



Robot-assisted laparoscopic versus open ureteral reimplantation for pediatric vesicoureteral reflux: a systematic review and meta-analysis

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Abstract

Objective To compare the efficacy and safety of robot-assisted laparoscopic ureteral reimplantation (RALUR) and open ureteral reimplantation (OUR) in treating primary pediatric vesicoureteral reflux (VUR) based on published literature.

Methods A comprehensive literature search of PubMed, Embase, Cochrane Library, CBM, CNKI and VIP databases was conducted to identify studies comparing the outcomes of RALUR with OUR for treating primary pediatric VUR. The last search was in January 2017. Summarized mean differences (MDs) or odds ratios (ORs) with 95% confidence intervals (CIs) were used to assess the differences in outcomes between RALUR and OUR.

Results A total of six studies containing 7122 children with primary VUR were included in this analysis. Significantly longer operation time was needed for RALUR than OUR (MD 66.69 min, 95% CI 41.71–91.67, $P < 0.00001$), while the RALUR group had significantly fewer days of hospital stay (MD – 17.80 h, 95% CI – 21.18 to – 14.42, $P < 0.00001$) and postoperative Foley placement (MD – 0.32 days, 95% CI – 0.57 to – 0.07, $P = 0.01$). No significant differences were found in estimated blood loss during operation, success rate, complications, and postoperative analgesia usage between the two groups. In subgroup analyses, a significantly higher rate of short-term postoperative complications in RALUR was found compared with OUR (OR 3.17, 95% CI 1.72–5.85, $P = 0.0002$).

Conclusions Our study indicates that compared with OUR, RALUR is also an effective surgical approach for primary pediatric VUR and could help patients return to society more quickly; however, short-term postoperative complications of RALUR should be considered cautiously.

Keywords Meta-analysis · Open ureteral reimplantation · Pediatric vesicoureteral reflux · Robot-assisted laparoscopy ureteral reimplantation · Systematic review

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Introduction

Vesicoureteral reflux (VUR) is a common health problem in pediatric urology, occurring in approximately 1% of children [1]. Impairment of renal function may be caused by VUR through recurrent urinary tract infection and pyelonephritis [2]. Ureteral reimplantation was the initial surgical correction method for pediatric VUR. Laparoscopic approach for VUR was introduced as early as 1993 [3], and robot-assisted laparoscopic approach followed about one decade later [4]. Although open ureteral reimplantation (OUR) is still the gold standard in surgical treatment of pediatric VUR [5, 6], the application of robot-assisted laparoscopic ureteral reimplantation (RALUR) has been growing in popularity [7, 8].

Although OUR offers a high and durable success rate for pediatric VUR [9], less invasive techniques have also been developed to minimize surgical damage. However, the conventional laparoscopic approach failed to achieve a similar success rate compared to OUR [10, 11]. With the development of robotic instrumentation, RALUR was applied in clinical practices and has been proven to relieve postoperative pain, shorten the recovery phase and have a shorter learning curve than the conventional laparoscopic approach [12–14].

With the increased use of RALUR, wide-ranging success rates have been reported [15–18], and the conclusive evaluation of RALUR seemed important. However, few available studies exist that investigated the efficacy of RALUR for treating pediatric VUR compared with traditional OUR, and most of these studies were limited by a small sample of cases based in a single institution. Additionally, both the current European Association of Urology (EAU) and American Urological Association (AUA) guidelines on VUR in children do not recommend RALUR as a routine procedure for surgical correction of pediatric VUR due to a lack of reports and evidence [6, 19]. Therefore, we conducted this systematic review and meta-analysis to assess the efficacy of RALUR for treating primary pediatric VUR compared with OUR, aiming to provide further evidence and guidelines for clinicians.

Materials and methods

The systematic review and meta-analysis were conducted in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) guidelines.

Search strategy

A comprehensive electronic literature search of PubMed, Embase, and Cochrane Library was conducted to obtain studies comparing the outcomes of RALUR and OUR for treating primary pediatric VUR. The search terms used were “‘robot-assisted laparoscopic’ or ‘robotic assisted laparoscopic’”, “‘open’ or ‘open surgery’ or ‘open approach’”, “‘ureteral reimplantation’ or ‘ureteral reimplant’ or ‘UR’”, and “‘vesicoureteral reflux’ or ‘VUR’”. References of all included studies were also checked for potential records. The last search was performed on January 2017, and no language restriction was applied.

Inclusion and exclusion criteria

Comparative studies concerning the efficacies or outcomes of RALUR versus OUR for the surgical correction of primary pediatric VUR were included in this analysis.

