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ORIGINAL ARTICLE

Robot-assisted laparoscopic extravesical versus conventional laparoscopic extravesical ureteric reimplantation for pediatric primary vesicoureteric reflux: a systematic review and meta-analysis

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Abstract
To perform a systematic review and meta-analysis comparing the outcomes of robotic-assisted laparoscopic extravesical ureteric reimplantation (RALUR) with conventional laparoscopic extravesical ureteric reimplantation (LEVUR) for primary vesicoureteric reflux in children. We searched the databases to identify all papers of RALUR and LEVUR between 2001 and 2020. Systematic review was performed to identify patient data, age, reflux grades, laterality, duration of surgery, time to discharge, success rate and complications. Heterogeneity was reported with I^2 statistics and publication bias was assessed by Doi curve and Luis Furuya-Kanamori index. Pooled data from both groups were compared with Student's t test and Fisher's exact test, wherever appropriate. From a total of 43 articles screened, 28 articles were included (18 RALUR and 10 LEVUR). The I^2 statistics for RALUR and LEVUR showed heterogeneity of 86% and 25%, respectively. Both groups had comparable minor publication bias. RALUR had higher proportion of grade 5 VUR ($p<0.001$) and bilateral reimplantations ($p<0.001$). The success rate of RALUR was significantly lower than that of LEVUR (97.6% vs. 93.4%, $p=0.0018$). RALUR took a significantly longer duration for surgery compared to LEVUR, both for unilateral and bilateral cases ($p<0.001$). The complication rate was not significantly different: 6.6% for RALUR and 5.35% for LEVUR ($p=0.32$). The most common complication in both groups was post-operative urinary retention in bilateral cases. Articles on LEVUR reported more consistent success. RALUR series had higher proportion of grade 5 cases and bilateral reimplantations. RALUR reported longer operative time and lower success compared to LEVUR, with a complication rate comparable to LEVUR.

Keywords Ureteric · Reimplantation · Robot-assisted · Laparoscopic · Vesicoureteric · Reflux · Extravesical · Systematic · Review · Meta-analysis

Background

Ureteric reimplantation (UR) is a common operation for vesicoureteric reflux (VUR) performed by pediatric urologists. In the last two decades, with the popularity of minimally invasive surgical (MIS) techniques, there is increased utilization of MIS techniques for UR. Wang et al. [1] observed that the number of MIS procedures for VUR in the USA increased ninefold between 2005 and 2012 compared to 1998–2004, while there was a simultaneous reduction in open UR procedures. Laparoscopic extravesical UR (LEVUR) is an adaptation of the Lich–Gregoir technique, and several reports confirmed its applicability as an alternative to open UR [2–11]. With the wider availability of robotic systems, robot-assisted laparoscopic UR (RALUR) has grown rapidly over the last few years [12–29] with several publications describing the technique and results. However, while the technique and results of LEVUR have been published from centers all over the world, in contrast, most of the RALUR reports are from the USA alone.

Currently, robotic-assisted surgery is not easily available in many centers across the world, and until robotic-assisted surgery becomes available across the globe, conventional laparoscopic UR may have a definite role in anti-VUR surgery. Although RALUR made surgeon's life easier for

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dissection and suturing deep in the pelvis, with the benefit of improved ergonomics, some of these reports published inferior results with increased complications with RALUR [22, 23]. It is therefore prudent to know whether RALUR is worth adapting worldwide; the additional health-care investments required for robotic setup warrants a thorough review to see whether RALUR is superior, or at least equal and not inferior to LEVUR in terms of success and complications. We hypothesized that the addition of robotic assistance has improved the success or reduced the complications of LEVUR. In this systematic review and meta-analysis, we have tried to answer these questions.

Methods

Search strategy

Two investigators searched the databases: Pubmed (Medline), Publon, Index Medicus and Embase using the search terms: reimplantation (laparoscopic AND extravesical OR robotic) AND (child OR infant OR pediatric OR paediatric OR adolescent OR young), to identify all papers pertaining to RALUR and LEVUR in the pediatric population. MeSH terms were also utilized in the search. Cross citations and articles not included in the above sites were also identified by further search. Once identified from the database searches, these papers were further screened to identify those describing patient characteristics, including pre-operative, intra-operative and post-operative data.

