Review Article

Robot-assisted laparoscopic extravesical ureteral reimplantation (RALUR-EV): a narrative review

Soufiane Essamoud[1], Filippo Ghidini[2], Ciro Andolfi[2], Mohan S. Gundeti[3]

[1]Department of Pediatric Surgery, Mohammed VI University of Health and Science, Casablanca, Morocco; [2]Department of Pediatric Surgery, Colmar Children's Hospital (Pasteur II), Colmar, France; [3]Pediatric Urology, Section of Urology, Department of Surgery, The University of Chicago Comer Children's Hospital, Chicago, IL, USA

Contributions: (I) Conception and design: S Essamoud, C Andolfi; (II) Administrative support: C Andolfi; (III) Provision of study materials or patients: S Essamoud, F Ghidini, C Andolfi; (IV) Collection and assembly of data: S Essamoud, C Andolfi; (V) Data analysis and interpretation: All authors; (VI) Manuscript writing: All authors; (VII) Final approval of manuscript: All authors.

Correspondence to: Ciro Andolfi, MD. Department of Pediatric Surgery, Colmar Children's Hospital (Pasteur II), 1 Rue Dr Paul Betz, 68000 Colmar, France. Email: ciro.andolfi@ch-colmar.fr.

Background and Objective: In the last two decades, the treatment of vesicoureteral reflux (VUR) benefits from the introduction of robot-assisted laparoscopy surgery in pediatric population. This article aims to review the advantages of robot-assisted laparoscopic extravesical ureteral reimplantation (RALUR-EV) in pediatric patients with VUR and provides an update on surgical outcomes.

Methods: A literature search of PubMed and MEDLINE databases was conducted. All the articles, published between 2010 and 2022, describing clinical outcomes of patients with VUR after treatment with RALUR-EV, were considered to be relevant for the purpose of the study. The results were synthetized as a narrative review.

Key Content and Findings: Twenty-one studies were included. Of them, 19 (90.5%) presented a retrospective design. These articles involved 1,321 children and 1,914 ureters who underwent RALUR-EV. The mean age at the procedure was 6 years, and the mean follow-up length was 20.4 months. The overall success rate of surgery was 92.2% for patients and 90.9% per ureter. The mean operational time was 175.4 minutes for unilateral reimplantation and 200.3 minutes for bilateral reimplantation. The mean length of stay was 1.9 days.

Conclusions: The article discusses the adoption of RALUR-EV, its advantages, the heterogeneity of study protocols, and the evolution of surgical techniques. It also highlights the need for standardized protocols and prospective studies to further understand the advantages of RALUR-EV.

Keywords: Vesicoureteral reflux; robotic surgery; vesicoureteral reflux (VUR); robot-assisted laparoscopic extravesical ureteral reimplantation (RALUR-EV)

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Introduction

Vesicoureteral reflux (VUR) is the most common urological malformation in children and a frequent cause of urinary tract infection (UTI) (1). Even if the primary management plan is a watchful waiting approach, based on antibiotic prophylaxis and the evidence of spontaneous VUR regression, surgery should be considered the definitive treatment, according to the current European Association of Urology (EAU)/European Society for Paediatric Urology (ESPU) guidelines (2). Even though the surgical approach might differ from team's experiences and habits, the indications remain the same: severe UTIs despite the antibiotic prophylaxis, worsening of renal function, and lack of VUR improvement (3). Treatment options are endoscopic submucosal injection of bulking agents and intra- or extra-vesical ureteral reimplantation for failed endoscopic treatment, especially for children affected by persistent high-grade reflux (2). The evolution of the laparoscopic approach due to technical advances, such as smaller endoscopic instruments and high-resolution cameras, contributed to the development of minimally invasive surgery (MIS) for pediatric urology (4). Its advantages include faster recovery, shorter length of hospital stay (LOS), decreased post-operative pain (5), and better cosmetic results, as already reported for pediatric pyeloplasty (6). However, due to its technical complexity and the steep learning-curve, the widespread adoption of laparoscopy has been limited, especially for challenging procedures such as ureteroneocystostomy (UNC) (7). The introduction of the Da Vinci® robotic surgical system in the pediatric arena has been able to overcome those limits, thanks to faster learning-curves, enhanced depth perception, and improved motions skills (3,5,8). However, despite its critical technical advantages, it is still not widely adopted and modern guidelines does not put it as a gold-standard in the armamentarium for UNC (9,10). The main reasons seem to be procedure's high costs, longer operative time (OT) due to docking, no haptic feedback, and lack in uniformity of training (11,12).