Accordingly, convention abstracts, case reports, conference proceedings, reviews or repeated publications were excluded. Literature search and screening, including studies’ quality assessment and data extraction, were performed by two reviewers (TD and BL) independently, and discrepancies were resolved via open discussion.

Study quality assessment and data extraction

Criteria provided by the Oxford Centre for Evidence-based Medicine were applied to assess the level of evidence (LOE) for all included studies [20], and the quality of non-randomized controlled trials (non-RCTs) was also assessed by Newcastle–Ottawa Scale [21]. Literature with an assessment score reaching seven or more stars was considered to be of high quality.

Data of all eligible studies regarding the following factors were extracted: study design, country, period, successful outcome definition, participant information (number, age, VUR grade, follow-up time, and group matched characteristics), operation-related information (operative time, estimated blood loss, and intraoperative complications), and relevant outcomes (length of stay, success rate, postoperative complications, postoperative Foley placement, postoperative analgesia usage, and hospital cost). Mean values with standard deviation (SD) of continuous data were extracted, and event and total numbers of related classified data were also collected. We also contacted the original authors for complete data if necessary.

Study end points and statistics analysis

The aim of this analysis was to compare the outcomes of RALUR with OUR for primary pediatric VUR based on published articles. Thus, surgical outcomes available in original studies were regarded as end points of this analysis, including operative time, length of stay, success rate, intraoperative and postoperative complications, estimated blood loss in surgery, postoperative Foley placement, postoperative analgesia usage, and hospital cost. Additionally, the success of surgical correction was defined as postoperative resolution of VUR by voiding cystourethrogram and absence of postoperative febrile urinary tract infection.

In this analysis, RevMan analytical software package (Version 5.3, Cochrane Collaboration, Oxford, UK) was used to combine the extracted data of eligible studies. Summarized mean differences (MDs) with 95% confidence intervals (CIs) were applied to assess the differences of outcomes for continuous variables between RALUR and OUR. Pooled odds ratios (ORs) with 95% CIs of success and complication rates were calculated to evaluate the efficacy and safety. Heterogeneity of included studies was assessed using the Chi square test-based Q - and I^2 - statistics [22]. If no

heterogeneity was found with $P > 0.10$ in the heterogeneity test, the fixed-effect model was used to calculate the combined MD or OR values. Otherwise, a random-effect model was used. Only a two-sided $P < 0.05$ demonstrated that the results in the analysis were significant. Subgroup analyses were also conducted according to study design (comparative or cohort study), data source (single center or multiple centers), VUR laterality (unilateral or bilateral reimplantation), surgical technique (extravesical or intravesical reimplantation), and follow-up time (≤ 1 or > 1 year). The publication bias of all included studies was assessed by visual inspection of the inverted funnel plot.

Results

Eligible studies and characteristics

Six studies [8, 14, 15, 23–25] containing 7122 children with primary VUR were included in this systematic review and meta-analysis (Fig. 1). The characteristics of eligible studies are listed in Table 1. Included studies were performed

between 2003 and 2014 and published between 2011 and 2016. All studies were conducted in the USA. In six included studies, four were designed as retrospective comparative studies [14, 15, 23, 24], and the remaining two were retrospective cohort studies [8, 25]. In all 7122 patients, 441 received RALUR and 6681 underwent OUR.

Quality assessment of eligible studies

As shown in Table 1, according to the LOE assessment, all included studies were rated Level 3. Under the Newcastle–Ottawa Scale, four studies [14, 15, 23, 24] with scores ≥ 7 stars were considered to be of high quality, and the other two studies [8, 25] scored 6 stars.

Operation time

Five studies [14, 15, 23–25] compared the operation time of RALUR with that of OUR. Meta-analysis by a random-effect model indicated that a longer operation time was needed for RALUR than OUR (MD 66.69 min, 95% CI 41.71–91.67, $P < 0.00001$) (Fig. 2). The results of subgroup analyses for

