Comparison of the Safety and Efficacy between Transperitoneal and Retroperitoneal Approach of Laparoscopic Ureterolithotomy for the Treatment of Large (>10mm) and Proximal Ureteral Stones: A Systematic Review and Meta-analysis

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Purpose: We aimed to compare the safety and efficacy between laparoscopic transperitoneal ureterolithotomy (LTU) and laparoscopic retroperitoneal ureterolithotomy (LRU) in the treatment of large (>10mm) and proximal ureteral stones.

Materials and Methods: Electronic databases, including PubMed, EMBASE, Cochrane Library, Web of Science, and Scopus were searched through December 2019. Comparative studies comparing the two approaches were included. The primary outcome was a single-procedure success rate; the secondary outcomes included operative time, hospital duration, and complications (according to the Clavien-Dindo Grade). Newcastle–Ottawa scale (NOS) and the modified Jadad scale were used to evaluate the quality of the included studies. The Egger's test estimated publication bias. The meta-analysis was performed by Review Manager 5.3 and STATA 15.0.

Results: Seven studies, involving 125 participants in LTU group and 128 in LRU group, were included in the study. The results suggested that both single-procedure success rate and the rate of postoperative paralytic ileus were significantly higher in the LTU group than in the LRU group (95.2% vs 87.5%, 95% CI: .00-.16, RD = .08, *P* = .04; 10.4% vs 0, 95% CI: .02- .19, RD = .10, *P* = .02, respectively). No publication bias of the primary outcome was observed with the Egger's test (*P* = .117). No significant differences were noted in terms of operative time and hospital duration (95% CI: -18.95-8.80, MD = -5.08, *P* = .47; 95% CI: -.98- .58, MD = -.20, *P* = .61, respectively). Additionally, according to Clavien-Dindo Grade, the rates of major complications (>= Grade 3a) including open conversion (.8% vs 5.5%, 95%CI: -.11- .01, RD = -.05, *P* = .12), stone migration (8.1% vs 6.7%, 95% CI: -.08- .11, RD = .02, *P* = .76), vascular injury (5.4% vs 0, 95%CI: -.03- .14, RD = .05, *P* = .21) and ureteral stricture (1.3% vs 5.3%, 95% CI: -.11- .02, RD = -.04, *P* = .20), were comparable between the two groups.

Conclusion: In the treatment of large and proximal ureteral calculi, LTU has a significantly higher single-procedure success rate and a higher rate of postoperative paralytic ileus than LRU. However, the complication was well-tolerated. The small sample size and limited, including studies, were the main limitations.

Keywords: laparoscopy; meta-analysis; retroperitoneal; transperitoneal; ureterolithiasis; ureterolithotomy

INTRODUCTION

The treatment of large proximal ureteral stones is complicated.[1] Although ureterorenoscopy (URS) and extracorporeal shockwave lithotripsy (SWL) are the most common procedures, however, multiple sessions are required.[2] This drawback promotes the usage of laparoscopic ureterolithotomy (LU) due to its high stone-free rate (SFR). Traditionally, LU was realized through the retroperitoneal approach. As laparoscopic retroperitoneal ureterolithotomy (LRU) is at risk of stone migration to the kidney, the new method of laparoscopic transperitoneal ureterolithotomy (LTU) is attempted[3]. However, different opinions have emerged during the exploration of these two approaches. LTU is recommended to the less-experienced surgeons by Abat et al.[4] for its broader operation field and familiar anatomy. However, another study reported that LTU and LRU were comparable in terms of efficiency and safety and surgeons could perform the procedure dependent on personal preference.[5] Due to such controversy, A comprehensive study of this issue was needed. Thus, we conducted a meta-analysis with an attempt to understand these two approaches comprehensively.

MATERIALS AND METHODS

This meta-analysis was performed based on the guidelines outlined in the Preferred Reporting Items for Systematic Reviews and Meta-analysis (PRISMA) statement.[6]

Search strategy

We conducted a systematic search of electronic databases, including PubMed, EMBASE, Cochrane Library, Web of Science, and Scopus (through December 2019) to identify all relevant studies. The search strategy was combining with following terms without language restriction: ('laparoscopic ureterolithotomy' OR 'LU') AND ('proximal' OR 'upper') AND ('ureteral stone' OR 'ureteral stones' OR 'ureteral calculi' OR 'ureteral calculus' OR 'ureteral lithiasis'). And references of included studies were manually identified for relevant records. The titles and abstracts of identified studies were independently screened by two reviewers

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Table 1. Characteristics and quality evaluation of including studies.

