6% (Grade 1), 2.9% (Grade 2), 11.3% (Grade 3), and 2.9% (Grade 4). No patients remained at Grade 5.

Table 4. Mean reflux grade before and after treatment in the intervention group.

Treatment Stage	Mean Grade	N	Standard Deviation	Minimum	Maximum
Before	3.1	35	0.70	1.0	5.0
After	0.6	35	1.17	0.0	4.0

The mean VUR grade in the intervention group was 3.1 (±0.70) before treatment and decreased to 0.6 (±1.17) after treatment. These values are presented in Table 4.

Table 5. Mann–Whitney U test comparing reflux grades before and after treatment in the intervention group.

Test Parameter	Value
Rank Sum – Pre	1756.000
Rank Sum – Post	729.000
U Statistic	99.000
Z Score	6.03
p-value	< **0.0001**

The reduction in reflux grade following intervention was statistically significant. The Mann–Whitney U test yielded a U statistic of 99.000, with a Z score of 6.03 and a p-value less than 0.0001, indicating a significant difference in reflux grade distributions before and after treatment (Table 5).

Table 6. Clinical manifestations of urinary tract infections in both groups.

UTI Indicator	Response	IG Count	IG %	CG Count	CG %
Fever Associated with UTI	Yes	28	80.0%	31	88.6%
	No	7	20.0%	4	11.4%
Symptomatic UTI Presentation	Yes	32	91.4%	34	97.1%
	No	3	8.6%	1	2.9%

Fever associated with urinary tract infection (UTI) was reported in 80.0% of patients in the intervention group (IG) and 88.6% in the control group (CG). Symptomatic UTI presentation occurred in 91.4% of IG patients and 97.1% of CG patients (Table 6).

Table 7. Recurrent urinary tract infections in the intervention group.

Recurrent UTI	IG (n=35)	%
Yes	11	31.4%
No	24	68.6%
Total	35	100%

As shown in Table 7, 31.4% of patients in the intervention group experienced recurrent urinary tract infections (UTIs), while 68.6% had no recurrence during follow-up.

Table 8. Presence of renal scarring (DMSA Scan).

Renal Scarring	IG (n=35)	%	CG (n=35)	%
Yes	8	22.9%	10	28.6%
No	27	77.1%	25	71.4%
Total	35	100%	35	100%

Renal scarring, as assessed by DMSA scan, was present in 8 patients (22.9%) in the intervention group and 10 patients (28.6%) in the control group. The remaining 27 patients (77.1%) in IG and 25 patients (71.4%) in CG showed no evidence of scarring (Table 8).

Table 9. Mean renal function (post-therapeutic evaluation) by kidney side and group.

Kidney Side	Group	Mean (%)	N	SD (%)	Min (%)	Max (%)
Left	IG	43.9	28	24.12	12.0	85.0
Left	CG	59.6	17	14.42	39.0	90.0
Right	IG	39.6	28	21.56	13.0	88.0
Right	CG	41.9	17	17.51	18.0	86.0

Post-treatment renal function assessment showed that the mean function of the left kidney was 43.9% (SD = 24.12) in the intervention group and 59.6% (SD = 14.42) in the control group. On the right side, the mean renal function was 39.6% (SD = 21.56) in the intervention group and 41.9% (SD = 17.51) in the control group (Table 9). Renal function data were available for 28 patients in the intervention group and 17 in the control group.

Non-parametric tests (Mann–Whitney U and Wilcoxon signed-rank) were applied to assess between-group and within-group renal function differences (Tables 10 and 11).

Table 10. Mann–Whitney U test for post-treatment renal function between groups.

Kidney Side	Rank Sum IG	Rank Sum CG	U	Z	p-value
Left	544.500	490.500	138.500	-2.318	0.020
Right	621.500	413.500	215.500	-0.515	0.607

Mann–Whitney U test results showed a statistically significant difference in post-treatment left kidney function between groups (U = 138.5, Z = –2.318, p = 0.020), while no significant difference was observed for the right kidney (U = 215.5, Z = –0.515, p = 0.607) (Table 10).