Fig. 1 Flow diagram of study selection

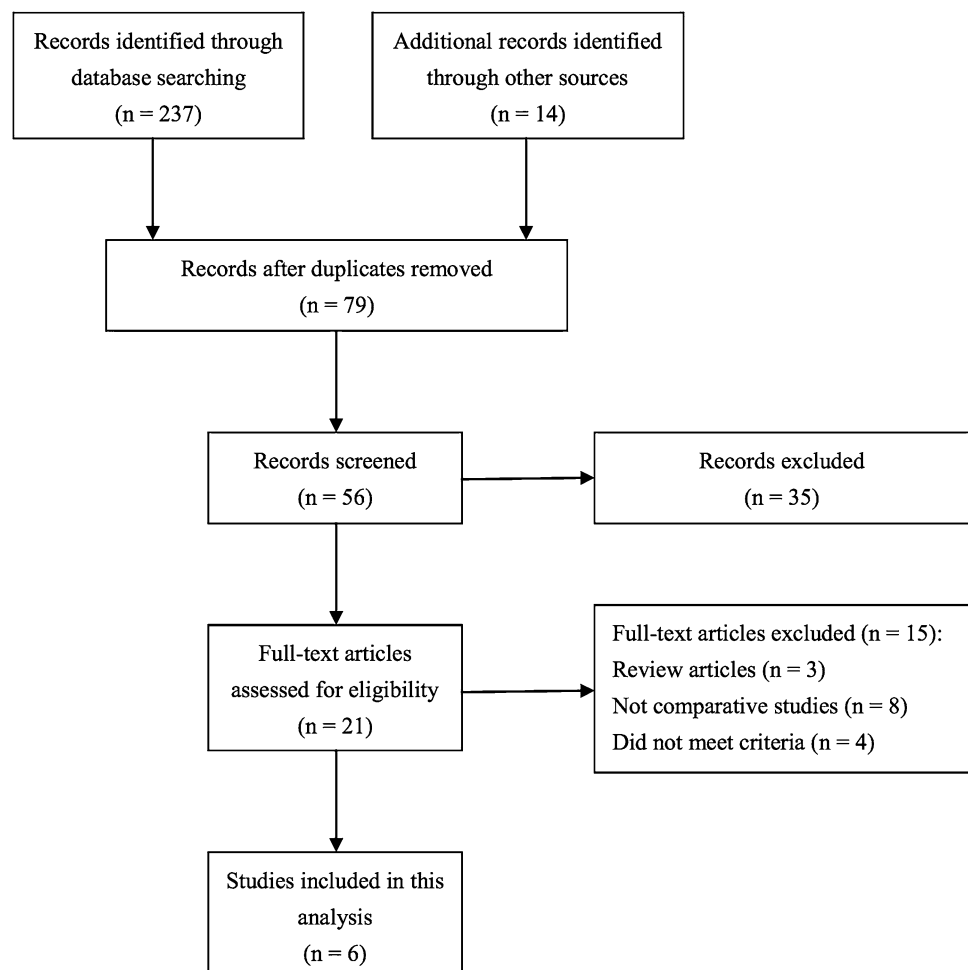


Table 1 The baseline characteristics of included studies

References	Country	Study period	Study design	LOE	Groups	No. of pts	No. of ureters repaired	Mean age (years)	Mean VUR grade	Group matched characteristics	Mean follow-up time (months)	Quality scores
Smith et al. [14]	USA	2006–2009	Retrospective comparative study	3	Robot group	25	33	5.8	3.5	Gender, age, weight, and VUR grade	22.5	*****
Marchini et al. [15]	USA	2007–2010	Retrospective comparative study	3	Open group	25	46	4.2	3.4	Gender, age, weight, and VUR grade	14	*****
Schomburg et al. [23]	USA	2008–2010	Retrospective comparative study	3	Open group	39	66	7.6	NA	Gender, weight, and VUR grade	20	*****
Arlen et al. [24]	USA	2013–2014	Retrospective comparative study	3	Open group	20	26	4.3	3.1	Gender, VUR grade, and renal function	16.6	*****
Bowen et al. [8]	USA	2009 and 2012	Retrospective cohort study	3	Open group	41	41	2.4	2.6	Gender, race, and comorbidity	NA	*****
Kurtz et al. [25]	USA	2003–2013	Retrospective cohort study	3	Open group	5062	NA	4.3	NA	Gender and comorbidity	3	*****
					Open group	1494	4					

Points of Newcastle-Ottawa Scale score, one star means one point
LOE level of evidence, VUR vesicoureteral reflux

operation time are shown in Table 2, and all revealed that significantly longer operation time was needed for RALUR compared with OUR.

Length of stay

The length of hospital stay between RALUR and OUR groups was compared in five studies [8, 14, 15, 23, 24]. Pooled data demonstrated that the RALUR group had a significantly shorter hospital stay time than the OUR group (MD – 17.80 h, 95% CI – 21.18 to – 14.42, $P < 0.00001$) without heterogeneity ($I^2 = 38\%$, $P = 0.15$) (Fig. 3). Table 3 demonstrates the subgroup analyses of length of hospital stay between these two groups, and all results indicated that significantly shorter time of hospital stay was needed by RALUR than OUR.

