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A multi-institutional European comparative study of open versus robotic-assisted laparoscopic ureteral reimplantation in children with high grade (IV—V) vesicoureteral reflux

Simone Sforza [a,*], Beatriz Bañuelos Marco [b], Bernhard Haid [c], Numan Baydilli [d], Muhammet Irfan Donmez [e], Anne-Françoise Spinoit [f], Irene Paraboschi [g], Lorenzo Masieri [a], Lukas Steinkellner [c], Yusuf Ilker Comez [h], Rianne J.M. Lammers [i], Lisette Aimée 't Hoen [j], Fardod O'Kelly [k], Edoardo Bindi [l], Yusuf Kibar [m], Mesrur Selçuk Silay [h]

* Correspondence to: Simone Sforza, Department of Pediatric Urology, University of Florence, Meyer Hospital, Gaetano Pieraccini Street 24, 50139 Florence, Italy. simone.sforza1988@gmail.com (S. Sforza)

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Summary

Introduction
Traditionally, open ureteral reimplantation (OUR) has been the standard treatment for primary vesicoureteral reflux (VUR) requiring reimplantation. Robotic-assisted laparoscopic ureteral reimplantation (RALUR) is gaining popularity and high success rates have been reported.

Objective
In this multi-institutional study, we aimed to compare the perioperative and postoperative outcomes of OUR and RALUR for high-grade (IV + V) VUR in children.

Study design
A retrospective evaluation was performed collecting data from 135 children (0—18 years) who underwent high grade VUR surgical correction at nine European institutions between 01/01/2009 and 01/12/2020, involving either open or robotic approaches. Institutional review board approval was obtained. Patients with lower grades of VUR ($\leq$III), previous history of open or endoscopic ureteral surgery, neurogenic bladder, or refluxing megaureter in need of ureteral tapering were excluded. Pre-, peri- and post-operative data were statistically compared.

Results
Overall, 135 children who underwent either OUR ($n = 68$), or RALUR ($n = 67$) were included, and their clinic and demographic features were collected. The mean age of the open group was 11 months (interquartile range [IQR] 9.9—16.6 months), in the RALUR group it was 59 months (IQR 29—78mo) ($p < 0.01$); the open cohort had a weight of 11 kg (IQR 9.9—16.6 kg) while the RALUR group had 19 kg (IQR 13—25 kg) ($p < 0.01$). No significant differences were found for intraoperative (1.5 % vs 7.5 %, $p = 0.09$) or for postoperative complication rates (7.4 % vs 9 %, $p = 0.15$). Favorable outcomes were reported in the RALUR group: shorter time to stooling (1 vs 2 days), fewer indwelling urethral catheter days (1 vs 5 days), perioperative drain insertion time (1 vs 5 days) and a shorter length of hospital stay (2 vs 5 days) ($p < 0.01$). The success rate was 94.0 % and 98.5 % in the open and RALUR groups, respectively. The long-term clinical success rates from both groups was comparable:42 vs 23 months for open and RALUR, respectively.

[a]Department of Pediatric Urology, University of Florence, Meyer Children Hospital, Florence, Italy [b]Department of Urology, Charité University Clinic, Division of Paediatric Urology, Berlin, Germany [c]Department of Pediatric Urology, Ordensklinikum Linz, Hospital of the Sisters of Charity, Linz, Austria [d]Department of Pediatric Urology, Erciyes University Faculty of Medicine, Kayseri, Turkey [e]Division of Pediatric Urology, Department of Urology, Istanbul Faculty of Medicine, Istanbul University, Istanbul, Turkey [f]Department Urology ERN Centre, Ghent University Hospital, Ghent University, 9000 Ghent, Belgium [g]Department of Pediatric Urology, Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico, Milano, Italy [h]Department of Urology, Biruni University, Division of Paediatric Urology, Istanbul, Turkey [i]Department of Urology, University Medical Center Groningen, 9713 GZ Groningen, the Netherlands [j]Department of Paediatric Urology, Sophia Children's Hospital, Erasmus University Medical Center, 3015 GD Rotterdam, the Netherlands [k]Division of Paediatric Urology, Beacon Hospital, DK18 AK68 Dublin, Ireland [l]Pediatric Surgery Unit, Salesi Children's Hospital, Ancona, Italy [m]Department of Urology, University, Koru Hospital, Ankara, Turkey

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Summary table Preoperative and postoperative data.