Study ID	Preop-imaging	Postop-imaging	Country	Study Period	Study Type	Stone Characteristics	No. Surgeon(s)	Surgical Experience	F/u (mon)	Quality Score
Abat 2016	KUB, US IVU, NCCT	NA	Turkey	Nov. 2011 to Mar. 2013	Retro-	Proximal	2	Limited	14.84 ± 7.46/ 35.56 ± 9.11	6
Almeida 2009	KUB, US IVU, CT	KUB	Brazil	Jan. 2004 to Nov. 2007	Pro-	Large(>10mm), proximal	1	Limited	1	8
Pierluigi 2009	US, IVU CT	NA	Italy	2004 to 2006	Pro-	Large(>10mm), proximal, impacted	2	Limited	12	8
Khalil 2015	CT	NA	Egypt	Jan. 2012 to Sep. 2013	RCT	Large(>15mm), proximal, impacted	NA	NA	12	8
Wisoot 2010	KUB	NA	Thailand	Jul. 1997 to Dec. 2007	Retro-	Large(>15mm), impacted	3	NA	18	7
Vishwajeet 2013	KUB, US IVU	KUB, IVU US	India	Jan. 2009 to May 2012	RCT	Proximal	1	NA	14/15	5a
Chiu 2015	NA	NA	China	Dec. 2009 to Sep. 2014	Retro-	Large(>15mm), proximal, impacted	1	Experienced	3	8

Abbreviations: Preop- imaging, preoperative imaging examinations; postop- imaging, postoperative imaging examinations; KUB, Kidney; Ureter; and Bladder X-ray; US, ultrasound; IVU, intravenous urogram; NCCT, non-contrast computed tomography; NA, not available; retro-, retrospective comparative study; pro-, prospective comparative study; F/u, follow up.
a Quality evaluated by the modified Jadad scale, the others were evaluated by NOS.

(Hualin and Han) following deduplication. Then, full texts or conference abstracts were obtained for further identification of their eligibility.

Inclusion and Exclusion Criteria

The including trials met the following requirements:
1) Study types: randomized controlled trials (RCTs) and non-randomized comparative studies.
2) Patients with large (>10mm) and proximal ureteral calculi.
3) Comparison between LTU and LRU.
4) Report on the primary outcome and at least one of the secondary outcome measures mentioned below.
5)Reviews, animal studies, case reports, and non-comparative studies were excluded.

Data extraction and outcome measures

Two reviewers (Hualin, Han) extracted data from including literature independently, including baseline characteristics and data of outcome measures. 1) baseline characteristics included first author, time of publication, country, recruitment duration, study design, stone characteristics, number of surgeon(s) and patients, gender proportion, body mass index (BMI) and average age, stone size, and laterality. 2) Outcome measures were single-procedure success rate (defined below), operative time, length of hospital duration, and complications.
The primary outcome was a single-procedure success rate. It was defined as reaching stone-free status at a single-one procedure without an open conversion re-

Table 2. Demographic and baseline characteristics of included patients.

Study ID	Sample Size(n)	Age (years)	BMI (kg/m^2)	Stone Size(mm)	Stone Side(R:L)	Gender (M:F)	Single-procedure Success Rate	Operative Time(mins)	Hospital Duration(days)
Abat 2016	25/25	38.96±17.01/ 47.8±14.1	NA	16.62±4.78/ 20.12±5.18	6:19/ 11:14	6:19/ 15:10	21/20	147±36.54/ 106.4±38	2.94±1.69/ 7.12±4.47
Almeida 2009	15/19	43.2±16.7/ 43.8±15.7	NA	12.5±2.6/ 13.6±3.8	10:6/ 8:10	8:7/ 12:7	15/15	100(70-180)/ 105(90-120)	3(2-3)/ 2(2-3)
Pierluigi 2009	18/17	42(25-60)/ 40(28-61)	22.3(20.6-35.7)/ 21.6(20.2-31.8)	23(15-45)/ 22(13-35)	NA	NA	17/17	68(48-130)/ 103(69-147)	4(2-7)/ 5(2-10)
Khalil 2015	13/11	37.6±13.2/ 44.6±7.9	25.9±2.8/ 28.09±4.4	15.5±3.7/ 15.8±3.02	5:8/ 5:6	9:4/ 8:3	13/7	116.2±21.8/ 137.3±17.9	5.4±1.2/ 5±0.8
Wisoot 2010	11/28 44.2	42.1/	NA	17.8/ 18.2	NA	NA	11/27	128.3(75-180)/ 125.9(75-270)	8.8/ 4.1
Vishwajeet 2013	24/24	37.75±10.61/ 39.16±11.49	NA	18±3.6/ 17±3.8	14:10/ 8:16	14:10/ 13:11	23/22	83.12±8.3/ 84.1±6.4	3.125±0.74/ 2.67±0.63
Chiu 2015	19/4	54.47±10.75/ 51.5±17.91	25.31±2.82/ 28.2±4.19	20.2±6.4/ 18±2.2	NA	15:4/ 3:1	19/4	102.3±33.9/ 111.25±8.3	5±1.76/ 5.25±1.26