Table 11. Wilcoxon matched pairs test – change in renal function within groups

Comparison	N	T	Z	p-value
IG Left: Pre vs Post	26	165.000	0.267	0.790
CG Left: Pre vs Post	17	65.500	0.521	0.603
IG Right: Pre vs Post	24	38.500	3.186	0.001
CG Right: Pre vs Post	15	37.000	1.306	0.191

Within-group comparisons using the Wilcoxon matched pairs test showed a statistically significant improvement in right kidney function in the intervention group (Z = 3.186, p = 0.001). No significant change was observed in left kidney function in either group, nor in right kidney function in the control group (Table 11).

Table 12. Mean serum creatinine values by group.

Group	Mean (µmol/L)	N	SD	Min	Max
IG	62.5	35	13.22	38.0	88.0
CG	57.4	22	23.21	26.0	139.0

The mean serum creatinine concentration was 62.5 µmol/L (SD = 13.22) in the intervention group and 57.4 µmol/L (SD = 23.21) in the control group. Serum creatinine data were missing for 13 patients in the control group.

Minimum and maximum values ranged from 38.0 to 88.0 µmol/L in the intervention group and from 26.0 to 139.0 µmol/L in the control group (Table 12).

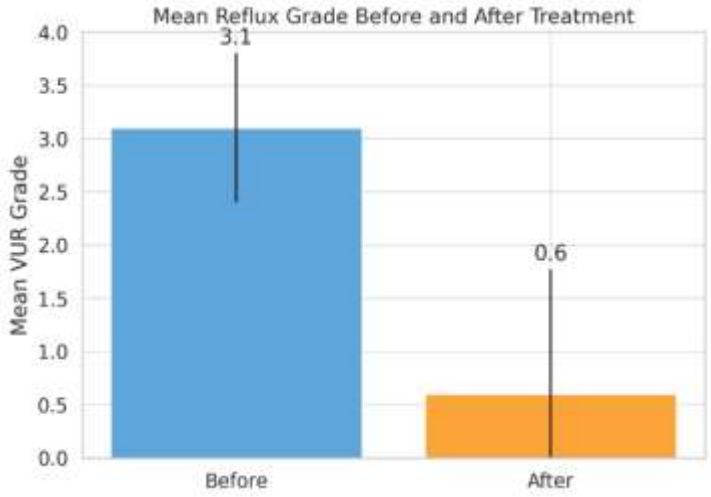

Figure 1. Mean reflux grade before and after treatment

The mean VUR grade decreased from 3.1 (±0.70) before treatment to 0.6 (±1.17) after treatment. The figure depicts group mean values with corresponding standard deviation error bars to illustrate variability in reflux severity before and after intervention (Figure 1).

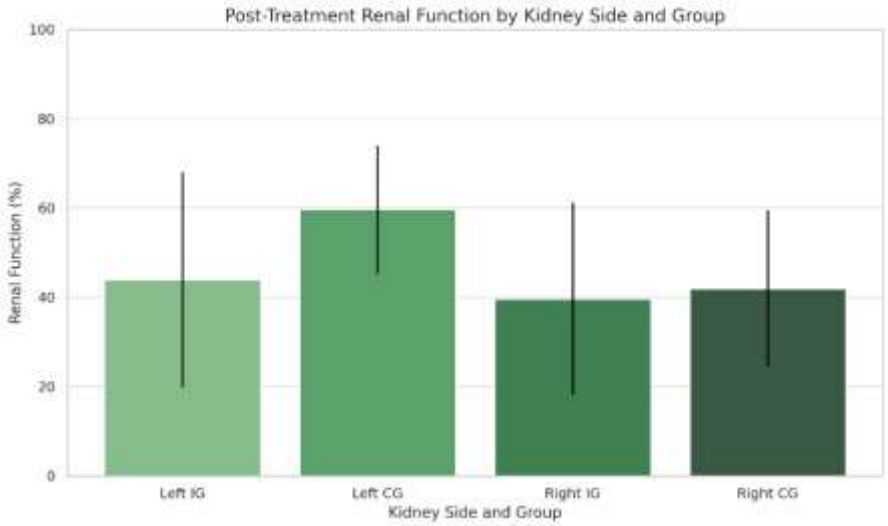

Figure 2. Post-treatment renal function by kidney side and treatment group

The mean post-treatment function of the left kidney was 43.9% (SD = 24.12) in the intervention group and 59.6% (SD = 14.42) in the control group. For the right kidney, mean function was 39.6% (SD = 21.56) in the intervention group and 41.9% (SD = 17.51) in the control group. Error bars represent standard deviation (Figure 2).