Inclusion and exclusion criteria

We included both prospective and retrospective series on RALUR and LEVUR published from 2001 to 2020. We did not include articles that described vesicoscopic reimplantation. We included all studies pertaining to children up to 18 years. We excluded non-English language articles, review articles, case reports and education articles. Duplicate publications were identified and removed. The remaining articles were evaluated on a seven-point scale; each article was scrutinized for information regarding seven points, which included the number of patients/ureters, age, grades of VUR, operating time, success, hospital stay and complications. Only those articles that provided information on at least four of the seven parameters were included. Articles with grossly incomplete data and errors in reporting were excluded.

Study appraisal and synthesis

The systematic review was carried out according to the preferred reporting items (PRISMA) guidelines for systematic and meta-analysis [30]. Both authors assessed titles and abstracts for inclusion and with discussion came to agreement upon included studies. Figure 1 describes the methodology followed in this systematic review and meta-analysis.

Data analysis

Meta-analysis of proportions was carried out using MetaXL 5.3 (Epigear International© 2010–2016). Heterogeneity was reported with I^2statistics, with 0–40% not important, 30–60% moderate, 50–90% substantial, and 75–100% considerable. Heterogeneity was analyzed within RALUR and LEVUR groups for the success rate, the main parameter of this study. Publication bias within each group was assessed graphically and quantitatively using the Doi plot and Luis Furuya-Kanamori (LFK) index [31], respectively. From the pooled data in each group, outcomes such as mean age, reflux grades, laterality, duration of surgery, time to discharge, success and complications were compared between the two groups with Student's *t* test and Fisher's exact test, wherever appropriate.

Results

Study selection

Figure 1 shows the study selection process, where a total of 43 records were identified from the search for RALUR or LEVUR in children. Four records were excluded for duplication of the study population in the reporting, causing an overlap, and six for lack of full data and/or error in reporting. Five review articles were also removed, leaving a total of 28 articles for analysis. This included 18 articles on RALUR and 10 articles on LEVUR. Regarding geographic distribution, RALUR was reported mainly from the USA (Asia 1, USA 17), while LEVUR was reported from across the globe from many countries (Asia 3, Europe 5, North America 3, South America 1), with some being multicenter reports in both groups. The summary of data from individual RALUR and LEVUR articles is given in Table 1, while the comparative pooled data from both groups are given in Table 2.

Assessment of publication bias

The Doi plots and LFK index in both groups are given in Fig. 2. The LFK index was − 1.32 for RALUR and − 1.33 for LEVUR, indicating only minor asymmetry (minor negative publication bias) in both groups.

Meta-analysis of success rate

For the purpose of this analysis, success was defined as the complete resolution of VUR on post-operative imaging