Success rate

The efficacy of RALUR versus OUR for surgical correction of pediatric VUR was evaluated in four comparative studies [14, 15, 23, 24], of which in all studies the mean follow-up time was longer than 1 year (range 14–22.5 months). The results of the meta-analysis demonstrated that no significant difference was found in the success rate between the two groups (OR 1.13, 95% CI 0.43–2.99, $P = 0.80$) without heterogeneity ($I^2 = 0\%$, $P = 0.85$) (Fig. 4). In subgroup analyses, none of the subgroups indicated a significant difference in the success rate (Table 4).

Postoperative complications

Five studies [14, 15, 23–25] compared the number of complications after RALUR with OUR. Significant heterogeneity ($I^2 = 71\%$, $P = 0.004$) existed, and no significant difference was found between RALUR and OUR in the number of postoperative complications (OR 0.77, 95% CI 0.28–2.15, $P = 0.62$) (Fig. 5). According to the sensitivity analysis, we found statistically significant heterogeneity in the study performed by Kurtz et al. [25], while in the other four studies [14, 15, 23, 24] no heterogeneity ($I^2 = 0\%$, $P = 0.79$) was found.

Kurtz et al. [25] conducted a retrospective cohort study from multiple centers. They found that the rate of postoperative complications in the RALUR group was significantly higher than in the OUR group (OR 3.17, 95% CI 1.72–5.85, $P = 0.0002$) after a 3-month follow-up (Table 5). The four other studies [14, 15, 23, 24] were retrospectively designed in a single center and had a follow-up time longer than 1 year. In this subgroup, no significant difference in the rate of postoperative complications was found between RALUR and OUR (OR 0.50, 95% CI 0.25–1.01, $P = 0.05$) (Table 5).

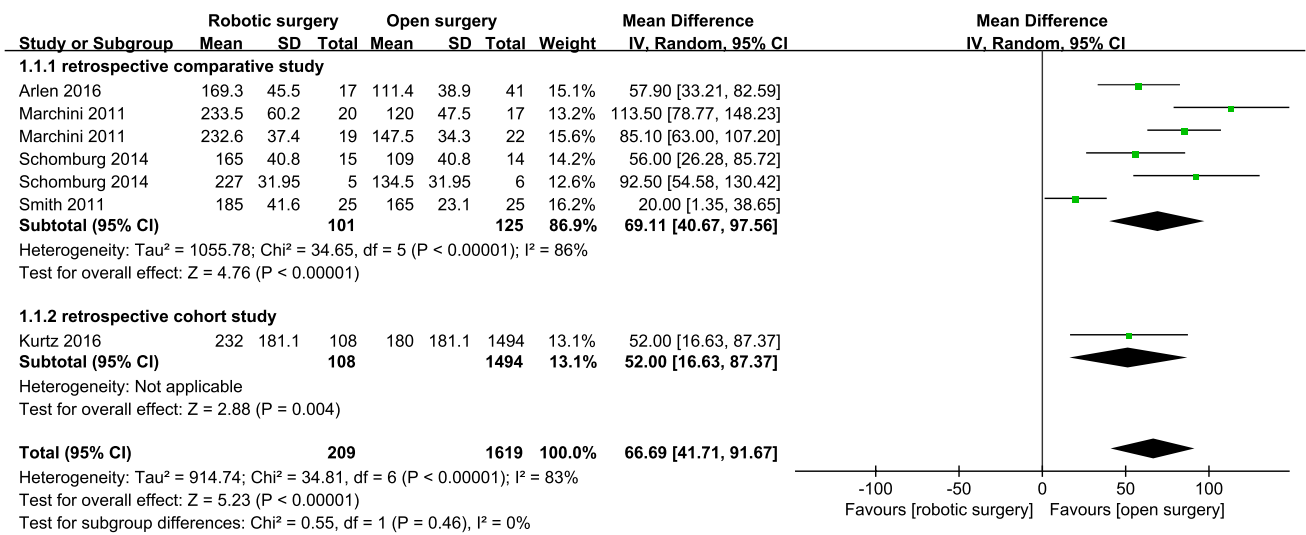


Fig. 2 Forest plot for comparison of the operation time between the RALUR and OUR groups

Table 2 Subgroup analyses for comparison of the operation time between the RALUR and OUR groups

Subgroups	Number of eligible studies	Heterogeneity		Combined results	
		I ² (%)	P	MD (min)	95% CI
Comparative studies	4	86	< 0.00001	69.11	40.67 to 97.56
Cohort studies	1	NA		52.00	16.63 to 87.37
Single center	4	86	< 0.00001	69.11	40.67 to 97.56
Multiple centers	1	NA		52.00	16.63 to 87.37
Unilateral reimplantation	2	57	0.13	42.46	18.27 to 66.65
Bilateral reimplantation	2	76	0.04	64.58	10.19 to 118.97
Extravesical reimplantation	4	86	< 0.0001	65.86	33.00 to 98.72
Intravesical reimplantation	1	NA		85.10	63.00 to 107.20