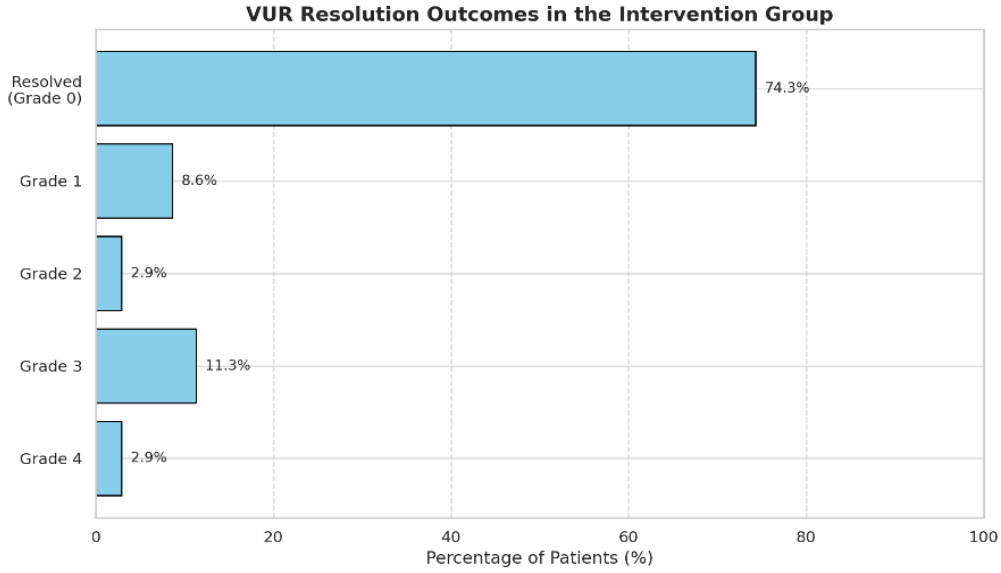

Figure 3. VUR resolution outcomes in the intervention group

Post-treatment assessment of VUR grades in the intervention group (n = 35) showed that 26 patients (74.3%) had complete resolution (Grade 0). Grade 1 was present in 3 patients (8.6%), Grade 2 in 1 patient (2.9%), Grade 3 in 4 patients (11.3%), and Grade 4 in 1 patient (2.9%). No patients remained at Grade 5. The figure illustrates the full range of residual reflux grades following intervention (Figure 3).

Radiological Findings in Representative Cases

All patients in the study underwent initial diagnostic evaluation using voiding cystourethrogram (VCUG), which remains the gold standard for identifying and grading vesicoureteral reflux (VUR). As illustrated in (Figure 4), a typical micturating cystourethrogram (MCUG) reveals retrograde contrast opacification of the ureters and renal pelvicalyceal systems, allowing for precise anatomical classification of reflux severity. Despite the associated radiation exposure, MCUG continues to provide unmatched diagnostic reliability for initial VUR detection.

To evaluate renal parenchymal function and assess post-inflammatory scarring, all patients underwent technetium-99m dimercaptosuccinic acid (DMSA) scintigraphy. (Figure 5) presents a representative DMSA scan from the cohort, showing cortical radiotracer uptake bilaterally.

Areas of diminished uptake were interpreted as evidence of renal scarring, a critical parameter in determining long-term renal prognosis and therapeutic strategy.

In selected cases—specifically those with persistent or recurrent febrile urinary tract infections (UTIs) but no reflux visible on standard imaging position installation contrast cystography (PIC) was utilized. As demonstrated in (Figure 6), no reflux was evident on the conventional MCUG image (Panel A), whereas the subsequent PIC cystography (Panel B) detected Grade II left-sided VUR. This case highlights the potential of PIC to uncover occult or intermittent reflux, supporting its inclusion in extended diagnostic algorithms for patients with discordant clinical and radiological findings.