		Group A (Open; n = 68)	Group B (Robot; n = 67)	p-value
Male, n. %		45 (66.2 %)	40 (59.7 %)	0.43
Grade of VUR, n. %	4	62 (91.2 %)	35 (52.2 %)	<0.01
	5	6 (8.8 %)	32 (47.8 %)	
Month, median; IQR		18; 15-54	59; 29-78	<0.01
Kg, median; IQR		11; 9.9—16.6	19; 13-25	<0.01
Side, n. %	Left	25 (36.8 %)	24 (35.8 %)	0.90
	Right	23 (33.8 %)	21 (31.3 %)	
	Bilateral	20 (29.4 %)	22 (32.8 %)	
Type of approach, n. %	Extraperitoneal	68 (100 %)	/	<0.01
	Transperitoneal	/	67 (100 %)	
Type of intervention, n. %	Lich-gregoire	31 (45.6 %)	67 (100 %)	<0.01
	Cohen	37 (54.4 %)	/	
Procedure, n. %	Unilateral	48 (70.6 %)	45 (67.2 %)	0.66
	Bilateral	20 (29.4 %)	22 (32.8)	
Operative time, median; IQR		100; 86-116	120; 118-140	<0.01
Satava intraoperative complication, n. %	No	67 (98.5 %)	62 (92.5 %)	0.09
	Grade 1	1 (1.5 %)	5 (7.5 %)	
Clavien Dindo postoperative complication, n. %	No	63 (92.6 %)	61 (91 %)	0.15
	Grade 1	5 (7.4 %)	4 (6 %)	
	Grade 3	/	2 (3 %)	
Time to stool, median; IQR		2; 1-3	1; 1-1	<0.01
Time to flatus, median; IQR		0: 0-1	1: 1-1	0.28
Days of catheter, median; IQR		5; 2-5	1 1-1	<0.01
Days of drainage, median; IQR		5; 3-5	1; 1-3	<0.01
Lenth of stay, median; IQR		5; 3-6	2; 1-2	<0.01
Follow up month, median; IQR		42; 10-51	23; 11-37	0.67
Follow Up, n. %	Success	62 (94 %)	66 (98.5 %)	0.50
	Stenosis	1 (1.5 %)	1 (1.5 %)	
	Persistent low grade reflux	3 (4.5 %)	/	
Resurgery	No	62 (94 %)	66 (98.5 %)	0.35
	endoscopic	1 (1.5 %)	1 (1.5 %)	
	Open	3 (4.5 %)	/	

Discussion

This study reported a large multicentric experience focusing on high grade VUR. Furthermore, this study compares favorably to OUR in a safety analysis. There was also a trend towards higher success rates with RALUR utilizing an extravesical approach which has not been previously reported.

Conclusion

RALUR is an efficacious and safe platform to use during ureteral reimplantation for high grade VUR. The overall peri-operative and post-operative complication rates are at least equivalent to OUR, but it is associated with a faster functional recovery and time to discharge. Medium to long term success rates are also equivalent to OUR.

Introduction

The incidence of vesicoureteral reflux (VUR) in asymptomatic children is estimated at about 0.4—1.8 %. However, the incidence of VUR is significantly increased to 32 % in children presenting with recurrent UTIs [1]. Furthermore, in the presence of antenatal hydronephrosis, VUR can be detected postnatally in 16.2 % of patients [2].

The management of VUR generally involves a multidisciplinary approach to include both medical and surgical management. Patients are now individually risk-stratified to take into account and can differ according to individual risk stratification taking into account multiple factors as well as parental preferences. The modern trend of management for children with non-symptomatic low risk VUR is observation, because of the negligible risk of renal injury and the high chance of spontaneous resolution. Moreover, when low-risk VUR is symptomatic endoscopic treatment with injection of bulking agents still plays a role with good outcomes [3—5]. On the other hand, high risk VUR as well as symptomatic high grade VUR (grades IV and V) is an indication for surgical management with open ureteral reimplantation (OUR) as the gold standard approach [6—8].

There have been a number of publications examining the initial experiences and learning curves with robotic-assisted laparoscopic ureteral reimplantation (RALUR) in the last years, however some of these studies included all grades of VUR, as well as heterogeneous sets of patients. A clear advantage of the robotic approach compared to open series has not yet been demonstrated [9,10]. Comparative, large multicenter studies focusing on the treatment of high risk and high grade VUR with RALUR have also yet to be performed. Thus, due to underpowered data sets, it is hard to quantify the actual incidence and prevalence of complications in this cohort of patients [7,11—14].