Data was presented as "LTU/LRU"
Abbreviations: R, right; L, left; M, male; F, female; NA, not available.

Table 3. Intra- or postoperative complications classified by the modified Clavien-Dindo Grade (*P* value was calculated by using MH test).

Grade	No. Complications (%)		*P* Value
	LTU	LRU	
Grade 1	8 (6.4%)	9 (7.03%)	
Prolonged drainage Retroperitoneal hematoma	6 (4.8%)	2 (1.6%)	7 (5.47%)
	2 (1.56%)	.95	.74
Grade 2	22 (17.6%)	13 (10.16%)	
UTI	12 (9.6%)	12 (9.38%)	.87
Transfusion	3 (2.4%)	1 (.78%)	.49
Paralytic ileus	7 (5.6%)	0	.02
Grade 3a	-	-	
Grade 3b	10 (8%)	16 (12.5%)	
Open conversion	1 (.8%)	7 (5.47%)	.12
Stone migration	5 (4%)	4 (3.13%)	.76
Vascular injury	3 (2.4%)	0	.21
Ureteral stricture	1 (.8%)	5 (3.91%)	.20
Grade 4a	1 (.8%)	0	
Pulmonary embolus	1 (.8%)	0	.45
Total complications	41 (32.8%)	39 (30.47%)	

quirement or auxiliary procedures requirement due to stone migration. Secondary outcomes included length of hospital stay, operative time, minor and complications. Complications were classified according to the Clavien-Dindo Grade.[7] Additionally, complications of more than Grade 3a were regarded as major ones. Prolonged drainage was defined as urine leakage requiring drainage for more than 72 hours.[4,5,8,9] And paralytic ileus was defined as the absence of bowel sound lasting for over 36 hours.[2,4,8]

Any disagreements were resolved by discussion or consultation with a third reviewer (Gang).

Evaluation of study quality

Comparative studies included RCTs and non-randomized comparative studies. The modified Jadad scale was used to assess the methodological qualities of RCTs, while, Newcastle–Ottawa scale (NOS) was used for non-randomized comparative studies. The results were listed in **Table 1**.

Statistical analysis

The risk difference (RD) was used for dichotomous variables, while the mean difference (MD) was used for continuous ones. Forest plots were used to present the results of our meta-analysis. The Z test determined all the pooled effects, and $p < 0.05$ was considered statistically significant. *P* values of dichotomous and continuous variables were calculated by Mantel–Haenszel (MH) test and Inverse-Variance (IV) weighting, respectively. Chi square-based Q test and I^2 tests were used to assess the quantity of heterogeneity among these studies. When I2 < 50 %, $p > 0.1$, the pieces of evidence