In another representative case, MCUG clearly demonstrated high-grade bilateral VUR with retrograde filling of both ureters and collecting systems (Figure 4), typical of Grades IV–V. This imaging pattern was pivotal in determining the need for interventional management, further underscoring the clinical value of detailed anatomical imaging in VUR.

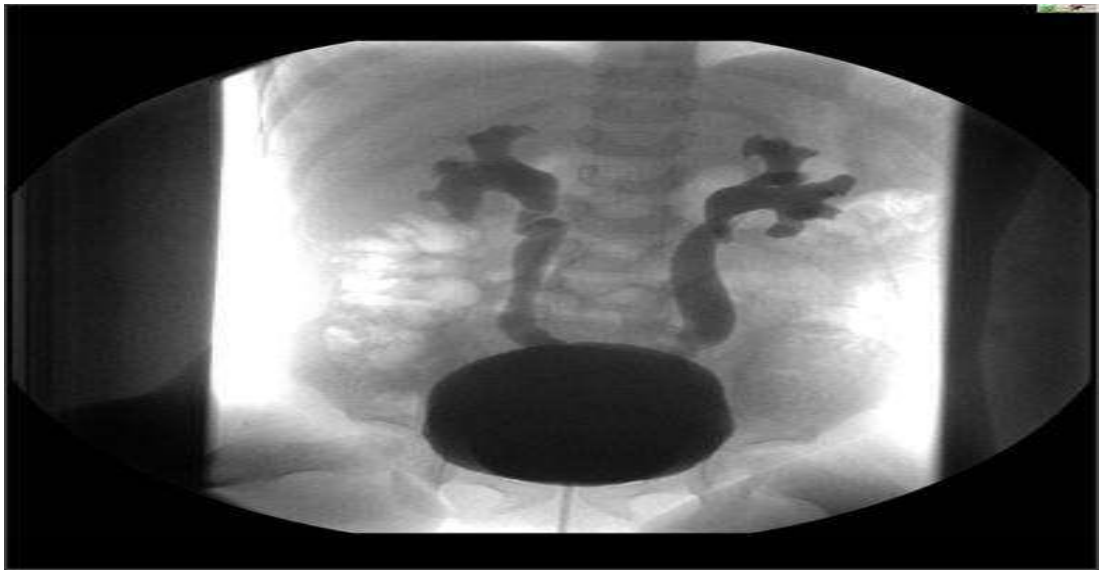

Figure 4. Bilateral vesicoureteral reflux on MCUG

Micturating cystourethrogram (MCUG) showing bilateral vesicoureteral reflux with retrograde opacification of both ureters and pelvicalyceal systems. This image demonstrates a high-grade, symmetrical reflux pattern, confirming the diagnostic accuracy of MCUG in identifying and grading severe VUR

In the evaluation of long-term renal parenchymal health, DMSA scintigraphy was used to assess cortical scarring and differential kidney function. Figure 5 shows a representative scan used in the study, highlighting radiotracer distribution across the renal cortices. Areas of reduced uptake correlate with scarring and serve as objective markers for renal damage due to recurrent or high-grade reflux.