The present study aims to compare the clinical success rate between children treated with an OUR or a RALUR approach. The secondary objective is determinate any potential differences in peri-operative and postoperative complications between the open surgery and RALUR approaches.

Material and methods

This study was carried out by the Pediatric Urology Working Group of EAU Young Academic Urologists. Institutional review board approval was obtained prior to the study according to the local ethics committee guidelines. All preoperative, perioperative and follow up data of consecutive primary VUR patients classified as a minimum of a unilateral grade IV or V treated with OUR or RALUR in different pediatric centers were enrolled (Department of Pediatric Urology, University of Florence, Meyer Children Hospital, Florence, Italy; Department of Pediatric Urology, Ordensklinikum Linz, Hospital of the Sisters of Charity, Linz, Austria; Department of Urology, Charité University Clinic, Berlin, Germany; Division of Paediatric Urology, Department of Urology, Biruni University, Istanbul, Turkey; Division of Paediatric Urology, Department of Urology, University, Koru Hospital, Ankara, Turkey; Pediatric Surgery Unit, Salesi Children's Hospital, Ancona, Italy; Department of Pediatric Urology, Erciyes University Faculty of Medicine, Kayseri, Turkey).

Inclusion criteria for this study included those in whom informed consent was provided, age less than 18 years at the time of surgery and grade IV or V VUR confirmed by voiding cysto-urethrography (VCUG). The study period was 01/01/2009 to 01/12/2020. Patients with lower grades of VUR ($\leq$III), age over 18 years, a previous history of ureteral surgery, neurogenic bladder, or refluxing megaureter in need of ureteral tapering were excluded.

All the operations were performed by eleven highly experienced surgeons from these referral centers. The surgical approach (open/robotic) and reimplantation technique were according to the preference of the operating surgeon. The latter included the Lich-Gregoire and Cohen techniques for OUR and Lich-Gregoire for RALUR [9,15].

Focusing on the RALUR approach all the patients were operated in a classic supine position with a Foley catheter positioned in the bladder. The first 8-mm trocar was always positioned in the umbilicus using an open Hasson's technique to produce a camera port, and pneumoperitoneum was carried out at a pressure of 10—12 mmHg. Bilateral 8-mm working ports were inserted at 7—9 cm apart from the camera port along the mid-clavicular line, and a 5-mm assistant port was then placed to be used by the bed-side surgeon. The patient was placed in the Trendelenburg position and the da Vinci robot was docked over the patient's feet. an incision was made in the peritoneum just above the posterior bladder wall on the affected side and then the ureter was dissected. The ureter was mobilized by careful dissection to avoid injuring the vas deferens or uterine artery. A polyglactin acid suture hitch stitch may be placed to draw the bladder to the opposite side and enhance visualization. The bladder was filled with saline and a 2.5—3 cm detrusor incision was made to the level of the mucosa. The detrusor muscle was then separated from the mucosa laterally, establishing the muscular flaps used to create the detrusor tunnel. The detrusor flaps were then wrapped around the ureter and reapproximated using 4—0 polyglactin. In duplex systems, both the ureters were reimplanted in the same way in a common detrusor sheath.

Both with OUR or RALUR JJ stent catheters were positioned according to surgeon preference in the Cohen's reimplantation and only in exceptional circumstances in the Lich-Gregoire cohort (solitary kidney or duplex system) in a retrograde fashion way. Wound drains, urethral or suprapubic catheters were also placed at the end of the procedure according to the surgeon preference. [16] All patients were managed with continuous antibiotic prior to surgery and discontinued post-operative after 30 days. In case a pigtail was placed, the antibiotic prophylaxis continued until it was removed.

Non-parametric and descriptive data of the cohort were recorded. The collected data included preoperative features such as symptoms, associated anomalies and VUR grade. Intraoperative and perioperative characteristics such as surgical approach, operative time, complications, length of stay (LOS) and time to stool were similarly assessed. Complications were classified according to the Satava (intraoperative) and modified Clavien Dindo (postoperative) systems [17,18]. Intraoperative complications were defined as all events occurring between the induction of anesthesia and patient awakening that could potentially cause injury and required unplanned surgical maneuvers. Postoperative complications were defined as any event occurring until the 90th postoperative day, which altered the normal postoperative including delayed discharge. Follow-up carried out according to each center individual algorithm, with indications for re-surgery were similarly assessed.