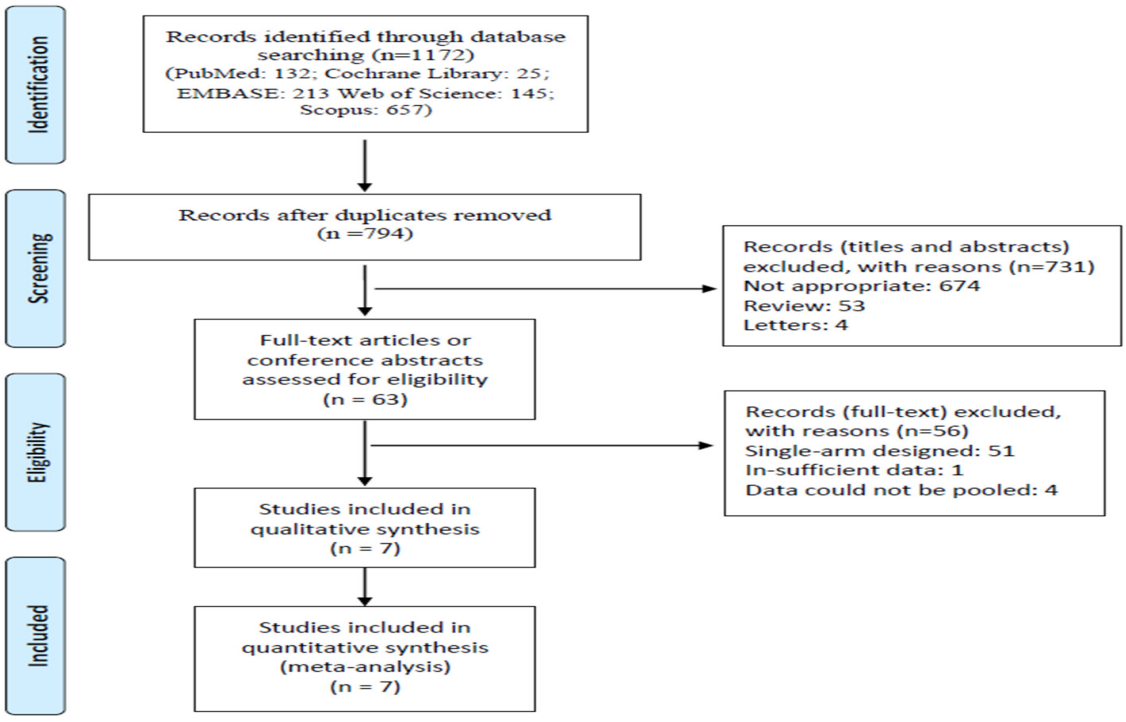

Figure 1. Flow diagram of included studies.

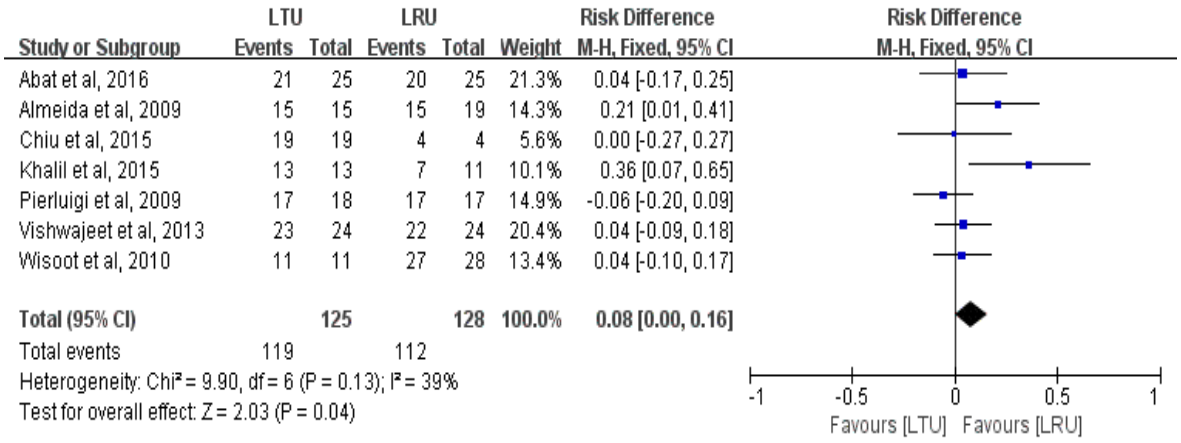

Figure 2. Forest plot of comparison: single-one procedure success rate.

were thought to be acceptable heterogeneity, we used the fixed-effects model. Otherwise, the random-effects model was applied. Publication bias was evaluated with the Egger's regression asymmetry test. Review Manager 5.3 (Cochrane Collaboration, Oxford, UK) was used to analyze the aggregate data. STATA 15.0 (College Station, Texas, USA) was used to identify publication bias and generate Eggers plot.

RESULTS

Search process and study characteristics

The systematic search identified 1172 relevant studies. After further screening, seven studies (2 RCTs and five non-randomized comparative studies),[2,4,5,8-11] involving 125 participants in LTU group and 128 in LRU group, satisfied our inclusion criteria. The process of study identification is detailed in Figure 1. Except for one conference abstract,[11] the full texts of the left six studies were obtained. Overall, the quality of non-randomized comparative studies was very high, with only one study[4] having a NOS of 6, and two RCTs[8,10] had a modified Jadad scale of 5. The characteristics of included studies were listed in **Table 1**. Demographic and baseline characteristics of enrolled patients were presented in **Table 2**.

