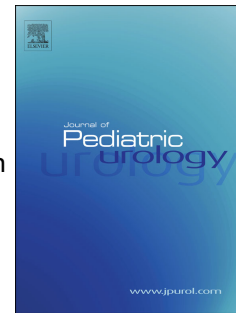


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PII: S1477-5131(25)00707-7

DOI: <https://doi.org/10.1016/j.jpurol.2025.105716>

Reference: JPUROL 105716

To appear in: *Journal of Pediatric Urology*

Received Date: 11 August 2025

Revised Date: 9 December 2025

Accepted Date: 29 December 2025

Please cite this article as: Moreno Bencardino C, Rickard M, Dos Santos J, Pippi Salle JL, Romao R, Chua ME, Lorenzo AJ, Should the presence of ipsilateral lower pole vesicoureteral reflux impact the decision to offer a uretero-ureterostomy for children with duplication anomalies?, *Journal of Pediatric Urology*, <https://doi.org/10.1016/j.jpurol.2025.105716>.

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Should the presence of ipsilateral lower pole vesicoureteral reflux impact the decision to offer a uretero-ureterostomy for children with duplication anomalies?

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Should the presence of ipsilateral lower pole vesicoureteral reflux impact the decision to offer a uretero-ureterostomy for children with duplication anomalies?

Keywords:

Duplex system; lower pole reflux; uretero-ureterostomy

Abbreviations:

iLPR: Ipsilateral lower pole vesicoureteral reflux

IQR: Inter-quartile range

LP: Lower pole

SFU: Society of Fetal Urology (hydronephrosis grading system)

UP: Upper pole

UTI: Urinary tract infection

UU: Uretero-ureterostomy

VCUG: Voiding cystourethrogram

VUR: Vesicoureteral reflux

Abstract:

Objective: To evaluate whether the presence of ipsilateral lower pole vesicoureteral reflux (iLPR) should influence surgical decision-making in cases of associated upper pole (UP) pathology otherwise amenable to a uretero-ureterostomy (UU).

Methods: We conducted a single-institution retrospective review of 41 pediatric patients with duplex system anomalies who underwent UU over five years. Patients were segregated into two groups: those without evidence of iLPR (including those with unknown reflux status), and those with documented iLPR. Primary outcomes included postoperative urinary tract infections (UTIs), surgical complications, and improvement/resolution of hydronephrosis.

Results: Of 41 patients, 11 had confirmed iLPR. Demographics, preoperative ultrasound findings, and clinical presentation were comparable between groups. We followed a stent-free, radiation-free, open surgical technique, with most patients discharged within 24 hours. Complication rates—including UTIs, infected stumps, and anastomotic leaks—were similar between groups and not statistically significant. During postoperative surveillance, UTIs occurred in 21% of the no/unknown-iLPR group and 36% of the LPR group ($p = 0.55$), though most were isolated events. UP hydronephrosis improved or resolved in over 90% of cases, with no significant difference between groups.

Conclusion: UU is a safe and effective surgical option for managing duplex UP anomalies, even in the presence of reflux. Our findings challenge historical exclusion of iLPR patients from UU consideration and suggest that routine preoperative VCUGs may not be necessary, particularly in the absence of other indications for obtaining a cystogram.

Introduction

Upper pole (UP) pathology of a duplex system can be associated with the development of recurrent urinary tract infections (UTIs), loss of kidney function and urinary incontinence due to obstruction or ectopic ureteral insertion. Several surgical techniques have been described to address this condition, including UP heminephrectomy, UP ureteral ligation, common sheath reimplantation (CSR), and uretero-ureterostomy (UU) [1], [2]. Among these, UU represents a widely employed strategy, offering a practical solution that can be performed with minimal morbidity and low risk of damage to the ipsilateral lower pole (LP) moiety. Over the years, this approach has been extensively studied, with several articles highlighting its safety and efficacy, even in cases with minimal or absent UP function [3], [4], [5]. Concurrently, the need for other time-honoured interventions appears to have decreased substantially[6]

Despite the progressive broadening of indications for UUs, the practice of routinely obtaining a preoperative voiding cystourethrogram (VCUG) as well as excluding cases with ipsilateral lower pole reflux (iLPR) remains widely accepted. Understandably, many practitioners refrain from performing surgery without documentation of the child's reflux status and exclude patients with iLPR from undergoing a UU due to concerns around leaving unaddressed an associated condition [5], [7], [8]. iLPR's presumed impact on postoperative outcomes, particularly UTIs, kidney scarring and the need for additional interventions, represents a largely theoretical yet important source of uncertainty.