Success was defined as no symptoms (UTIs) in the follow-up period, and no worsening of hydronephrosis compared to preoperative findings on ultrasound recorded after at least the first nine months of surgery. VCUG was not routinely performed (we recorded only eight patients with this exam), unless a patient exhibited recurrent febrile UTIs in order to assess for failure. All the patients presented a minimum follow up of 9 months. All preoperative, perioperative and postoperative data were recorded by medical doctors.

Results

Overall, 135 patients were included in the analysis. Their characteristics are summarized in both Table 1 and Table 2. The open group included 68 patients, while the robotic group included 67 patients.

VUR grade IV occurred in 62 children (91.2 %) in the open group and 35 (52.7 %) in the robotic cohort, while grade V VUR occurred in 6 children (8.8 %) and 32 (47.8 %) respectively in each group ($p < 0.01$). Patients in the OUR group were significantly younger (11 months, IQR 9.9–16.6 vs 59 months IQR 29–78; $p < 0.01$) and lighter compared to the RALUR group (11 kg, IQR 9.9–16.6 kg, vs. 19 kg IQR 13–25 kg; $p < 0.01$). VUR grade V was more represented in the RALUR group, however patient age was also significant (32 [47.8 %] vs 6 [8.8 %] months; $p < 0.01$).

Table 2 outlines the overall intraoperative and postoperative features of each approach. OUR is always performed extraperitoneal (100 % of the cases), while RALUR was performed through a transperitoneal extravesical Lich-Gregoire approach in every case ($p < 0.01$).

In the open group, 31 patients (45.6 %) underwent Lich-Gregoire technique using an extravesical approach, whereas the other 37 children (54.4 %) underwent a transvesical Cohen technique. In the open group a JJ stent was placed in 24 patients (35.9 %). In the RALUR group, only 3 patients had a JJ stent placed (two cases with a solitary kidney and one with a duplex collecting system).

The operative time was significantly different between the two groups: 100 min (IQR 86–116min) in the open group, and 120 min (IQR 118–140min; $p < 0.01$) in the robotic cohort. There were no significantly reported differences in intraoperative (1.5 % vs 7.5 %, $p = 0.09$) or postoperative complication rates (7.4 % vs 9 %, $p = 0.15$). In the RALUR cohort, there were four mild episodes of bleeding and two minimal bladder mucosal injuries during detrusorotomy, with one patient experiencing both. There was one Satava grade one complication with a small vaginal injury which was repaired with primary suture without further incident in the OUR cohort.

In the postoperative period, there were two recorded Clavien 3b complications in the RALUR group: one child experienced long-standing pain and hydronephrosis managed by JJ stent placement, and another who experienced JJ stent migration requiring ureteroscopy in a patient with a solitary kidney. The other complications of both groups included postoperative fever requiring antibiotic treatment (Clavien 1). Favorable outcomes were reported in the robotic group with shorter time to stool (2 vs 1 days; $p < 0.01$), and fewer catheter and surgical drain days (5 vs 1 days; $p < 0.01$), as well as a significantly lower length of hospital stay (LOS) (5 vs 2 days; $p < 0.01$).

The long-term clinical success rates were 94 % in the open, and 98.5 % in and the robotic group, with a median follow-up of 42 months (IQR 10–51mo) and 23 months (IQR 11–37mo) respectively ($p = 0.50$). The patient of the RALUR group who was managed with JJ stent placement in the postoperative period presented during follow-up with a low-grade VUR and, after four months, was treated by secondary endoscopic correction.

Table 3 provides a comparative summary of unilateral and bilateral procedures. In the unilateral groups, the

Table 1 Overview of preoperative data of the patients.

