



Systematic review and cumulative analysis of the managements for proximal impacted ureteral stones

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Abstract

Purpose To compare the efficacy and safety of different treatment options for the management of proximal impacted ureteral stones (PIUS).

Methods A systematic literature search using Pubmed, Medline, Embase and Cochrane Library was conducted to obtain studies concerning different managements for PIUS up to Jan 2018. Summary odds ratios (ORs), standard mean differences (SMDs) or weighted mean differences with their 95% confidence intervals (CIs) were calculated to compare the efficacy and safety of all included treatment methods, registered in PROSPERO under number CRD42018092745.

Results A total of 15 comparative studies with 1780 patients were included. Meta-analyses of final stone-free rate (SFR) favored percutaneous nephrolithotomy (PCNL) over ureteroscopic lithotripsy (URL) (OR 10.35; 95% CI 5.26–20.35; $P < 0.00001$), laparoscopic ureterolithotomy over URL (OR 0.11; 95% CI 0.05–0.25; $P < 0.00001$) and URL over extracorporeal shockwave lithotripsy (OR 0.47; 95% CI 0.28–0.77; $P = 0.003$). As to complications, PCNL had a significantly higher blood transfusion rate (OR 7.47; 95% CI 1.3–42.85; $P = 0.02$) and a lower ureteral injury rate (OR 0.15; 95% CI 0.04–0.52; $P = 0.003$) compared with URL. It also shared a significantly lower stone-retropulsion rate (OR 0.03; 95% CI 0.01–0.15; $P < 0.0001$) and higher treatment costs (SMD = 2.71; 95% CI 0.71–4.70; $P = 0.008$) than URL.

Conclusions Our meta-analysis suggested that PCNL might be the best option for PIUS owing to its higher successful rate. Complications such as hemorrhage could be decreased by the application on mini-PCNL.

Keywords Proximal impacted ureteral stones · Managements · Systematic review · Meta-analysis

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Introduction

Impacted ureteral stones are defined as stones remaining in one position for more than 2 months. Consequently, the distal part of the ureter is difficult to be studied by intravenous urography even after a long interval following contrast injection [1]. Long-term proximal impacted ureteral stones (PIUS) may result in pain, urinary tract infection, hydronephrosis, and even loss in renal function. Fortunately, with the improvement of optic systems, miniaturization of endoscopic equipment and cumulative experience in endoscopic surgeries, various surgical techniques have been in use for treatment of PIUS, including extracorporeal shockwave lithotripsy (SWL), ureteroscopic lithotripsy (URL), percutaneous nephrolithotomy (PCNL) and laparoscopic ureterolithotomy (LU).

Though most treatments have been used to treat PIUS, the optimal choice of treatment remains controversial.

Previous studies [2–7] have made comparisons on the efficacy and safety of different managements for PIUS patients. Nevertheless, sample size in these studies was quite small and their results were uncertain and inconclusive. One published meta-analysis stated that mini-PCNL should be considered as the preferred technique for PIUS with a higher stone-free rate (SFR) and similar complications compared with URL [8]. However, this study only compared PCNL and URL, and some original articles meeting its criteria were not included. Comparisons between other PIUS management options are still under debate.

The European Association of Urology (EAU) Guidelines on urolithiasis demonstrate that URL is an option for PIUS, while PCNL could be considered for larger PIUS with dilated renal collecting system. In addition, LU should be performed on conditions when endoscopic lithotripsy or SWL fails [9]. Nevertheless, the levels of evidences are relatively low. The guidelines of American Urological Association (AUA) even do not have specific statements on treating PIUS [10]. Therefore, to provide more detailed information and higher level of evidences (LOE), we performed a systematic review and meta-analysis to compare the efficacy and safety of all possible surgical methods of PIUS, aiming to guide urologists towards the best recommended treatments.

Materials and methods

The comprehensive prospective protocol of our review was preconditioned according to the preferred reporting items for systematic reviews and meta-analysis [11], including objective, literature-search strategy, inclusion and exclusion criteria, study selection, data extraction, methods of statistical analysis and outcome measurements. Protocol of this study was registered in PROSPERO under number CRD42018092745.

Search strategy

A literature strategy search using Pubmed, Medline, Embase and Cochrane Library was performed thoroughly to obtain relevant studies comparing different managements for PIUS up to Jan 2018. Comparative studies regarding any available treatments were included. Search terms used were “‘proximal’ or ‘upper’” and “‘impacted’ or ‘incarcerated’” in combination with “‘ureteral stones’ or ‘ureteral calculus’”. References of all included studies were also scanned to identify potential records. Language of eligible studies was restricted to English.