At our institution, we currently favor addressing obstruction and ectopia first, by managing obstructed UP ureters associated with a ureterocele with an endoscopic puncture, and ectopic ureters or obstructed UPs without a ureterocele with a UU, regardless of the presence of reflux. Effectively, we expanded the indications for a UU by questioning the clinical significance of otherwise asymptomatic reflux to the LP ureter and, therefore, the need to document its presence. Initially, this was limited to patients without UTIs and no evidence of infected UP systems. After experiencing favourable outcomes, we evolved to not performing routine VCUGs in this population in the absence of infection, unless there is clear evidence that the presence of iLPR would lead to a change in management.

Following this management philosophy and based on the hypothesis that the presence of iLPR does not impact the outcomes of UUs, we present herein a retrospective study that aims to compare

the outcomes of performing this surgery in children with or without iLPR. We sought to provide insight into the clinical implications of iLPR in this context and address whether its presence should preclude UU as a treatment option.

Methods

We conducted a retrospective review of our duplex system database, identifying consecutive patients who underwent a UU procedure over five years. Inclusion criteria focused on patients with duplex systems presenting with worsening UP hydroureteronephrosis, UP parenchymal thinning, UP pyonephrosis, or urinary incontinence who underwent UU as a standalone surgical intervention. Patients who underwent concurrent procedures, such as ureteral reimplantation or LP injection of a bulking agent, were excluded.

Preoperative evaluation consisted of serial ultrasounds to monitor kidney morphology and the degree of associated hydronephrosis, as well as selective VCUGs. When diagnosed, iLPR was categorized as low (I–II) or high-grade (III–V) based on conventional classification [9]. Hydronephrosis was graded using the Society for Fetal Urology system [10], labelling grades 3 and 4 as high-grade. Additional collected variables included the patient's age, sex, circumcision status, clinical presentation, use of antibiotic prophylaxis, and presence of presentation and breakthrough UTIs.

UUs were performed following a stent-free and radiation-free (i.e. no fluoroscopy for retrograde pyelograms) standardized open technique. Initially, the LP ureter is cannulated through endoscopy with an open-ended catheter, which is left externalized and tied to a foley catheter during the procedure. This is done under USN guidance (agitated saline is injected through the stent and LP position is confirmed); this is, to facilitate the future intraoperative identification of the LP ureter. Briefly, a small (2-2.5 cm) ultrasound-guided incision was performed in the inguinal region, fashioned at the point of shortest distance between the skin and the ureters. The distal aspect of the UP ureter was dissected as low as possible towards the bladder. The end-to-side anastomosis was fashioned with running absorbable sutures. Both the open-ended catheter and the indwelling Foley catheter are removed at the completion of the case. The procedure is typically performed as day surgery, expecting most patients to be discharged within 6-12 hours. This is facilitated by the regular use of regional (abdominal wall) ultrasound-guided blocks and the adoption of many of the steps outlined in our pyeloplasty pathway [11], which positively accelerates postoperative recovery.

A priori defined outcomes were captured by recording the incidence of UTIs and infected stumps - often-negative urine cultures with inflammatory systemic response and ultrasound findings of a

collection of the stump -, use and duration of prophylactic antibiotics, resolution or degree of hydronephrosis improvement on ultrasound, and the need for additional surgical interventions. Follow-up duration was also recorded for each patient. We defined a successful outcome as hydronephrosis improvement or resolution in asymptomatic children without recurrent UTIs or incontinence after toilet training.

For comparison purposes, patients were divided into two groups: those with absent or unknown reflux status and those with documented iLPR. By definition, children with unknown reflux status did not have a preoperative VCUG since birth.

Statistical analyses were conducted to contrast outcomes between groups, following accepted methods for continuous and categorical variables. A p-value of less than 0.05 was considered statistically significant.

Results

Demographic information is presented in **Table 1** and postoperative outcomes in **Table 2**. A total of 41 patients were included, with 30 patients in the absent/unknown VUR group and 11 in the iLPR group. Baseline characteristics, perioperative findings, surgical outcomes, and postoperative results are summarized below.