		Group A (Open; n = 68)	Group B (Robot; n = 67)	p-value
Gender, n. %	Male	45 (66.2 %)	40 (59.7 %)	0.43
	Female	23 (33.8 %)	27 (40.3 %)	
Diagnosis, n. %	prenatal	23 (33.8 %)	26 (38.8 %)	0.54
	post natal	45 (66.2 %)	41 (61.2 %)	
Grade of VUR, n. %	4	62 (91.2 %)	35 (52.2 %)	<0.01
	5	6 (8.8 %)	32 (47.8 %)	
Associated anatomical anomaly, n. %	None	49 (72.1 %)	55 (82.1 %)	0.56
	Solitary kidney	1 (1.5 %)	2 (3 %)	
	UPJO	1 (1.5 %)	1 (1.5)	
	Duplex system	11 (16.2 %)	7 (10.4 %)	
	Upper pole ureterocele & duplex system	5 (7.3 %)	/	
	Other	1 (1.5 %)	2 (3 %)	
Comorbidity, n. %		6 (8.8 %)	8 (11.9 %)	0.55
Scintigraphy	Normal	12 (17.6 %)	7 (10.4 %)	0.43
	minimalchangeunilat	26 (38.2 %)	32 (47.8 %)	
	minimalchangebilat	7 (10.3 %)	11 (16.4 %)	
	severechangeunilat	18 (26.5 %)	14 (20.9 %)	
	severechangebilat	5 (7.4 %)	3 (4.5 %)	
Month, median; IQR		18; 15-54	59; 29-78	<0.01
Kg, median; IQR		11; 9.9–16.6	19; 13-25	<0.01
Side, n. %	Left	25 (36.8 %)	24 (35.8 %)	0.90
	Right	23 (33.8 %)	21 (31.3 %)	
	Bilateral	20 (29.4 %)	22 (32.8 %)	

Table 2 Data regarding perioperative and postoperative data.

		Group A (Open; n = 68)	Group B (Robot; n = 67)	p-value
Type of approach, n. %	Extraperitoneal	68 (100 %)	/	<0.01
	Transperitoneal	/	67 (100 %)	
Type of intervention, n. %	Lich-Gregoire	31 (45.6 %)	67 (100 %)	<0.01
	Cohen	37 (54.4 %)	/	
Type of strategy, n. %	Extravesical	31 (45.6 %)	67 (100 %)	<0.01
	Intravesical	37 (54.4 %)	/	
Procedure, n. %	Unilateral	48 (70.6 %)	45 (67.2 %)	0.66
	Bilateral	20 (29.4 %)	22 (32.8)	
Pig tail placement, n. %		24 (35.3 %)	3 (4.5 %)	<0.01
Days of pig tail removal, n. %		31; 29-40	31; 30-32	0.50
Operative time, median; IQR		100; 86-116	120; 118-140	<0.01
Satava intraoperative complication, n. %	No	67 (98.5 %)	62 (92.5 %)	0.09
	Grade 1	1 (1.5 %)	5 (7.5 %)	
Clavien - Dindo postoperative complication, n. %	No	63 (92.6 %)	61 (91 %)	0.15
	Grade I	5 (7.4 %)	4 (6 %)	
	Grade III	/	2 (3 %)	
Time to stool, median; IQR		2; 1-3	1; 1-1	<0.01
Time to flatus, median; IQR		0: 0-1	1: 1-1	0.28
Days of catheter in situ, median; IQR		5; 2-5	1 1-1	<0.01
Drain placement, n. %	No	62 (91.2 %)	64 (95.5 %)	0.18
	Yes	6 (8.8 %)	16 (23.9 %)	
Days of drain removal, median; IQR		5; 3-5	1; 1-3	<0.01
Length of stay, median; IQR		5; 3-6	2; 1-2	<0.01
Follow up in months, median; IQR		42; 10-51	23; 11-37	0.67
Follow-up, n. %	Success	62 (94 %)	66 (98.5 %)	0.50
	Stenosis	1 (1.5 %)	1 (1.5 %)	
	Persistent low grade reflux	3 (4.5 %)	/	
	Persistent high grade reflux	0	/	
Lost at Follow-up, n.		2	/	/
Re-do intervention	No	62 (94 %)	66 (98.5 %)	0.35
	Endoscopic	1 (1.5 %)	1 (1.5 %)	
	Open	3 (4.5 %)	/	
	Robot	0	/	

operative time was in favor of the open procedure: 96 min (IQR 81—110min) vs 120 min (IQR 110—140min; $p < 0.01$). The complications and follow-up data are equivalent in both groups. However, some perioperative outcomes were significantly better in the RALUR group including catheterization days (3 [IQR 2—5days] vs 1 [IQR 1—3days]) and LOS ($p < 0.01$).

Table 4 provides a sub-analysis of the outcomes of Lich-Gregoire technique in both the OUR and RALUR cohorts. Patients in the open group were younger, lighter, more likely to have unilateral VUR, and had a shorter operative time (94 min [IQR 80—107min] versus 120 min [IQR 118—140min], $p < 0.01$). The intraoperative and postoperative complication rates were not significantly different, however RALUR resulted in a faster post operative recovery with lower time to stool, time to flatus, fewer catheter days and LOS.