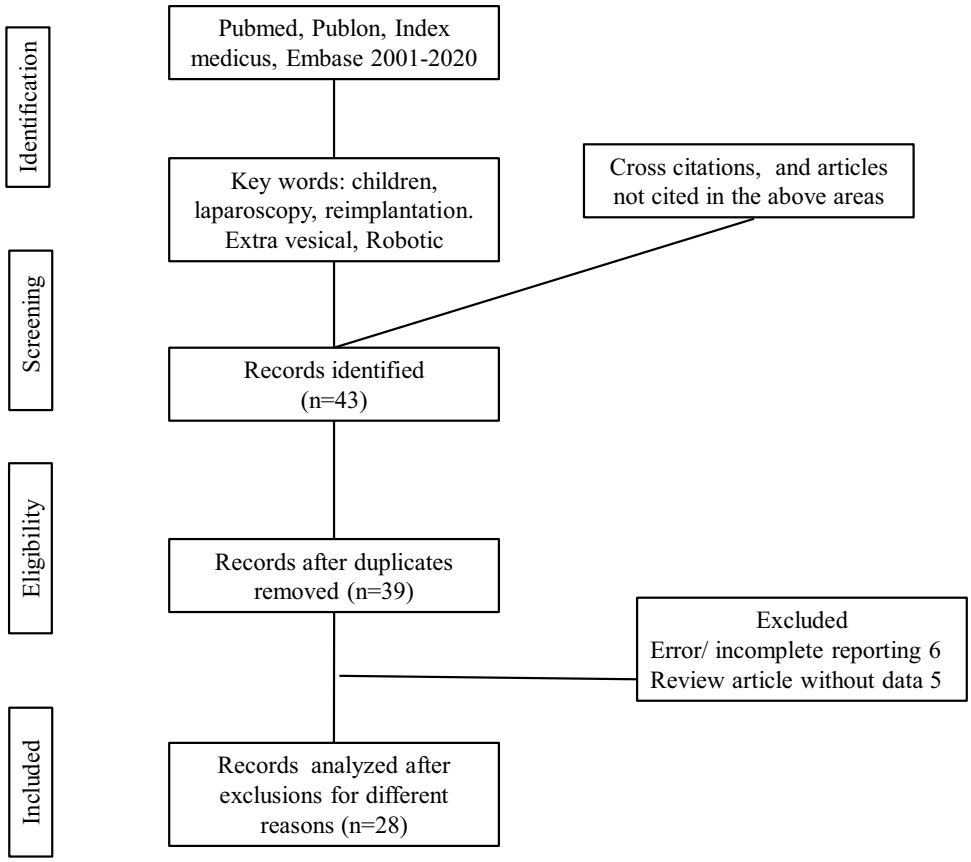

Fig. 1 PRISMA-compliant flow chart demonstrating assessment of eligibility of articles for inclusion in analysis. PRISMA: Preferred Reporting Items for Systematic Reviews and Meta-Analyses

(radiographic success). The I^2statistics for RALUR success showed high heterogeneity for success rate with I^2 of 86% (95% C.I 79–65%). In contrast, the I^2statistics for LEVUR success showed low heterogeneity with I^2 of 25% (95% C.I 0–64%). Figure 3 shows the forest plot of studies on RALUR and LEVUR groups. The overall success rate of RALUR was 1667/1783 [93.4% (95% C.I 88–97%)], while the overall success rate of LEVUR was 673/696 [97.6% (95% C.I 95–98%)]. This difference in success rate (LEVUR > RALUR) was statistically significant ($p = 0.0018$; χ^2).

General outcomes

Table 1 shows the individual outcomes of all the studies and Table 2 shows the pooled outcomes of parameters compared. The mean age at operation was comparable between both groups (5.8 years for RALUR and 5.6 years for LEVUR, $p = 0.542$; Fisher's). Among papers that provided grade, the proportion of grade 5 VUR was significantly higher in RALUR compared to LEVUR (7.65% vs. 2.2%, $p < 0.001$; χ^2). Similarly, the proportion of bilateral reimplantations was significantly higher ($p < 0.001$; χ^2) at 45% in RALUR compared to 33% in LEVUR.

Duration of surgery

The mean (sd) duration of surgery for unilateral procedure was 171 (30.7) min for RALUR and 107 (30.1) min for LEVUR. The mean (sd) duration of surgery for the bilateral procedure was 223 (38.1) min for RALUR and 161 (35.8) min for LEVUR. For both unilateral and bilateral procedures, RALUR took a significantly longer duration ($p < 0.001$; Fisher's).

Time to discharge

The mean (sd) time to discharge was 1.8 (1.5) days for RALUR and 1.6 (0.4) days for LEVUR. Overall, RALUR patients took a significantly longer time to get discharged ($p = 0.002$; Fisher's).