Therefore, we aimed to review the current literature to highlight the potential advantages of robot-assisted laparoscopic extravesical ureteral reimplantation (RALUR-EV) in pediatric patients and to provide an up-to-date status of the art concerning this innovative approach. Our goal was to collect the current evidence for pediatric surgeons and urologists who wants to embrace this new approach. We present this article in accordance with the Narrative Review reporting checklist (available at https://tp.amegroups.com/article/view/10.21037/tp-23-336/rc).

Methods

A literature search of PubMed and MEDLINE databases was conducted to identify all relevant articles published between 2010 and 2022, describing clinical outcomes of patients with VUR after treatment with RALUR-EV. The string search was ('vesico-ureteral reflux' OR 'VUR') AND ('robot') AND ('reimplantation' OR 'ureteroneocystostomy' OR 'RALUR' OR 'RALUR-EV'). The entire string with MeSH terms is reported in Appendix 1. We also used the filter "age" by choosing "birth-18 years old" to limit our search to articles related to pediatric populations. The references of extracted articles were also reviewed to identify additional pertinent studies. Inclusion criteria were: studies published in the English language; studies that specifically diagnosed VUR; studies of patients treated with robot-assisted surgery; studies that explicitly described the clinical outcomes for pediatric patients; and studies that contained original data. Exclusion criteria were: studies that did not clearly state the outcomes; those with insufficient original data; articles that reported data included in other selected references; reviews; case reports; and commentary or opinion pieces. One author extracted the data from the included studies and the other author checked the extracted data. Disagreements were resolved by discussion. The following data were extracted from each article: first author; year of publication; number of patients and ureters treated; patients' age; OT; LOS; treatment successes, failures, and complications; and follow-up interval. The primary endpoint of the study was surgical success rate, which was treated as a dichotomous variable (success or failure). All the details about the search strategy are summarized in *Table 1*.

Results of the literature search

Initial PubMed search with the term with "robot ureteral reimplantation" showed 122 results. All articles referred to robot-assisted extravesical ureteral reimplantation were included. Twenty-one studies studying 1,321 children with VUR who underwent RALUR-EV were included in this review. They were performed between 2003 and 2019 and published between 2010 and 2019.

Six were retrospective comparative studies (13-18), 13 were retrospective cohort studies (1,12,19-29) and two were prospective cohort studies (30,31). From all the 1,321 children, we enumerated 1,914 ureters that were reimplanted with the extravesical approach with robot-assisted surgery.

Mean age at the procedure was 6 (range, 2.3–10) years. Mean follow-up length was 20.4 (range, 7.4–39) months. The mean total OT was 175.4 (range, 92.2–291) minutes for unilateral reimplantation and 200.3 (range, 108–285) minutes for bilateral reimplantation. The mean LOS was 1.9 (range, 0.9–7.4) days.

Success of surgery was assessed differently in these studies. Either clinically without systematic urethrocystograms (UCG), but done solely after a subsequent febrile UTIs (14,16,17,20,21,25,30), or systematically during the post-operative period, and finally

Table 1 The search strategy summary

Items	Specification
Date of search	March 01, 2023
Databases searched	PubMed and MEDLINE databases
Search terms used	('vesico-ureteral reflux' OR 'VUR') AND ('robot') AND ('reimplantation' OR 'ureteroneocystostomy' OR 'RALUR' OR 'RALUR-EV')
Timeframe	From January 2010 to December 2022
Inclusion and exclusion criteria	Inclusion criteria: English language; pediatric patients; diagnosis of VUR; robot-assisted surgery; clear clinical outcomes; original data
	Exclusion criteria: insufficient data; overlapping data; reviews; case reports; commentary and opinion pieces
Selection process	One author extracted the data under the supervision of the others. Disagreements were resolved by discussion
Additional consideration	Primary endpoint: surgical success rate

VUR, vesicoureteral reflux; RALUR-EV, robot-assisted laparoscopic extravesical ureteral reimplantation.

when family asks for an objective proof (21). The overall success rate regarding patients was 92.2%, whereas the overall success rates per ureter was 90.9%. Failure was defined as febrile UTI when assessed clinically, as persistent VUR on UCG when assessed radiologically. In some studies (12-19,22,24,25-29,31), failure rate was assessed per patients and was 4.3%. In others (1,20-23,26,30), it was assessed per ureter only or in addition to per patients, failure rate per ureter was 7.3%. All data are resumed in *Table 2*.

Summary

The evidence about spontaneous resolution of VUR, the initial conservative management, which relies on continuous antibiotic prophylaxis, and the global spread of subureteric injection of bulking materials in the last two decades drastically reduced the need for ureteral reimplantation. Nevertheless, traditional surgery still plays a relevant role in the treatment of VUR.

Hence, the current EAU/ESPU guidelines strongly recommend ureteral reimplantation for the patients affected by persistent high-grade VUR. Moreover, the current guidelines classify pediatric patients in different groups according to the risk of UTI breakthrough and renal impairment. Surgery should be offered in the children considered at high-risk (2).