The extravesical procedure success rate was not statistically different (RALUR 97 % vs OUR 87.1 %, $p = 0.12$), with only one patient submitted to re-surgery in the RALUR group versus four patients of the open cohort ($p = 0.05$).

Discussion

Surgical intervention in VUR is indicated in high-risk cases, often with high-grade VUR. OUR is accepted as the gold standard in the treatment of children with primary high grade VUR [6]. During the last decade, minimally invasive reconstructive surgery has become an attractive alternative to open approaches in children with the main goal of decreasing morbidity, providing faster recovery, better cosmetic outcomes and achieving historically high success rates associated with open surgery [16,19,20]. Although the use of the robotic platform for VUR started to spread out with many smaller series published, no data focusing on high grade VUR are reported in literature resulting in a lack of results concerning the group most difficult to treat.

Table 3 Data regarding all patient subgroups.

		Open unilateral procedure; n = 48	Robot unilateral procedure; n = 45	p-value	Open bilateral procedure; n = 20	Robot bilateral procedure; n = 22	p-value
Post natal diagnosis, n.%		31 (64.6 %)	12 (26.7 %)	0.36	14 (70 %)	8 (36.8 %)	0.20
Grade of VUR, n. %	4	44 (91.7 %)	24 (53.3 %)	<0.01	18 (90 %)	11 (50 %)	<0.01
	5	4 (8.3 %)	21 (46.7 %)		2 (10 %)	11 (50 %)	
Scintigraphy, n. %	Normal	10 (20.8 %)	4 (8.9 %)	0.08	2 (10 %)	3 (13.6 %)	0.07
	minimalchangeunilat	21 (43.8 %)	31 (68.9 %)		5 (25 %)	1 (4.5 %)	
	minimalchangebilat	5 (10.4 %)	1 (2.2 %)		2 (10 %)	10 (45.5 %)	
	severechangeunilat	11 (22.9 %)	9 (20 %)		7 (35 %)	5 (22.7 %)	
	severechangebilat	1 (2.1 %)	/		4 (20 %)	3 (13.6 %)	
Month, median; IQR		18; 15-54	67; 29-89	<0.01	21; 15-56	51; 30-63	0.03
Kg, median; IQR		11; 9.9—16.1	20; 13-25	<0.01	12.4; 10—17.1	16.5; 12-22	0.02
Type of approach, n. %	Extraperitoneal	48 (100 %)	/	<0.01	20 (100 %)	/	<0.01
	Transperitoneal	/	45 (100 %)		/	22 (100 %)	
Type of intervention, n. %	Lich-Gregoire	31 (64.6 %)	45 (100 %)	<0.01	/	22 (100 %)	<0.01
	Cohen	17 (35.4 %)	/		20 (100 %)	/	
Type of strategy, n. %	Extravesical	31 (64.6 %)	45 (100 %)	<0.01	/	22 (100 %)	<0.01
	Intravesical	17 (35.4 %)	/		20 (100 %)	/	
Pig tail placement, n. %		15 (27.1 %)	3 (6.7 %)	<0.01	9 (45 %)	/	<0.01
Operative time, median; IQR		95; 81-110	120; 110-140	<0.01	112; 99-123	127; 120-150	<0.01
Satava intraoperative complication, n. %	No	47 (98.5 %)	41 (91.1 %)	0.14	20 (100 %)	21 (95.5 %)	0.33
	Grade 1	1 (1.5 %)	4 (8.9 %)		/	1 (4.5 %)	
Clavien - Dindo postoperative complication, n. %	No	44 (91.7 %)	40 (88.9 %)	0.65	20 (100 %)	21 (95.5 %)	0.33
	Grade 1	4 (8.3 %)	3 (6.7 %)		/	1 (4.5 %)	
	Grade 3	/	2 (4.4 %)		/	/	
Time to stool, median; IQR		1; 1-3	1; 1-2	0.57	2; 1-3	1; 1-1	<0.01
Time to flatus, median; IQR		0: 0-1	1: 1-1	0.48	0; 0-1	1; 1-1	0.96
Days of catheter insitu, median; IQR		3; 2-5	1 1-3	<0.01	6; 5-6	1; 1-1	<0.01
Drain placement, n. %	No	42 (87.5 %)	32 (71.1 %)	0.50	20 (100 %)	19 (86.4 %)	0.08
	Yes	6 (12.5 %)	13 (28.9 %)		/	3 (13.6 %)	
Days of drain removal, median; IQR		5; 3-5	2; 1-3	<0.01	/	1; 1-1	/
Length of stay, median; IQR		5; 3-6	2; 1-2	<0.01	7; 6-7	2; 1-2	<0.01
Follow-up, n. %	Success	43 (91.5 %)	43 (95.8 %)	0.52	19 (100 %)	22 (100 %)	1.00
	Stenosis	1 (2.1 %)	2 (4.4 %)		/	/	
	Persistent low grade reflux	3 (6.3 %)	/		/	/	
	Persistent high grade reflux	/	/		/	/	
Lost at follow-up, n.		1	/	/	1	/	/
Re-do intervention	No	43 (91.5 %)	44 (97.8 %)	0.37	20 (100 %)	22 (100 %)	1.00
	Endoscopic	3 (6.4 %)	1 (2.2 %)		/	/	
	Open	1 (2.1 %)	/		/	/	
	Robot	0	/		/	/	