Baseline Characteristics

The median (inter-quartile range [IQR]) age at baseline was 2 (1, 4) in the no/unknown VUR group and 1.7 (1, 4) months in the iLPR group ($p=0.92$). The most common associated ureteral abnormalities were ureterocele (4; 13% no/unknown VUR vs. 2; 18% in iLPR) and ectopic ureter (26; 87% in no/unknown VUR vs. 9; 82% in iLPR) ($p=0.65$). Continuous antibiotic prophylaxis (CAP) was prescribed preoperatively in 28 patients (93%) of no/unknown VUR patients and 10 (91%) iLPR patients ($p=1.00$), with a mean CAP duration of 11 (IQR 5,19) months and 16 (IQR 12, 23) months, respectively ($p = 0.2$).

Preoperative Findings

UP dilation was present in all patients, with 25 (83%) of the no/unknown VUR patients and 10 (91%) of the iLPR patients having high-grade hydronephrosis ($p=1.00$). UP ureter dilation was observed in 26 (87%) of the no-VUR patients and 11 (100%) of the LPR patients ($p=0.56$). The median (IQR) maximum upper ureter diameter was similar between groups (13; [11, 19] mm for no/unknown VUR vs. 13 [9, 16] mm for iLPR; $p=0.44$). LP hydronephrosis was noted in 6 (23%) of the no/unknown VUR patients and 2 (20%) of the iLPR patients ($p=1.00$). Only 4 patients in the no/unknown VUR group had ipsilateral LP ureteral dilation, and a VCUG was performed in all of them, ruling out the presence of iLPR. Two of them had UP reflux, suggesting ectopia at the bladder neck (i.e. so-called refluxing-obstructed megaureter).

Surgical Data

The median (IQR) age at surgery for primary UU was 10 (7, 19) months in the no/unknown VUR group and 13 (6, 21) months in the iLPR group ($p=0.66$). For cases following ureterocele incision or ureterostomy closure, the median age at surgery was 17 (13, 22) months for no/unknown VUR patients and 10 months for LPR patients ($p = 0.40$). For the no/unknown VUR, 6 (20%) had an

internalized stent placed, compared to none in the iLPR group. These patients correspond to the first patients that were operated on, we have completely migrated to a stent-free technique as described. All patients were discharged the within 24 hrs.

Postoperative Outcomes

Incidence of postoperative complications -including UTIs, infected stumps and urinary leaks- was not statistically different between the no/unknown VUR and iLPR groups (10%, 13% and 7% vs. 9%, 18% and 0% respectively; $p=0.83$). During postoperative surveillance, UTIs occurred in 21% of the no/unknown VUR patients and 36% of iLPR patients ($p = 0.55$). Notably, only 5 patients in the no/unknown reflux status group did not undergo a VCUG, and none of these children experienced a UTI during postoperative monitoring.

To ensure that the “unknown reflux status” patients were not skewing the results, we performed a *post hoc* analysis with these children excluded and found that the rate of infections after UU remained statistically non-significant (16.7% vs 31.3%; $p=0.25$).

One patient in the iLPR group required further procedures during follow-up, which were related to the presence of an infected ureteral stump. In the no/unknown VUR group, one patient required further intervention for an anastomotic leak and one for an infected ureteral stump.

Follow-Up

Post-operative monitoring time was 28 (15, 38) months and 21 (13, 53) months for the no/unknown VUR and iLPR groups, respectively ($p=0.33$). A degree of persistent UP dilatation was observed in 46% of cases with no/unknown VUR and 50% of iLPR cases ($p=0.1$); however, 28 (93.3%) vs. 10 (91%), respectively, had either resolved or improved hydronephrosis at the last follow-up. No further surgical procedures were needed for this reason.

Discussion

This study aimed to evaluate UU outcomes with a specific focus on the impact of documented iLPR when compared to children with absent or unknown VUR status. Our findings suggest that this surgical procedure is safe and effective irrespective of the reflux status of the lower moiety, and that in most cases, a routine preoperative cystograms can be avoided. Importantly, no statistically significant differences were observed in key postoperative outcomes between the groups. These results also highlight that postoperative complications, including UTIs within 30 days after surgery, were comparable. Although a higher proportion of patients with iLPR experienced an infection during surveillance (>30 days after surgery; 36% vs. 20%), this difference did not reach statistical significance. Of note, other series have reported on the rate of postoperative UTIs (within 30 days) at around 5-21% [4], [5], [7], numbers that are comparable to ours.