Primary outcomes

Single-procedure success rate

Patients in LTU group had significantly higher single-procedure success rate than those in LRU group (95.2% vs 87.5%, 95% CI: .00-.16, RD = .08, *P* = .04, **Figure 2**). For the primary outcome, the publication bias was not observed with the Egger's test (*P* = .117; **Figure 3**).

Secondary outcomes

According to the Clavien-Dindo Grade, complications were listed in Table 3. No significant differences were observed in terms of operative time (95% CI: -18.95-8.80, MD = -5.08, *P* = .47, Figure 4) and length of hospital stay (95% CI: -.98- .58, MD = -.20, *P* = .61, Figure 4). However, significant heterogeneity was reported (I^2 = 87%, I^2 = 90%, respectively, Figure 4). Additionally, according to the Clavien-Dindo Grade, major complications between two groups were similar in terms of open conversion (.8% vs 5.5%, 95%CI: -.11- .01, RD = -.05, P = .12, Figure 5), stone migration (8.1% vs 6.7%, 95% CI: -.08- .11, RD = .02, *P* = .76, Figure 5), vascular injury (5.4% vs 0, 95%CI: -.03- .14, RD = .05, *P* = .21, Figure 5) and ureteral stricture (1.3% vs 5.3%, 95%

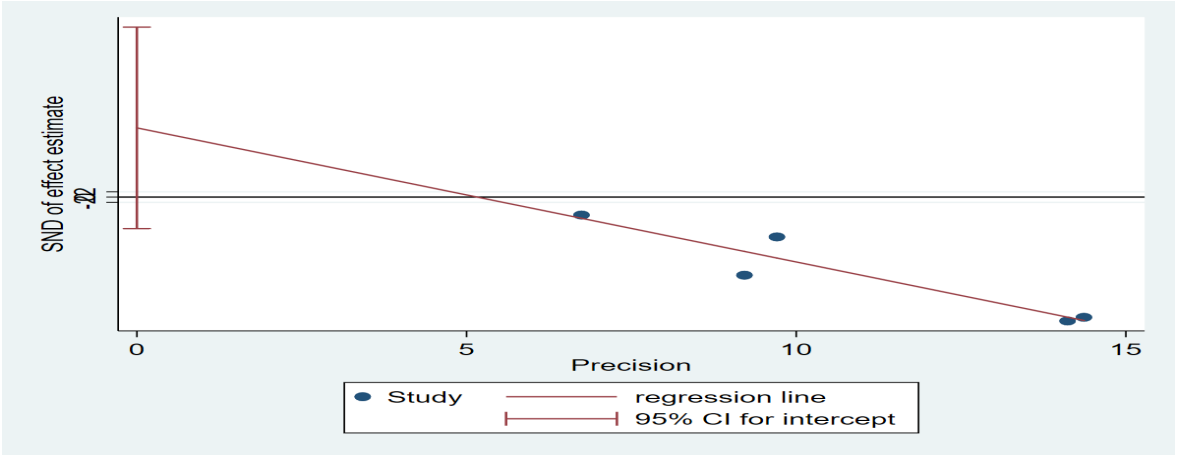

Figure 3. Eggers plot for the single-one procedure success rate.