IQR: interquartile rate.

Table 4 Overview of extravesical procedures.

		Group A (Open; n = 31)	Group B (Robot; n = 67)	p-value
Post natal diagnosis, n.%		23 (74.2 %)	41 (61.2 %)	0.20
Grade of VUR, n. %	4	31 (100 %)	35 (52.2 %)	<0.01
	5	/	32 (47.8 %)	
Scintigraphy, n. %	Normal	5 (16.1 %)	7 (10.4 %)	0.56
	minimalchangeunilat	10 (32.3 %)	32 (47.8 %)	
	minimalchangebilat	5 (16.1 %)	11 (16.4 %)	
	severechangeunilat	10 (32.3 %)	14 (20.9 %)	
	severechangebilat	1 (3.2 %)	3 (4.5 %)	
Month, median; IQR		18; 15-68	59; 29-78	<0.01
Kg, median; IQR		10.9; 9.9—16.2	19; 13-25	<0.01
Side, n. %	Left	13 (41.9 %)	21 (31.3 %)	<0.01
	Right	18 (58.1 %)	24 (35.8)	
	Bilateral	/	22 (32.8 %)	
Type of approach, n. %	Extraperitoneal	31 (100 %)	/	<0.01
	Transperitoneal	/	67 (100 %)	
Type of intervention, n. %	Lich-Gregoire	31 (100 %)	67 (100 %)	/
	Cohen	/	/	
Pig tail placement, n. %		/	3 (4.5 %)	0.23
Operative time, median; IQR		94; 80-107	120; 118-140	<0.01
Satava intraoperative complication, n. %	No	31 (100 %)	62 (92.5 %)	0.11
	Grade 1	/	5 (7.5 %)	
Clavien-Dindo postoperative complication, n. %	No	30 (96.8 %%)	61	0.31
	Grade 1	1 (3.2 %)	4	
	Grade 3	/	2	
Time to stool, median; IQR		1; 1-2	1; 1-1	<0.01
Time to flatus, median; IQR		1; 0-1	1: 1-1	<0.01
Days of catheter removal, median; IQR		2; 2-3	1 1-1	<0.01
Drain placement, n. %	No	31 (100 %)	51 (76.1 %)	0.03
	Yes	/	16 (23.9 %)	
Days of drain removal, median; IQR		/	1; 1-3	/
Length of stay, median; IQR		3; 3-3	2; 1-2	<0.01
Follow Up, n. %	Success	27 (87.1 %)	65 (97 %)	0.12
	Stenosis	1 (3.2 %)	/	
	Persistent low grade reflux	3 (9.7 %)	2 (3 %)	
	Persistent high grade reflux	/	/	
Re-do intervention	No	27 (87.1 %)	66 (98.5 %)	0.052
	Endoscopic	3 (9.7 %)	1 (1.5 %)	
	Open	1 (3.2 %)	/	
	Robot	/	/	

IQR: interquartile rate.

Our multicenter study is the first to describe only grade IV and V VUR treated with RALUR vs. OUR. Our study confirms the feasibility of the robotic approach for high grade VUR in children, with faster recovery detected by an early time to stool and flatus, a statistically significant shorter LOS and complication rates similar to the open strategy. On the other hand, at the same time in literature, a national database of 1373 with VUR was analyzed, and the authors suggest that the differential for LOS is more related to institutional culture for open surgery than the use of robotics [21].

Focusing on the success rate, it is higher for RALUR for unilateral surgery (91.5 % vs 95.8 %) and after the extravesical Lich-Gregoir approach (97 % vs 87.1 %), although not statistically different. No previous publication looked into this comparison of techniques. On the other side, the OUR group presents the possibility of treatment of younger and lighter children with a shorter operative time, while the robotic approach still faces some technical instrumentation challenges when dealing with small children.