Complications

The complications reported in the various studies were classified according to the Clavien–Dindo classification [32]. All complications in either group were Clavien grade 1-3b; there were no Clavien grade 4 or 5 complications in either group. Four main complications were considered in the analysis: post-operative urinary retention, urine

Table 1 Details of studies included in RALUR and LEVUR

Author	No of units	Mean age (years)	Duration of surgery (min)	Time to discharge (days)	Success rate %	No of Clavien 1–3 complications
RALUR						
Peters [12]	27	5.8	NA	NA	88	3
Casale [13]	82	3.2	153	1.1	97.6	0
Smith [14]	33	5.9	235U;262B	1.4	97	4
Marchini [15]	27	8.6	209U;233B	1.3	85	6
Kasturi [16]	300	3.6	110	1	99.3	0
Chalmers [17]	22	6.3	237U;285B	1.3	91	0
Dangle [18]	40	5.4	NA	1.8	80	NA
Schomburg [19]	35	6.2	165U;227B	1	100	3
Akhavan [20]	78	7.2	NA	2	92.3	6
Hayashi [21]	15	7.6	217U;298B	7.4	93	0
Grimsby [22]	93	6.7	NA	NA	77	6
Herz [23]	72	5.2	206U;306B	1.6	85.2	10
Arlen [24]	13	9.3	169.3	1	100	1
Gundeti [25]	83	5.3	NA	2	82	1
Boysen [26]	363	6.4	152U; 198B	1.6	87.9	11
Boysen [27]	199	6.6	174U;218B	1.5	93.8	10
Sachdev [28]	230	5.9	161U' 208B	NA	97	14
Kim [29]	101	5	161U;205B	1.3	96	6
LEVUR						
Capolicchio [10]	31	7.3	NA	NA	96	2
Tsai [2]	14	3.4	170 U; 218 B	1.4	93	1
Lopez [11]	43	4.4	70 U; 124 B	1	100	2
Bayne [4]	144	6.7	NA	1.7	95	6
Riquelme [3]	95	4.5	105 U; 180 B	1.6	96	2
Javali [5]	98	9.5	102 U; 165 B	1.5	98	3
Esposito [6]	38	4.8	95 U; 128 B	2.4	89	2
Soulier [7]	159	3.9	96 U; 128 B	1.2	99	3
Badawy [8]	17	5	90 U	2	100	3
Bustangi [9]	57	4.2	127 U; 184 B	1.6	98	4

U unilateral; *B* bilateral; *NA* not available

Table 2 Metaanalysis of RALUR and LEVUR articles data

Summary	RALUR (1227 patients, 1783 ureters)		LEVUR (523 patients, 696 ureters)		Difference (*p* value)	
Mean (s.d) age in years	5.8 (1.4)		5.6 (2.9)		0.0542	
Bilateral cases	556/1227 (45%)		173/523 (33%)		<0.001	
% of ureters with grade 5 VUR (among papers that provided grade)	103/1345 (7.65%)		12/552 (2.2%)		<0.001	
Surgery Duration (min) Mean (sd)	Unilateral	Bilateral	Unilateral	Bilateral	<0.001 unilateral	<0.001 bilateral
	171 (30.7)	223 (38.1)	107 (30.1)	161 (35.8)		
Time to discharge (days) mean (sd)	1.8 (1.5)		1.6 (0.4)		0.0027	
Success rate	1667 (93.4%)		673 (96.7%)		0.0018	
Complication rate	81 (6.6%) retention 33, ureteric complications 40 port-site hernia 8		28 (5.3%) retention 9, ureteric complications 12		0.32	