MD mean difference, CI confidence interval, NA not applicable

The bold numbers mean the P value is < 0.05

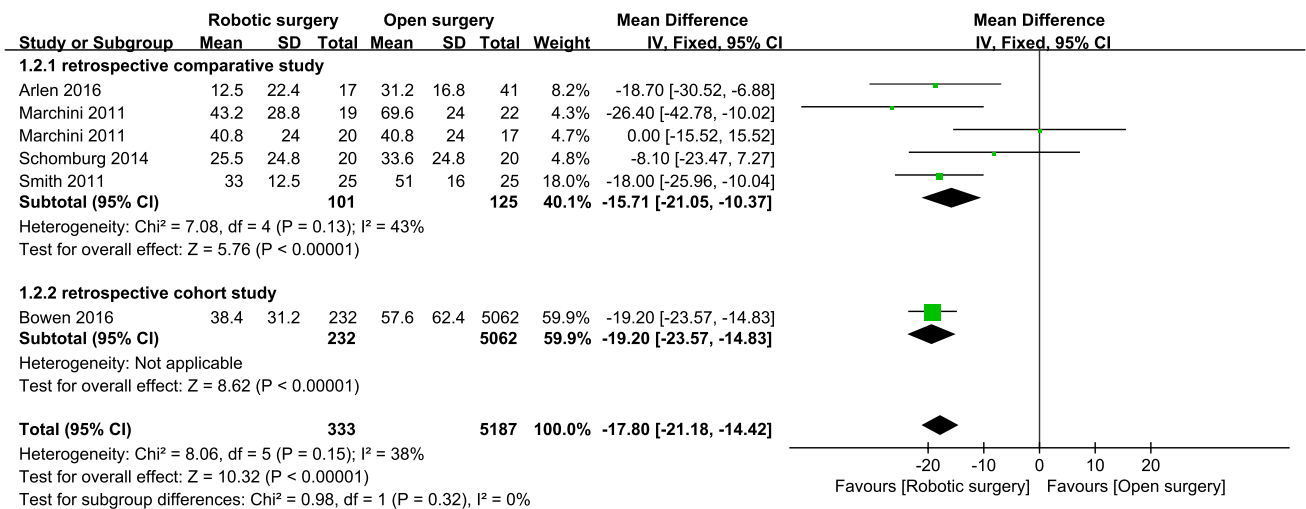


Fig. 3 Forest plot for comparison of the length of hospital stay between the RALUR and OUR groups

Table 3 Subgroup analyses for comparison of the length of hospital stay between the RALUR and OUR groups

Subgroups	Number of eligible studies	Heterogeneity		Combined results	
		I ² (%)	P	MD (h)	95% CI
Comparative studies	4	43	0.13	– 15.71	– 21.05 to – 10.37
Cohort studies	1	NA		– 19.20	– 23.57 to – 14.83
Single center	4	43	0.13	– 15.71	– 21.05 to – 10.37
Multiple centers	1	NA		– 19.20	– 23.57 to – 14.83
Unilateral reimplantation	1	NA		– 23.00	– 37.20 to – 8.80
Bilateral reimplantation	1	NA		– 14.00	– 27.68 to – 0.32
Extravesical reimplantation	4	43	0.15	– 14.44	– 20.09 to – 8.79
Intravesical reimplantation	1	NA		– 26.40	– 42.78 to – 10.02

MD mean difference, CI confidence interval, NA not applicable
The bold numbers mean the P value is < 0.05