A possible explanation of this aspect might be the link to the initial enrolled period that also included the learning curve of the robotic surgeons; originally the robotic platform was usually used only in older children and more in recent years experiences has started to be described also in infants [22]. In some cases, the robotic surgeons participating in this study could contribute younger patients, but in order to achieve reasonable long-term follow up (42 and

23 months for robotic and open groups, respectively), it was decided to only include those patients whose follow-up fell within these parameters.

It has been described that the lack of development of miniaturized robotic instruments suited to pediatric application, high costs and a paucity of appropriate training pathways can act as barriers to establishing RALUR as the first choice for surgical treatment of VUR and other anatomical anomalies in the pediatric population [23]. In this light, the open approach will still play a large role in reconstructive urology in infants and young children, for the foreseeable future.

This study assessed the safety of the robotic approach in high grade VUR, and demonstrates that there are no significant differences in the intraoperative and postoperative complication rates between open and robotic strategy. Peri-operative complications were rare and low grade. Two complications (Clavien 3b) were recorded in the post-operative period that necessitated access to the operative room in the RALUR cohort, while the others complications required antibiotic treatment (Clavien 1).

Boysen et al. similarly reported in a large multicenter experience (143 patients), an acceptable safety profile with 4.9 %, 0.8 and 5.6 % of Clavien Dindo grade 1,2 and 3 respectively. Those grade 3 complications included urine leak (n = 3, 2.1 %), ureteral obstruction (n = 2, 1.4 %), port site hernia (n = 1, 0.7 %), inability to deflate defective Foley catheter balloon requiring cystoscopic removal (n = 1, 0.7 %), and retained portion of drain following removal requiring laparoscopic retrieval (n = 1, 0.7 %). Transient urinary retention was seen in four patients (2.8 %, overall), all of them having undergone a bilateral procedure (7.1 % of bilateral cases). Among patients with retention, an indwelling catheter was required for a median of 3 days (range 2—14 days), all returning to spontaneous voiding [10]. In this series, none of our patients experienced urinary retention postoperatively. As previously reported a precise dissection at the junction between ureter and bladder is recommended, avoiding medial and caudal detrusor dissection [7,24,25]. In our series, although a large number of bilateral procedures were recorded, we didn't find any bladder dysfunction; this might be related to the particular attention to this previous issue.

Esposito et al. [9] conducted an international survey on RALUR of 55 patients with high grade VUR found only three (5.4 %) postoperative complications: One small urinoma which resolved spontaneously (Clavien 2) and two cases of persistent reflux, of which one required endoscopic injection (Clavien 3b). Other experiences have reported higher numbers of complications, but these studies presented their initial experiences with the robotic platform, or related to revision procedures, requiring tapering of the ureter. These cases were excluded in this series. It would appear that the robotic learning curve did not seem to influence success rate with only one relapse [26,27]. We strongly feel that the magnified vision and improved dexterity and ergonomics facilitated by the robot are clear advantages in improving surgical performance compared to open surgery. We expect that the rapid improvement of the learning curve will further allow for a reduction in operative time.

The present study had several limitations. The study design was retrospective and nonrandomized. Not all of the centers had the facilities and resources to offer a robotic approach moreover, eleven surgeons are involved with some different outcomes maybe related to the surgeon preference. Furthermore, a post-operative VCUG was not performed in all patients, and therefore the true radiological success rate is unknown. Finally, whilst the cosmetic outcome was outside the scope of this study, we believe it to be better in those patients undergoing RALUR. Further studies may be able to answer whether three/four 8 mm ports or a 5 cm open incision might be more cosmetically desirable.

The power of this study lies in the large multicentric experience of reporting and the focus on high grade VUR. Furthermore, this study has a relatively long follow-up period and compares favorably to OUR in a safety analysis. There was also a trend towards higher success rates with RALUR utilizing an extravesical approach which has not been previously reported.

Conclusion

RALUR is an efficacious and safe platform to use during ureteral reimplantation for high grade VUR. The overall peri-operative and post-operative complication rates are at least equivalent to OUR, but it is associated with a faster functional recovery and time to discharge. Medium to long term success rates are also equivalent to OUR. We believe that the robotic platform with its quick learning curve may be considered in all cases of ureteral reimplantation and that this should be reflected in conversations around informed consent in experienced centres.

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Conflict of interest

Nil.

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