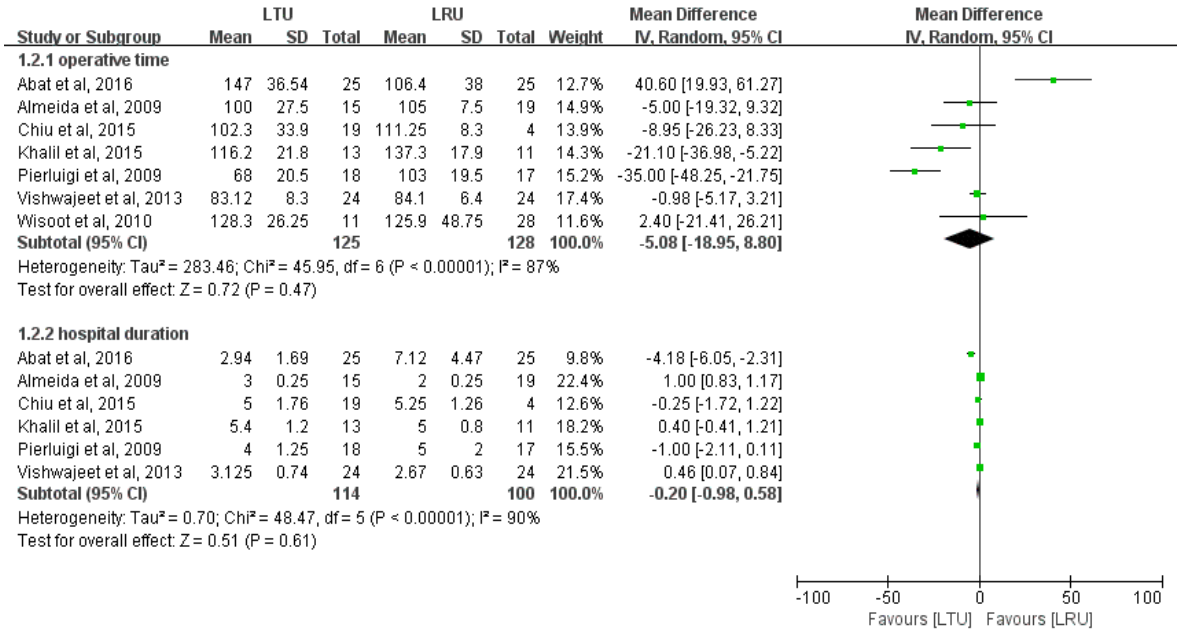

Figure 4. Forest plot of comparison: operative time and hospital duration.

CI: -.11- .02, RD = -.04, *P* = .20, **Figure 5**). One case in LTU group with Grade 4a complication (pulmonary embolus) was recorded in the study by Abat et al.[4] The patient was admitted to intensive care unit (ICU) for further treatment. Considering minor complications, except for paralytic ileus of which the morbidity was significantly higher in LTU group (10.4% vs 0, 95% CI: .02- .19, RD = .10, *P* = .02, **Figure 6**), no statistical differences were noted between two groups in terms of urinary tract infection (UTI) (21.8% vs 23.1%, 95% CI: -.17- .14, RD = -.01, *P* = .87, **Figure 6**), transfusion (4.2% vs 1.4%, 95% CI: -.04- .09, RD = .02, *P* = .49,

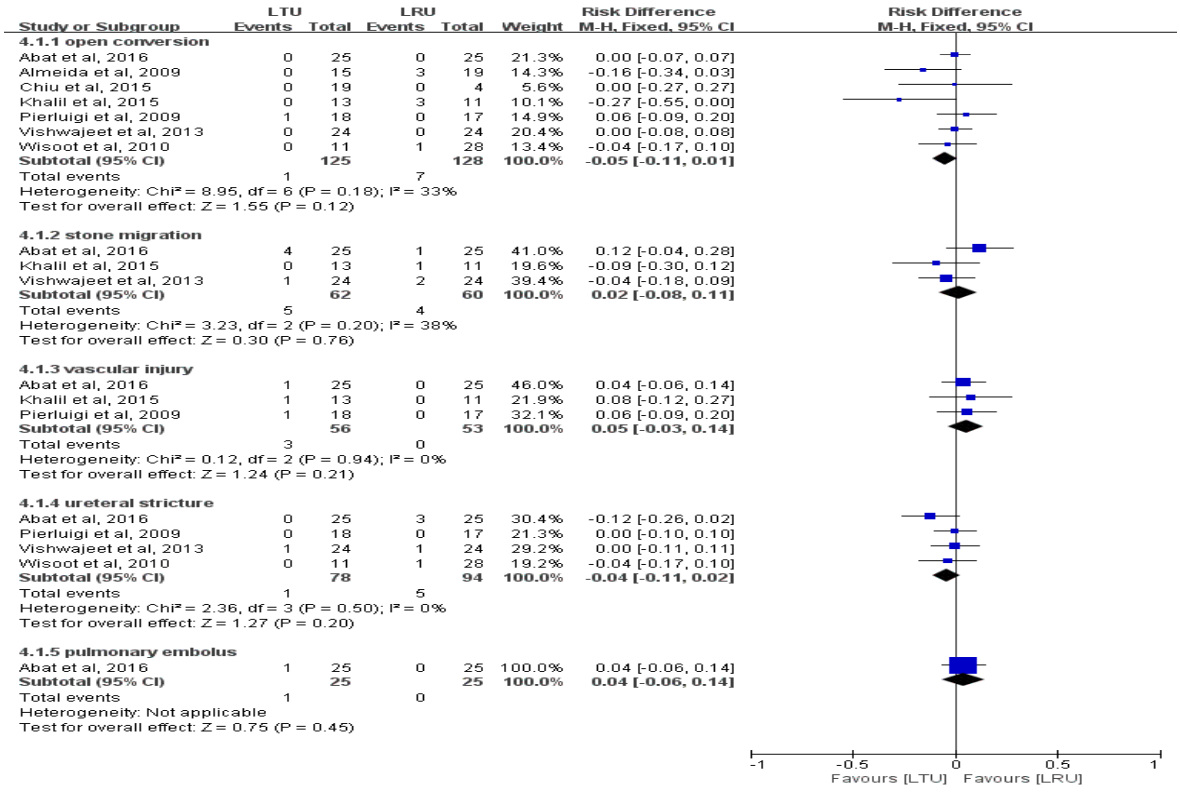

Figure 5. Forest plot of comparison: major complications.