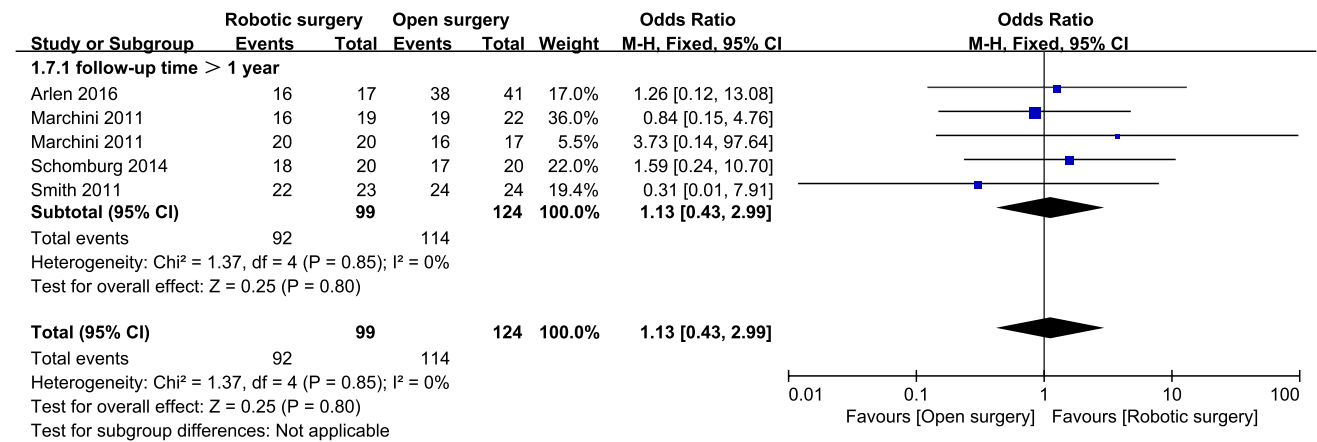


Fig. 4 Forest plot for comparison of success rates between the RALUR and OUR groups

Table 4 Subgroup analyses for comparison of success rates between the RALUR and OUR groups

Subgroups	Number of eligible studies	Heterogeneity		Combined results	
		I ² (%)	P	OR	95% CI
Comparative studies	4	0	0.85	1.13	0.43 to 2.99
Single center	4	0	0.85	1.13	0.43 to 2.99
Follow-up time > 1 year	4	0	0.85	1.13	0.43 to 2.99
Unilateral reimplantation	1	NA		1	1
Bilateral reimplantation	1	NA		0.12	0.00 to 3.17
Extravesical reimplantation	4	0	0.75	1.30	0.40 to 4.21
Intravesical reimplantation	1	NA		0.84	0.15 to 4.76

OR odds ratio, CI confidence interval, NA not applicable

Other comparisons

Intraoperative complications from both groups were recorded in four studies [14, 15, 23, 24]; however, no cases were reported in all studies. In addition, the estimated blood loss, postoperative Foley placement, and postoperative analgesia usage were compared in only two studies. The results of the above comparisons are listed in

Table 6. Significantly shorter days of postoperative Foley placement were found in RALUR than OUR. The hospital cost of RALUR and OUR was also compared in two studies [8, 25], of which both drew a conclusion that the cost of RALUR was significantly higher than that of OUR (median costs: \$32409 vs. \$22703, P < 0.001; median costs: \$9128 vs. \$7273, P = 0.049).