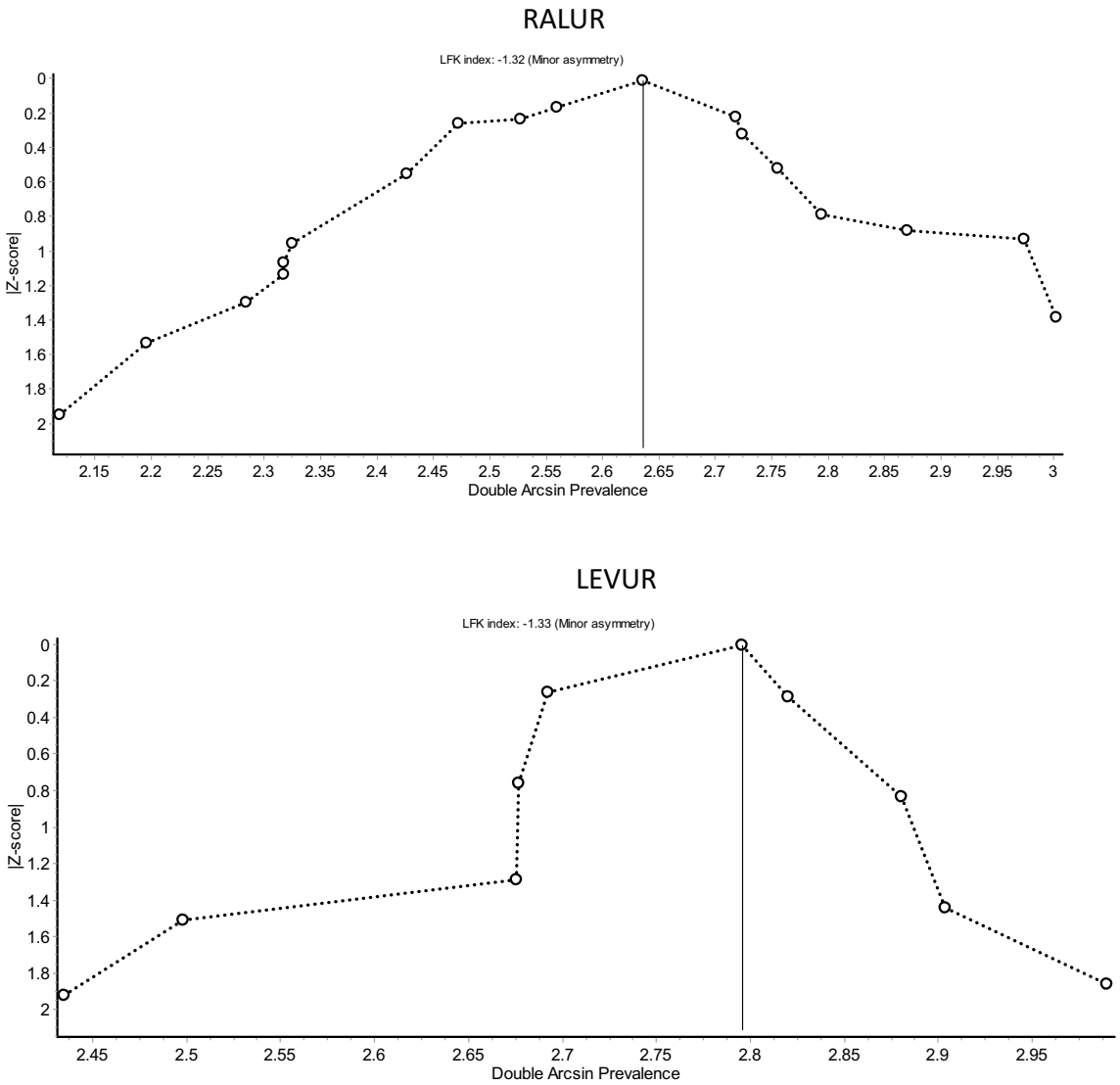

Fig. 2 Doi plots and LFK index for RALUR and LEVUR

leak, ureteric injury/obstruction and other specific procedure-related complication reported (like port-site hernia). The complication rate was comparable ($p = 0.32$, χ^2) for RALUR (6.6%) and LEVUR (5.3%). Among the complications reported in RALUR, 40/81 were ureteric injuries/leak/obstruction, 33/81 were urinary retentions and 8/81 were port-site hernias. Among the complications reported in LEVUR, 9/28 were urinary retention and 12/28 were ureteric complications.

Discussion

Although RALUR and LEVUR have been practiced for almost two decades, to our knowledge there have been no systematic reviews or meta-analysis comparing both MIS techniques. Both these techniques are similar adaptation of extravesical Lich–Gregoir technique with RALUR providing an ergonomic advantage to the surgeon and extra freedom in suturing deep within the pelvic cavity, but at a significantly higher cost. In a previous meta-analysis [33], RALUR was associated with higher early post-operative complications, reduced hospital stay and similar success rate compared with open UR. In this meta-analysis, we have compared the outcomes of RALUR and LEVUR so that our findings could help centers across the globe to decide whether to adopt the more expensive robotic technique that is currently popular in the USA.