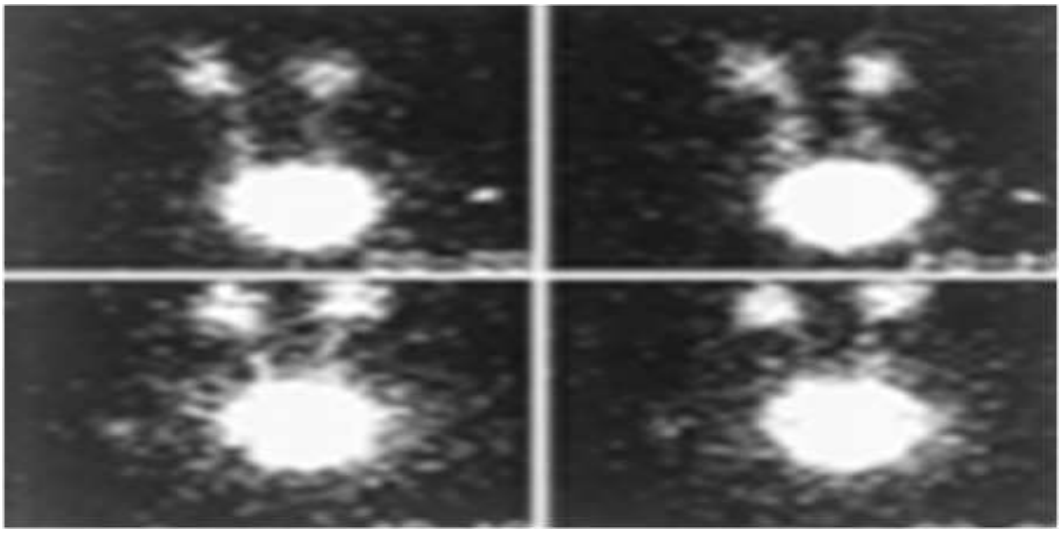

Figure 5. DMSA scintigraphy scan in pediatric VUR

Technetium-99m DMSA renal scintigraphy demonstrating radiotracer uptake in both kidneys. The scan provides functional evaluation of renal parenchyma and allows detection of cortical scarring, which is crucial for assessing long-term kidney damage in children with VUR. Areas of reduced uptake may indicate chronic scarring or previous pyelonephritis

In a subset of patients with persistent febrile UTIs and negative VCUG results, Position Installation Contrast (PIC) cystography was performed. In one representative case, no reflux was visualized on standard MCUG (Figure 6A); however, PIC imaging revealed a Grade II left-sided VUR (Figure 6B).

This underscores the potential value of PIC in detecting intermittent or occult reflux not apparent on conventional imaging. Such findings support the inclusion of PIC in diagnostic algorithms for clinically suspicious but radiologically inconclusive VUR cases.

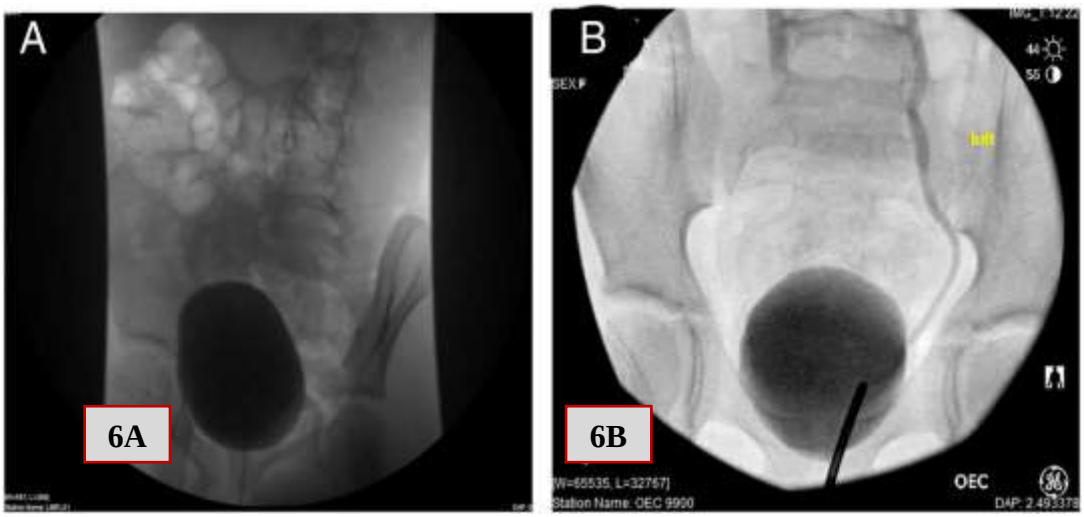

Figure 6. Comparison between MCUG and PIC in detecting occult vesicoureteral reflux
A. Standard micturating cystourethrogram (MCUG) showing no visible vesicoureteral reflux (VUR).
B. Position Installation Contrast (PIC) cystography of the same patient revealing Grade II left-sided VUR, previously undetected on MCUG.
This case highlights the diagnostic superiority of PIC in identifying intermittent or occult reflux in selected pediatric patients with persistent urinary tract infections

Discussion

In our study, 74.3% of patients who underwent endoscopic injection achieved complete reflux resolution (Grade 0), as shown in (Table 3) and illustrated in (Figure 3), aligning with published resolution rates, including the 2006 meta-analysis by Elder et al. [2] reporting 68–80% success in Grades II–IV. The effectiveness of bulking agents like Deflux has been well-documented in multiple reviews, and our data demonstrated a significant reduction in mean reflux grade after treatment, as detailed in (Table 4) and (Table 5) [4, 9, 10].