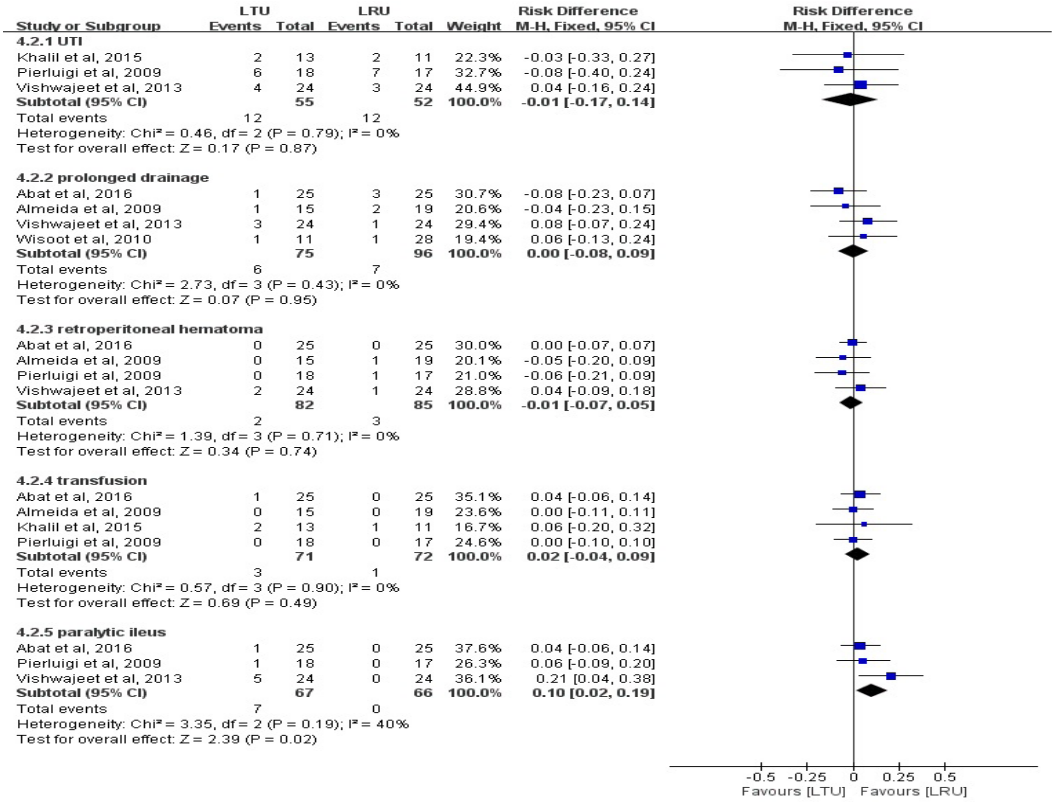

Figure 6. Forest plot of comparison: minor complications.

Figure 6), prolonged drainage (8% vs 7.3%, 95% CI: -.08- .09, RD = .00, *P* = .95, Figure 6), and retroperitoneal hematoma (2.4% vs 3.5%, 95% CI: -.07- .05, RD = -.01, *P* = .74, **Figure 6**).

DISCUSSION

For large(>10mm) and proximal ureteral stones, LU shows significantly higher SFR than URS.[8] It is still unclear which approach, transperitoneal or retro-peritoneal, is better in terms of efficacy and safety. Our results revealed that patients in the LTU group had a significantly higher single-procedure success rate than those in the LRU group. They suffered from a substantially higher proportion of postoperative paralytic ileus. However, it had to be admitted that the overall sample size and number of included studies were small, which was the main drawback of the study. Thus, theoretical significance may be clinically insignificant.