Acknowledging that the underlying infection risk profile of each patient is multifactorial, we sought to explore UTI cases further. Of the patients who experienced a postoperative surveillance UTI in the iLPR group, only one had high-grade reflux. Conversely, the other two patients in this group who had grade 4 reflux did not experience UTIs. Furthermore, despite the development of a UTI episode, at the last follow-up, all patients in this group had improvement in other outcome measures, and the infections remained an isolated event. For the no/unknown VUR group, we detected that many had evidence of bladder and bowel dysfunction at the time of developing an infection, which subsided after implementing conservative management recommendations. Only one child continued to experience recurrent UTIs, despite the absence of VUR.

These findings lead us to propose that the presence of UTIs in the postoperative surveillance period, for both groups, is potentially related to other factors (such as bladder bowel dysfunction) or represents isolated events, instead of being directly related to the presence of iLPR *per se*. Additionally, the duration and use of continuous antibiotic prophylaxis were similar in both groups, further supporting the comparable risk profile.

Previous studies have excluded patients with iLPR from being candidates for UU presumably due to concerns that neglecting to correct VUR by only diverting the UP system may adversely impact postoperative outcomes [3], [4], [7], [8]. This well-founded, albeit theoretical concern is based on three assumptions: that persistent VUR will lead to preventable infections, that correcting reflux will decrease the risk of infections, and that complications of not correcting it outweigh the

potential complications of concurrent anti-reflux procedures. Our findings challenge this belief, demonstrating that iLPR should not be considered an absolute contraindication to performing a UU. By including patients with iLPR, our study provides novel data that grants a broader understanding of the safety and efficacy of this surgical technique

A secondary aim of our study is to critically evaluate indications for VCUG in patients with a duplex system. In an otherwise asymptomatic child without recurrent infections, despite the presence of sonographic evidence of UP pathology, diagnosing iLPR appears to carry limited yield, as the presence of VUR does not preclude the child from having a UU. Pondering on this issue is timely, as there is a growing body of research that questions the value of routinely performing a cystogram in asymptomatic patients who may have reflux or children who experience their first UTIs, since a significant proportion of them do not warrant an intervention or experience a change in management [12]. Furthermore, minimizing radiation exposure -following the ALARA principle- is always welcome, and the instrumentation required for the test can trigger discomfort and infections, UTI, adverse events that can happen in 1-3.8% of the cases despite the use of prophylaxis [13]–[15]. Many of our patients did not experience preoperative UTIs; therefore, the indication for ordering a VCUG was solely based on ultrasound findings. We then suggest that there are limited indications for a VCUG in this population, and that the risks and benefits of performing this should be carefully reconsidered.

An additional concern surrounding the presence of iLPR is the potential impact VUR can have on complications and surgical outcomes. Regardless of the presence of iLPR, we found that patients experienced resolution or improvement in the degree of UP hydronephrosis, with no significant difference between the two groups. Similarly, children with and without iLPR experienced comparable rates of postoperative infections and surgical complications.

We posit that patients who experience postoperative infections due to the presence of reflux are candidates for endoscopic injection with a bulking agent or extravesical reimplantation as the ureterovesical junction of the LP ureter remains intact after a UU. Additionally, by preserving the trigone and intramural ureter, associated iLPR is also likely to experience improvement over time, as documented in many cases of primary VUR managed conservatively.

It could be argued that alternative procedures (such as CSR) for patients with reflux would yield similar or better results. Our dataset does not provide information to address this hypothesis;

nevertheless, we propose that these are more extensive procedures, associated with longer operative times, analgesic requirements and need for catheterization/stenting[16]–[20]. Moreover, just like any major reconstructive endeavour, CSR can be associated with issues related to obstruction or persistent reflux.

For instance, in a study where CSR with ureterocelectomy was indicated for cases of ectopic ureteroceles with LP high-grade reflux, the reported complication rate was up to 17.9% with a clear need for additional surgical procedures such as redo-CSR, ipsilateral nephrectomy due to postoperative decrease in kidney function, or endoscopic injections for persistence of VUR. Furthermore, the reported postoperative incontinence in 7.7% of the patients, secondary to bladder neck injury during reconstruction, is worrisome [18]. Other cohorts have reported postoperative incontinence rates of 6.3%[20]. Minimally invasive techniques, such as robotic-assisted interventions may have lower complication rates, however, as previously mentioned, a Foley catheter is often left for >24 hrs for unilateral cases and 48 hrs for bilateral cases [17] and hospital stays have been reported from 1.6-7 days [17], [19] and sometimes up to 26 days (with mean hospital stay of 6.8 days) in this last cohort. Importantly, UTIs during follow-up monitoring were reported to be around 25% for laparoscopic UU and 20.8% for common sheath reimplant[16], which is not too far from our results. We don't aim to make a direct comparison of UU against other methods, since this is not the scope of our study, however, the overall incidence of infections and complications appears to lend support to a less invasive approach, as advocated by our group.