For many years, open surgery approach was the main approach in ureteral reimplantation. Nowadays, two minimally invasive approaches have been introduced, consisting in the laparoscopic extravesical reimplantation and the transvesicoscopic reimplantation. A meta-analysis found similar outcomes for both the techniques, but the transvesicoscopic approach required more experienced skills and its spread was limited (32).

The superiority of the laparoscopic approach was demonstrated in the literature. Shi *et al.* (33) confirmed the advantages of short hospital stay, fast recovery, and minimal postoperative pain. Furthermore, Fernández-Alcaraz *et al.* (34), using a Lich-Gregoire-like laparoscopic procedure, had an acceptable success rate (99.2% *vs.* 100%), and a safe profile comparable to open surgery. They report a shorter hospital stay, less bleeding and less blood transfusion. Nevertheless, EAU/ESPU guidelines limit their use only to well-experienced centers.

The adoption of robot-assisted surgery progressed more rapidly in the adult population. It wasn't until the 2000s that we saw the first instances of RALUR-EV in pediatric cases. Studies on RALUR in children have a relatively short history of 15 years, in contrast to open surgery, which has been practiced for over 50 years. The concept was first described by Peters in 2004 (35). Since then, there has been a growing effort to implement this approach. However, its widespread adoption remains limited, despite its advantages like reduced postoperative pain and shorter hospital stays.

Its main objective is relatively the same: to protect the upper urinary tract in patients who fail conservative measures. It is achieved through a transperitoneal, extravesical approach, mimicking the Lich-Gregoire procedure (3).

Table 2 Summary of the papers included in the review

First name	Years	Study type	Patients (n)	Ureter (n)	Mean age (years)	Mean follow-up length (months)	Mean total OT unilateral (min)	Mean total OT bilateral (min)	LOS (days)	Intra-op complication rate (%)	Success rate (patient) (%)	Success rate (ureter) (%)	Failure rate (patient) (%)	Failure rate (ureter) (%)
Esposito (13)	2019	Retrospective comparative study	35	51	7.5	NA	159.5	202	2.6	0	100	NA	0	NA
Kawal (19)	2018	Retrospective cohort study	128	179	4	NA	NA	NA	NA	0	100	NA	0	NA
Boysen (30)	2018	Prospective cohort study	143	199	6.6	7.4	159	195	1.5	0	91.4	93.8	NA	2
Srinivasan (21)	2017	Retrospective cohort study	92	127	3.8	14	150	178	1.4	0	91.3	NA	NA	2
Boysen (20)	2017	Retrospective cohort study	260	363	6.4	NA	152	198	1.6	0	84.9	87.9	NA	3.6
Esposito (12)	2018	Retrospective cohort study	55	55	4.9	28	92.2	NA	2	0	96.3	NA	1.8	NA
Herz (22)	2016	Retrospective cohort study	54	72	5.2	NA	NA	NA	1.8	0	84.7	85.2	14.8	15.3
Arlen (14)	2016	Retrospective comparative study	17	20	9.3	16.6	169.3	NA	1	0	88.2	NA	0	NA
Gundeti (23)	2016	Retrospective cohort study	58	83	5.3	30	NA	NA	NA	0	NA	82	NA	18
Silay (24)	2015	Retrospective cohort study	89	114	5.4	NA	NA	NA	NA	0	NA	97.9	0	NA
Hayashi (15)	2014	Retrospective comparative study	9	15	10	NA	144	211.5	7.4	11.1	NA	93.3	0	NA
Dangle (1)	2014	Retrospective cohort study	29	40	5.4	NA	NA	NA	1.8	0	NA	80	NA	2.5
Schomburg (16)	2014	Retrospective comparative study	20	25	6.2	39	165	227	1	0	100	NA	0	NA
Grimsby (25)	2015	Retrospective cohort study	61	93	6.7	11.7	NA	NA	NA	2	72	NA	28	NA
Akhavan (26)	2014	Retrospective cohort study	50	78	6.2	9.5	NA	NA	2	0	NA	92.3	NA	7.7
Callewaert (27)	2012	Retrospective cohort study	5	10	6.8	28	NA	162	2	20	NA	90	0	NA
Chalmers (28)	2012	Retrospective cohort study	17	23	6.2	NA	237	285	1.3	0	87.5	90.9	5.8	NA
Kasturi (31)	2012	Prospective cohort study	150	300	3.5	NA	NA	108	0.9	0	99.3	NA	0.7	NA
Marchini (17)	2011	Retrospective comparative study	20	30	8.6	12	209	233.5	1.7	0	NA	100	5	NA
Smith (18)	2011	Retrospective comparative study	25	33	5.7	16	177	203	1.4	0	96	97	8	NA
Lee (29)	2010	Retrospective cohort study	4	4	2.3	33	291	NA	2.3	0	100	NA	0	NA

OT, operative time; LOS, length of hospital stay; NA, not available.