Before comparing both techniques, we tested the heterogeneity of success reported in both RALUR and LEVUR articles. We found low heterogeneity in LEVUR, with most articles reporting success rates in excess of 95%. However,

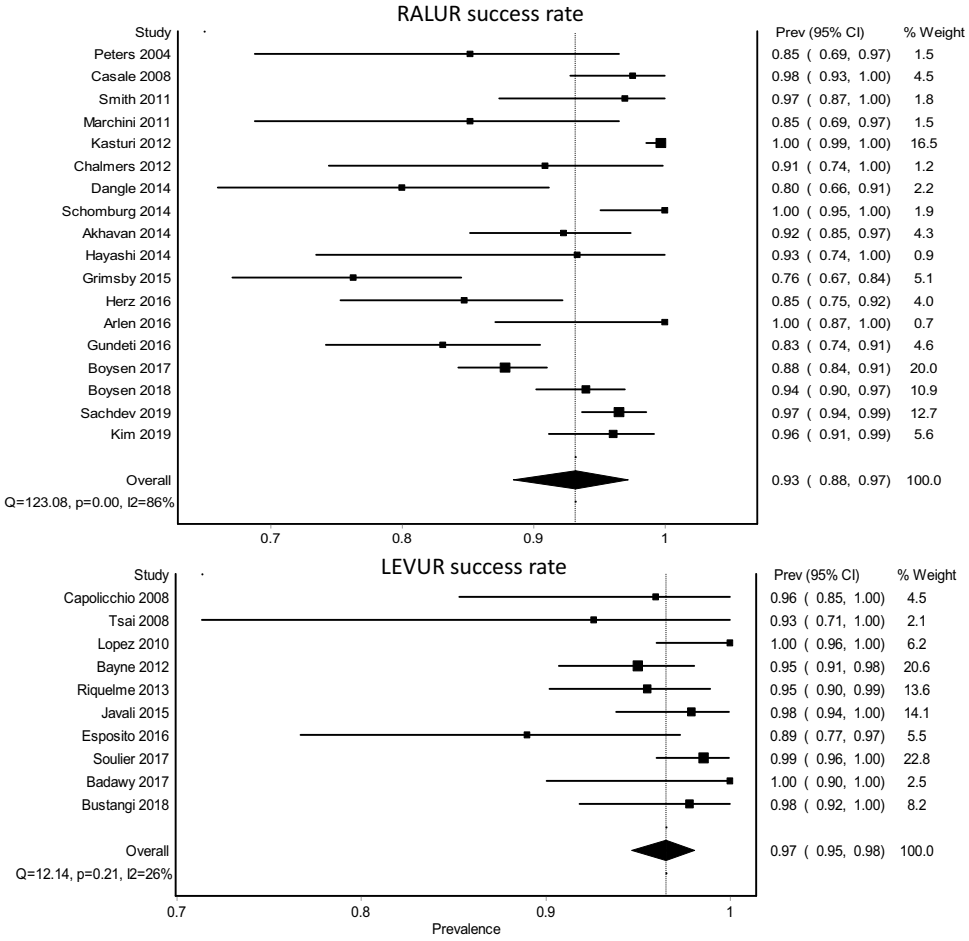

Fig. 3 Forest plots for success rate of RALUR and LEVUR

in the case of RALUR, there was significant heterogeneity, with reported success rates ranging from 77 to 100%. It is possible that LEVUR was performed by expert laparoscopic surgeons [5], which, coupled with the availability of tactile feedback, may account for uniformly high success rate seen with LEVUR. On the other hand with the availability of robotic technique, even relatively inexperienced surgeons might be attempting RALUR. There seems to be a definite learning curve for RALUR; Gundeti et al. [25] and Sachdev et al. [28] listed several modifications they incorporated along their RALUR learning curve, which seemed to improve their success and helped reduce complications over the years. Thus, even with robotic assistance, technical steps such as fine ureteric dissection and correct assessment of the length of submucosal tunnel (detrusorotomy) may require significant experience. Coupled with the lack of tactile sensation with robotic assistance, this learning curve may be responsible for the wide variation in RALUR results and the relatively poor results reported by some authors.