Renal outcomes in our cohort showed a statistically significant improvement in right kidney function within the intervention group, as shown in (Table 11). This is consistent with findings by Escolino et al., who reported improved renal parameters following successful endoscopic correction in similar populations [4]. Conversely, our conservative group showed no significant functional improvement, highlighting a potential limitation of antibiotic-only strategies in preserving renal integrity, especially in children with persistent or recurrent infections [5, 6, 11].

Recurrent UTIs were observed in 31.4% of the intervention group, as presented in (Table 7), a rate comparable to outcomes from meta-analyses by Wang et al. and Roussey-Kesler et al., which demonstrated that even after treatment, children with VUR remain at risk for infection recurrence [14,20-22].

The control group experienced higher overall UTI-related morbidity, consistent with Elmacı's findings on the limited long-term efficacy of amoxicillin prophylaxis [3]. Additionally, concerns regarding antibiotic resistance, treatment adherence, and growth impact have been raised by Guidos et al., suggesting that long-term prophylaxis may not be a benign approach [6].

While the mean left kidney function was lower in the intervention group post-treatment, as presented in (Table 9) and (Table 10), this likely reflects pre-existing renal damage rather than iatrogenic effect. In our cohort, renal scarring was observed in both groups with similar frequency, as shown in (Table 8). This finding is consistent with studies by Läckgren et al. and Chang et al., which emphasize that renal damage often occurs early—sometimes prenatally—and may not be fully reversible with either treatment strategy [1, 9].

Endoscopic failure was observed in a minority of our patients, with some showing residual reflux post-treatment. Factors such as high-grade reflux, injection technique, and anatomical variation have been implicated in other reports as contributors to endoscopic treatment failure [5, 13, 19].

Lanfranchi et al. and González et al. underscored the importance of experience, proper bulking agent deposition, and reflux grade in determining procedural success [5, 10]. Tekin et al. further supported the utility of endoscopic correction even in infants with complicated high-grade VUR, demonstrating encouraging results with early intervention [18].

Despite its invasiveness, endoscopic treatment has been associated with improved quality of life. Schwentner et al. reported that successful resolution of reflux through injection therapy led to marked psychosocial improvements, including reduced anxiety and better urinary control [15]. These non-clinical outcomes may weigh heavily in parental and physician decision-making, especially when evaluating short- versus long-term burden.

Machine learning-based prediction models, such as those proposed by Tafazoli et al., may play a future role in identifying patients who would benefit most from early intervention versus conservative observation [17]. Until such personalized models are widely available, real-world studies such as ours provide valuable guidance in selecting and stratifying treatment modalities.

Ultimately, while both treatment modalities have roles in the management of VUR, our findings reinforce the benefit of endoscopic treatment in achieving timely reflux resolution, reducing recurrent infections, and potentially preserving renal function—especially in children with moderate-to-severe reflux grades. Conservative therapy remains appropriate for selected patients with low-grade reflux or strong likelihood of spontaneous resolution but requires diligent follow-up and parental adherence.

Conclusion

This study supports the efficacy of endoscopic injection therapy as a minimally invasive, safe, and clinically beneficial approach for managing primary VUR in pediatric patients. Compared to conservative therapy, endoscopic treatment achieved higher rates of reflux resolution, reduced recurrence of UTIs, and showed potential benefits in renal functional outcomes, particularly in moderate-to-high-grade cases.

Nonetheless, conservative management remains a valid option in selected patients with low-grade reflux, provided there is close follow-up and good adherence. Renal scarring, often established early, may persist despite either treatment, underscoring the importance of early diagnosis and risk stratification.

These findings advocate for an individualized treatment approach in pediatric VUR, balancing reflux severity, infection history, renal function, and family preferences to optimize both clinical outcomes and quality of life.

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