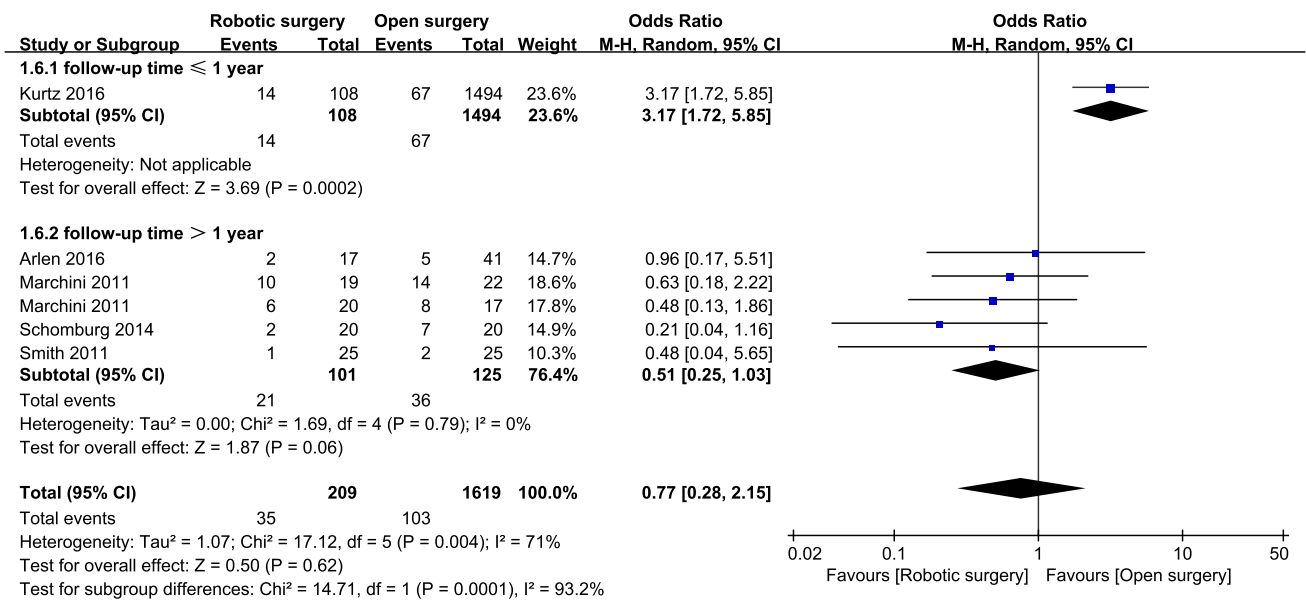


Fig. 5 Forest plot for comparison of postoperative complications between the RALUR and OUR groups

Table 5 Subgroup analyses for comparison of postoperative complications between the RALUR and OUR groups

Subgroups	Number of eligible studies	Heterogeneity		Combined results	
		I ² (%)	P	OR	95% CI
Comparative studies	4	0	0.79	0.50	0.25 to 1.01
Cohort studies	1	NA		3.17	1.72 to 5.85
Single center	4	0	0.79	0.50	0.25 to 1.01
Multiple centers	1	NA		3.17	1.72 to 5.85
Follow-up time ≤ 1 year	1	NA		3.17	1.72 to 5.85
Follow-up time > 1 year	4	0	0.79	0.50	0.25 to 1.01
Extravesical reimplantation	4	0	0.68	0.45	0.19 to 1.05
Intravesical reimplantation	1	NA		0.63	0.18 to 2.22

OR odds ratio, CI confidence interval, NA not applicable

The bold numbers mean the P value is < 0.05

Table 6 Other comparisons between the RALUR and OUR groups

Comparisons	Eligible studies	Heterogeneity		Combined results	
		I ² (%)	P	MD	95% CI
Estimated blood loss	[15] and [23]	54	0.11	− 0.28 ml	− 3.79 to 3.23
Postoperative Foley placement	[15] and [23]	40	0.19	− 0.32 days	− 0.57 to − 0.07
Postoperative analgesia usage	[14] and [23]	90	0.002	− 0.30 mg/kg	− 0.70 to 0.10

MD mean difference, CI confidence interval

The bold numbers mean the P value is < 0.05

Publication bias

Through the inverted funnel plot, no publication bias was detected for all results in this meta-analysis.

Discussion

To the best of our knowledge, this is the first systematic review and meta-analysis comparing the efficacy and safety

of RALUR and OUR for treating primary pediatric VUR. A total of six studies containing 7122 patients were included in this analysis. Our results indicated that patients receiving RALUR had a significantly longer operation time as well as shorter days of hospital stay and postoperative Foley placement than those receiving OUR. In addition, no significant differences were found in the estimated blood loss during operation, success rate, intraoperative and postoperative complications, and postoperative analgesia usage between the two groups. However, subgroup analyses in our study revealed that RALUR could induce more short-term postoperative complications. Therefore, compared with OUR, RALUR may also be considered as an effective surgical approach for primary pediatric VUR and could help patients shorten the time spent in the hospital to return to society more quickly; however, short-term postoperative complications of RALUR should be carefully considered.

Consistent with previous reports [14, 23, 24], our results indicated that RALUR was associated with longer operation time compared with OUR. It is reasonable and understandable that a surgical approach requiring dismembering and/or tapering lasts longer. Smith et al. [14] demonstrated that the operation time of RALUR was significantly longer, while the total operating room time did not demonstrate any differences. Schomburg et al. [23] also indicated that the bilateral procedure required a nearly twofold robotic console time than the unilateral procedure. Therefore, it is suggested that the bulk of time difference mainly resulted from the time in the operation itself and could not be attributed solely to robot setup time. Nevertheless, it has been shown that surgeons with adequate surgical experiences are more familiar with the RALUR technique, and thus less operation time is needed with increased robotic experience [26].

In this analysis, we found that RALUR was associated with shorter hospital stay and postoperative Foley placement than OUR. It is not surprising that as a minimally invasive approach, RALUR could accelerate the recovery of patients compared with an open approach. Postoperative analgesia usage of patients was compared in two studies [14, 23], and although the pooled results showed no significant difference, less analgesic usage in the RALUR group was reported in both studies. Therefore, a positive result in postoperative analgesia usage is also expected if the number of eligible studies is sufficient.