The retrospective nature of this study is a notable limitation, and the relatively small sample size may limit the generalizability of our findings as well as the ability to detect a statistically significant difference. Admittedly, not all patients underwent VCUGs preoperatively, increasing the risk of bias and potentially leading to iLPR reflux under-diagnosis in a minority of cases. Moreover, our follow-up time is modest, and it is possible that patients with reflux may demonstrate a higher risk of UTIs over time. Future prospective studies with larger cohorts are warranted to validate our findings and explore the long-term outcomes of UU in this population.

Nevertheless, despite these limitations, we propose that the presented analyses have value. To our knowledge, this offering represents the first study to assess the impact of iLPR on the clinical outcomes of duplex system patients, calling into question the need to routinely perform cystograms and concurrently correct reflux when addressing upper tract pathologies. As a single-institution

271 experience, we provide encouraging results with a standardized, minimally invasive, stent-free,
272 and radiation-free open surgical technique. If validated, our data has the potential to impact
273 practice, expanding the indications for UU while challenging time-honoured dogmas.

274

Conclusion

Our study shows that UU is a viable surgical option for duplex systems with UP pathology, even in the presence of LP reflux. These findings support the possibility of avoiding a cystogram in otherwise asymptomatic children. By expanding UU candidacy to include patients with iLPR, this study supports broader consideration for this versatile surgical technique and encourages re-evaluation of traditional diagnostic pathways in the management of pathology related to duplex systems.

Conflict of Interest statement:

None

Funding:

None

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Table 1. Baseline characteristics

	No VUR/unknown (n=30)	iLPR (n=11)	p value
Age baseline (months) median (IQR)	2 (1, 4)	1.7 (1, 4)	0.92
Males (n/%)	4 (13)	4 (36)	0.43
Circumcised	0 (0)	2 (18)	
Uncircumcised	4 (13)	2 (18)	
Associated UP ureter pathology (n/%)			0.62
Ureterocele	4 (13)	2 (18)	
Ectopic ureter	26 (87)	9 (82)	
UP hydronephrosis at baseline visit (n/%)	20 (100)	11 (100)	1.00
UP SFU grade 3 or 4 (n/%)	25 (83)	10 (91)	1.00
UP ureter dilation (n/%)	26 (87)	11 (100)	0.56
Maximum UP ureter diameter (mm) median (IQR)	13 (11, 19)	13 (9, 16)	0.44
LP hydronephrosis at baseline visit (n/%)	6 (23)	2 (20)	1.00
LP ureter dilated (n/%)	1 (4)	0 (0)	1.00
Maximum LP ureter diameter (mm) median (IQR)	12 (-)	-	
Age at surgery (months) median (IQR)			0.66
Primary UU	10 (7, 19)	13 (6, 21)	
After ureterocele incision or cutaneous ureterostomy	17 (13, 22)	10 (-)	
Preoperative VCUG (n/%)	25 (83)	11 (100)	0.30
Presence of LP VUR (n/%)			
Low grade (1-3)	NA	8 (73)	
High grade (4-5)		3 (27)	
Antibiotic prophylaxis	28 (93)	10 (91)	1.00
Preoperative UTI			
Yes	11 (37)	5 (45)	
No	19 (63)	6 (54)	

Median duration of prophylaxis (months) median (IQR)	11 (5, 19)	16 (12, 23)	0.20
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Table 2. Outcomes and complications

	No VUR/unknown (n=30)	iLPR (n=11)	p value
UP hydronephrosis at last follow-up [n (%)]	13 (46)	5 (50)	1.00
Complications [n (%)]			
UTI	3 (10)	1 (9)	0.83
Infected Stump	4 (13)	2 (18)	
Urine leak	2 (7)	0 (0)	
Postoperative surveillance UTI (>30 days) [n (%)]	6 (21)	3 (30)	0.55
Median follow-up in months (IQR)	28 (15, 38)	21 (13, 53)	0.33

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