In the present meta-analysis, the success rate of LEVUR was significantly higher than that of RALUR (96.7% vs. 93.4%, $p = 0.0018$). This difference may be partly due to the higher proportion of bilateral reimplantations ($p = 0.001$) and higher proportion of grade 5 VUR cases ($p = 0.001$) in RALUR compared with LEVUR. Although this may imply that RALUR may be the preferred technique for grade 5 VUR and bilateral reimplantation, some authors [23] reported that bilateral RALUR had lower success than unilateral RALUR. As discussed earlier, the learning curve of RALUR may also have contributed to the lower success in some reports. The lower preference of LEVUR in bilateral cases may be due to the risk of postoperative urinary retention with bilateral LEVUR. However, the same risk exists with bilateral RALUR also. To reduce this risk, nerve-sparing technique has been reported in both RALUR [13] and LEVUR [2].

The duration of surgery was significantly longer for RALUR than LEVUR (for both unilateral and bilateral cases). This may be due to the extra time-consuming docking time for the robot. Apart from this extra step, the higher proportion of grade 5 VUR cases in the RALUR group may also partly account for the longer operative time. It is likely that dissection of the dilated ureters of grade 5 VUR and the creation of longer detrusorotomies for reimplantation were more time consuming.

The mean post-operative hospital stay was longer for RALUR compared to LEVUR (1.8 vs. 1.6 days). However, despite statistical significance, this finding probably has limited clinical significance, since most children in both groups were discharged after overnight hospital stay. For practical purposes, it can be safely concluded that the hospital stay was comparable in both groups.

Although some authors [22, 23] have reported higher complications with RALUR, in this meta-analysis we did not find any significant difference in overall complication rate between RALUR (6.6%) and LEVUR (5.3%). The predominant complication in both groups was post-operative urine retention, especially in bilateral cases. However, this review did not find any difference in post-operative urinary retention in bilateral cases between both the groups [RALUR 33/556 (5.9%) versus LEVUR 9/173 (5.2%), $p = 0.852$]. Ureteric injuries/leak/obstructions were reported higher in RALUR (40/81) versus LEVUR (9/28), although this difference was not statistically significant. The specific complication reported only in RALUR was port-site hernia in eight cases, which required formal repair later. This complication was probably related to the use of larger ports in RALUR, and Sachdev et al. [28] reported that they modified their port closure technique to prevent this complication.

In an editorial on RALUR, Cannon and Ost [34] felt that comparison of MIS techniques should examine competitive surgical options concerning "QCCC" yield, comprising quality (success and complication rate), convalescence, cost and cosmesis. In the present review, we could compare the success, complications, duration of surgery and hospital stay between both groups. However, most publications of both RALUR and LEVUR have not clearly stated pain medication requirement, cost or cosmetic aspects for us to include in this meta-analysis. Further studies comparing RALUR and LEVUR should focus on these aspects also.

We acknowledge that systematic reviews and meta-analysis like this present some important limitations. The publications in both groups are cohort studies from different centers. Thus, there are no avenues to adequately control for significant confounders, such as reflux grade or laterality in any way. Similarly, there is no standardized reporting system and therefore the comparisons of complications are somewhat challenging to interpret. Thirdly, it is unclear what the surgeon experience is and how that might influence the outcomes. Fourthly, publication bias is an important limitation for any meta-analysis and systematic review. We tried to address these issues. The mean age of both groups was comparable, and there was only minor negative publication bias within both groups. So we are likely seeing the best outcomes, for both the robotic and laparoscopic approaches, as presented in the literature here. This, we think, gives credence to the results reported in this study.

In conclusion, both RALUR and LEVUR seem to be good alternatives to open ureteric reimplantation, with RALUR having lesser success rate and longer operative time compared to LEVUR. With regard to complication rate, there was no significant difference between the two techniques. With improved learning curve, it is likely that RALUR will catch up with LEVUR in terms of success rate also. Reduction in the cost of robotic setup, miniaturization of robotic instruments and standardization of RALUR technique resulting in consistent and improved outcomes are some of the major changes the world may like to see before the robotic approach gets accepted widely.

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Compliance with ethical standards

Conflict of interest None.

Ethical approval Not required.

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