OUR has long been the gold standard of surgical correction for pediatric VUR with high success rates [27]. Our results showed that the success rate of RALUR was as high as that of OUR on the basis of a one-year follow-up. Four included studies in our analysis reported success rates of RALUR and OUR with a mean follow-up time ranging from 14 to 22.5 months, and the average success rates of the two groups were nearly identical (92.9% for RALUR and 91.9% for OUR). Herz et al. [28] also

discovered a success rate of 85.2% for RALUR in a cohort with 54 children. Gundeti et al. [29] performed extravesical RALUR in 58 children and achieved a success rate of 87%. However, it is worth noting that some studies also reported wide-ranging success rates for RALUR [16–18]. Since no comparisons were conducted with open surgery, these studies were not eligible for our meta-analysis. As a result, although no significant difference in success rates between the two operation methods was found in our meta-analysis, the potentially unstable success rate of RALUR should also be considered.

Regarding postoperative complications, our results indicated that no significant difference existed between RALUR and OUR groups. Kurtz et al. [25] compared the 90-day complications between RALUR and OUR in a nationwide cohort of pediatric VUR patients, and they found that RALUR caused a significantly higher rate of 90-day complications than OUR. Although only one study compared the short-term postoperative complications between RALUR and OUR [25], the analyzed data were from multiple centers containing more than 1500 patients. Therefore, we should also focus on the short-term postoperative complications of RALUR. Furthermore, when the follow-up time was extended, the complication rate of RALUR was lower than half of that of OUR, with a P value of 0.05 in our analysis. In other words, although no significant difference has been identified yet, a significantly lower rate of postoperative complications in RALUR compared to OUR might be achieved if more eligible studies are included. Similar to our results, several previous studies also reported low complication rates of RALUR, ranging from 0 to 11% [16, 28–30]. Overall, RALUR has the advantage of fewer long-term postoperative complications compared with OUR.

In addition to the different operation methods, patients' age and VUR grade could also impact the outcomes of VUR patients. Among the six included studies, the age of patients was similar, and there was no significant difference between RALUR and OUR groups in the two studies [14, 15], while significantly older age for the RALUR group was observed in the other four studies [8, 23–25] ($P < 0.05$). Additionally, Bowen et al. [8] revealed that age was an independent factor associated with the use of RALUR vs OUR (OR 1.12, 95% CI 1.02–1.08, $P < 0.0001$). Differences in age may lead to different features of VUR and certainly cause disparate outcomes after operations. Unfortunately, the original studies did not conduct stratified analyses based on a similar age of pediatric patients, and so related subgroup analyses were unable to be performed in our meta-analysis. Therefore, older patient age in RALUR group should be regarded as an important confounding factor. Regarding the VUR grade, since no significant differences existed between the RALUR and OUR groups in all included studies, it did not affect the outcomes of the two operation methods in this study.

Several limitations should be addressed regarding this analysis. First, all studies included were retrospective, and most were conducted in a single center, which could lead to some potential biases in the results, such as selective and detective biases. No RCTs on this topic were conducted or published as of yet, and further high-quality multicenter RCTs are necessary to confirm our results. Second, all included studies were conducted in the USA, which will likely influence the applicability of our results to other countries. Third, the number of eligible studies for some comparisons, including the estimated blood loss, postoperative Foley placement and postoperative analgesia usage, was relatively small. In addition, due to a lack of related stratified analyses in original studies, we could not perform the subgroup analyses according to some important factors, including age, VUR grade, detailed surgical technique, and single or duplicated systems, which may affect the outcomes and prognoses of pediatric VUR patients.

Conclusion

Our meta-analysis indicated that patients receiving RALUR had a significantly longer operation time, but fewer days of hospital stay and shorter postoperative Foley placement than those receiving OUR. No significant differences existed in the estimated blood loss during operation, success rate, intraoperative and postoperative complications, and postoperative analgesia usage between RALUR and OUR. Subgroup analyses in our study demonstrated that RALUR induced more short-term postoperative complications than OUR. Therefore, compared with OUR, RALUR should be considered as an effective surgical approach for primary pediatric VUR, since it has a similar success rate and could help patients shorten the time spent in the hospital to return to society sooner. However, pediatric urologists should pay more attention to the short-term postoperative complications of RALUR, and further high-quality multicenter RCTs are still needed to confirm our results.

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Author contributions TD: project development, data collection, data analysis, and manuscript writing; BL: data collection, data analysis, and manuscript writing; LL: data collection and manuscript writing; XD: data collection; CC: data analysis; ZZ: manuscript editing; WZ: manuscript editing; WW: manuscript editing; GZ: project development and manuscript editing.

Compliance with ethical standards

Ethical approval No ethical approval was necessary due to its exclusive use of secondary data.

Conflict of interest The authors declare that they have no conflicts of interest.

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