The significantly higher single-procedure success rate in LTU group may be explained by the advantages of transperitoneal approach and drawbacks of retro-peritoneal approach, as well as open conversion rate. As we know, LTU owns advantages including a wider operating field, clear anatomical landmarks, and easy identification of the ureter. Contrarily, LRU has drawbacks including limited working space, lacking anatomic landmarks, and difficulty in suturing the ureter. Moreover, periureteral inflammatory adhesions because of long impaction time by large stones could contribute to relatively difficult identification of ureter in retroperitoneal approach.[8,10] Thus, open conversion rate was relatively higher in the LRU group (5.5% VS 0.8%) due to these drawbacks, although the difference was not significant. Moreover, Şahin et al[12] also reported one case in the LRU group who was converted to open surgery. With respect to postoperative complications, the rate of paralytic ileus was significantly higher in the LTU group. Surprisingly, only patients who had received LTU suffered from the complication.[2,4,8] The result was consistent with that of the study of Şahin et al.[12] Moreover, Khalil et al[10] described in their report that the average time to oral intake was significantly longer in the LTU group than in the LRU group (15.5 ± 2.8h VS 21.2 ± 4.9h, *P* = .002). This could be explained by the fact that LTU has disadvantages including intestine mobilization, peritoneal contamination with blood or urine leakage, and dissection or retraction of viscera. In LRU, lost blood does not come into the bowel and urine leakage would be contained within the retroperitoneal space and for cases with previous abdominal surgery, bowel injury could be prevented.[4] However, the complication was well-tolerated, and did not need surgical intervention.

It seemed that vascular injury only developed in the LTU group (**Table 3**). The outcome, however, revealed no significant difference between the two groups. In fact, patients in the LRU group still could suffer from the complication.[12] Among patients with vascular injury, two suffered from inferior vena cava injuries, who were managed by laparoscopy and open access,[2,4] respectively. Of note, surgeons in each study had limited laparoscopic experience. They just completed a laparoscopic training programme or were during their learning curve in laparoscopy. Besides, Pierluigi et al[2] reported 10 cases in the LRU group who developed peritoneal tearing when the surgeon tied to make pneumoperito-

neum, resulting in prolonged operative time. We also noticed that the outcomes of operative time and hospital duration revealed significant heterogeneity (I^2 = 87%, I^2 = 90%, respectively, **Figure 4**). The experience of the surgeon, which differed in studies included, may explain it. Because a surgeon who has initial experience in laparoscopy is unfamiliar with surgical procedures and the anatomy around ureter, resulting in being slow, and careful and needing more dissection and a prolonged operative time which causes an increase postoperative pain and dose of analgesic prescribed. Therefore, longer hospital stay is required due to pain management.[10] In brief, it was noteworthy that experience in laparoscopy mattered with respect to operative time and hospital stay, as well as morbidity of complications.

Three included studies reported their experience in the management of migrated stones.[4,8,10] URS, percutaneous nephrolithotomy (PCNL) and LU were adopted and these patients achieved complete SFR. Totally 5 stone migrations were reported in the study by Şahin et al[12] and were managed by SWL and ureteroscope successfully. For migrated stones, a combination of LU with endourologic lithotripsy through the laparoscopic ports (URS) may be better for that URS needs no laparoscopic ports[13], indicating that no more puncture was needed.

In this study, the incidences of prolonged drainage and ureteral stricture were similar between two groups. Some urologists believed that ureteral stent placement following LU could prevent urine leakage and stricture, while others opposed the opinion because stenting may add cost and discomfort to the patient.[8] One meta-analysis[14] in 2017 concluded that no significant difference was found in the rate of prolonged drainage between stented and stentless LU. However, ureteral stricture was not pooled in the analysis due to limited data. Future studies are needed to address this topic. Other minor complications including UTI and retroperitoneal hematoma were well-tolerated and were managed with conservative treatment. Although blood transfusion was needed for some cases, the overall rate (2.8%) was low. Overall, both two approaches were safe and efficient in the management of large and proximal ureteral stones. Interestingly, Nouralizadeh et al.[13] reported their experience in synchronous or metachronous bilateral laparoscopic stone surgery and the result revealed that this procedure was feasible for laparoscopic expertise. O'Kelly and colleagues[15] found that LU was safe in the management of partial duplex ureteric collecting system.

Even though this is the first meta-analysis to evaluate the efficacy and safety of two approaches in the management of large and proximal ureteral calculi, some limitations should be clarified. Firstly, the number of included studies and the sample sizes was relatively small. Secondly, the number and experience of surgeons varied among these studies, in addition to different study designs, contributing to certain biases. Thirdly, subgroup analysis was not applied due to limited data.

CONCLUSIONS

LTU has a significantly higher single-procedure success rate and paralytic ileus rate than LRU, but the complication is well-tolerated.

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CONFLICTS OF INTEREST

The authors report no conflicts of interest.

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