Moreover, indications for ureteral reimplantation have become less common compared to the 2000s. EAU guidelines encourage the tolerance of asymptomatic and low grade VUR in addition to the use of antibiotic prophylaxis waiting for its spontaneous regression (7). The decline of ureteral reimplantation as stated by Kurtz *et al.* (36) could explain more the lack of the adoption of RALUR overtime.

In the studies we reviewed, there was heterogeneity in the number of patients, their mean age, and the protocols used. A lot of information was also not specified in every study such as length of follow-up or LOS. Nevertheless, there are some observations we can make. Firstly, the mean LOS remains consistent, which is a key advantage of robot-assisted surgeries. In nearly every study, the incidence of peri-operative complications was non-existent. Callewaert *et al.* and Hayashi *et al.* found higher rate of peri-operative complications, which is probably due to a learning-curve effect (15,27).

The definition of surgical success or failure was also inconsistent, which may hinder the accurate assessment of its true value. This introduces a clear bias between those who evaluate it radiographically or clinically. This could potentially influence the decision for re-do surgeries, leading to increased morbidity for patients who might not undergo reoperation if treated by different teams. Yet, it's noteworthy that recent papers report higher success rates and lower failure rates. Surgeon team's experience and the evolution of material technology, development of higher-resolution camera with improvement of haptic sensations and 3D-vision could play a consequent role in surgery success.

Both RALUR and robot-assisted surgeries in general continue to evolve, both within individual teams and on a global scale. Regular publications contribute to improving success rates and reducing complications. In this sense, a relevant improvement was the LUAA technique described by Gundeti *et al.* (23). The LUAA technique modification consists in the adequate length of the detrusor tunnel (L), the use of a U stitch (U) at the uretero-vesical junction (UVJ) to mimic the advancement stitch along with the placement of a permanent ureteral alignment suture (A) and the inclusion of ureteral adventitia (A) in detrusorrhaphy to decrease ureteral slippage.

In cases of bilateral VUR, OT does not significantly differ compared to unilateral cases. The primary challenge in robot-assisted surgery lies in the extended docking time, which could be addressed through team experience and protocol standardization. The learning-curve might also reduce the OT. However, bilateral RALUR may pose greater challenges due to its involvement in per-operative lesions of the pelvic plexus nerve, leading to postoperative urinary retentions (12,17,18,22,24,26,27,29). Casale *et al.* (37) described a nerve sparing technique to avoid this complication. Adopted by Kasturi *et al.* (31), it seems to be effective in both their studies with no complication as such. The general rule in order to avoid lesions of the nerve plexus is a precautious use of electrocautery while dissecting, especially medially and inferior to the UVJ (31,37). For this reason, Gundeti *et al.* (23) proposed a Y-shaped nerve-sparing dissection around the UVJ with careful use of electrocautery. This surgical tip aimed to reduce the risk of post-operative urinary retention, especially in case of bilateral RALUR.

Other techniques have also been introduced to maximize surgical outcomes and decrease complications.

In order to avoid the risk of acute angulation of the ureter causing ureteral obstructions, Silay *et al.* (24) described a modified "top-down" suturing technique using interrupted sutures without the need for ureteral elevation or stent placement.

Undeniable benefits of this innovative approach are a faster learning-curves, enhanced depth perception and improved motions skills. Moreover, latest advances in robotic technology allowed a relevant improvement in the haptic feedback which is crucial for pediatric reconstructive surgery. On the other hand, limitations are represented by the procedure's cost and long OT due to docking. However, these limitations might be overcome by a widespread utilization robotic approach and structured teaching programs.

Efforts must be directed towards adopting robotic-assisted surgery as a mainstream method for treating children affected by VUR unresponsive to conservative and endoscopic management. Despite the extremely positive results of RALUR, current papers are too heterogenous to compare, and meta-analysis could not be performed, and further evidence should be produced to reach this goal. This is the main limitation of this paper.

Conclusions

RALUR-EV presented a consistent LOS when compared to traditional laparoscopy. However, the manipulation of the tissues and the intracorporeal sutures, which are crucial for reconstructive surgery, benefit from the enhanced ergonomics and 3D-vision. These aspects might reduce the risk of complications and ease the learning-curve for ureteral reimplantation performed by minimally invasive approach.

On the other hand, an increased OT and costs are considered the main negative aspects for robotic surgery. Once again, these limitations could be overcome by the learning-curve effect and a wide diffusion of this approach.

In conclusion, RALUR-EV might become a gold-standard treatment for unresponsive VUR in children, but further evidence should be required to support this approach and reach this target.

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