Inclusion and exclusion criteria

The selected studies were included based on the following criteria: (1) Comparative studies concerning the efficacy and safety of any available PIUS treatments; (2) Outcomes should consist at least two of the followings: SFR, overall complications, operation time, hospitalization time, blood transfusion, stone-retropulsion, postoperative fever, ureteral injury, auxiliary procedure and treatment costs. Accordingly, studies containing patients with serious urinary infection, musculoskeletal deformities, renal insufficiency, congenital abnormalities or solitary kidney were not included. Meanwhile, repeated publications, conference proceedings, non-published materials, editorials or reviews were also excluded from this analysis. Two reviewers performed study searching, quality assessments and data extractions independently, and disagreements were resolved by open discussion.

Study selection and data extraction

We screened the studies according to the inclusion and exclusion criteria. The authors of relevant studies were contacted to obtain incomplete data. Extracted data included: first author, year of publication, baseline patients’ characteristics, feature of stones, study period, study design, interventions, outcome measurements, variations in surgery techniques, statistical methods, and study conclusions.

Quality assessment and statistical analysis

The LOE of all included studies was assessed by the criteria provided by the Oxford Centre for Evidence-based Medicine [12]. The quality of non-randomized controlled trials (non-RCTs) was evaluated by Newcastle–Ottawa Scale (NOS) [13]. Additionally, the Cochrane risk of bias tool was applied to assess the methodological quality of RCTs [14].

Primary outcomes of this analysis were SFR and complications. Secondary outcomes included operation time, hospitalization time, stone-retropulsion rate, auxiliary procedures and treatment costs. Pooled odds ratios (ORs), standard mean differences (SMDs) or weighted mean difference (WMDs) were calculated to compare dichotomous and continuous variables, respectively. All results were reported with 95% confidence intervals (CIs). The Chi-square test based Q - and I^2 -statistic was used to test heterogeneity between studies. If heterogeneity was not significant ($P > 0.10$, $I^2 < 50\%$), fixed-effect model was adopted; otherwise, random-effect was applied. The results of the meta-analysis were expressed with forest graphs or tables. The Z test determined the pooled effects, and $P < 0.05$ was considered statistically significant. Subgroup analyses were

performed according to PCNL types, URL types and time points of SFR. Funnel plots and the Egger's test were used for potential publication bias [15]. All statistical analyses were performed by the software RevMan (version 5.3; Cochrane Collaboration, Oxford, UK) and STATA (version 13.0; StataCorp, College Station, Texas, USA).

Results

Characteristics and quality of eligible studies

After screening the titles and abstracts and then further reading the full texts, a total of 15 from 1255 studies [2–7, 16–24] containing 1780 patients were included in our analysis (Fig. 1). Table 1 shows baseline characteristics and quality assessments of all included studies. Among 15 of them, 2 [2, 3] conducted comparisons among PCNL, URL and LU, 7 [4, 16–21] compared PCNL with URL, 1 [5] compared PCNL with LU, 2 [6, 22] compared URL with LU, and other three [7, 23, 24] focused on comparison between URL and SWL. Regarding the study design and quality, 7 [2–4, 6, 16, 19, 21] were RCTs (LOE: 2a), 4 [5, 18, 20, 22] were retrospective case–controlled studies (LOE: 3) and the remaining 4 [7, 17, 23, 24] were prospective cohort studies (PCS) (LOE: 2b). The methodological quality of included studies was relatively high for all non-RCTs (NOS: 6 of 9

points) and RCTs were also in high qualities with points of 5 (the Cochrane risk of bias tools: score from 0 to 7).

Primary outcomes

Stone-free rate

Six studies [2–4, 16, 19, 21] compared the immediate SFR (I-SFR) after surgery between PCNL and URL. Meta-analysis by a fixed-effect model indicated that I-SFR favored PCNL over URL (OR 9.99; 95% CI 5.65–17.66; $P < 0.00001$) without heterogeneity ($I^2 = 0\%$, $P = 0.92$) (Fig. 2a). No obvious publication bias was detected through the inverted funnel plot.

Nine studies [2–4, 16–21] compared the final SFR (F-SFR) at the time of 1 month after surgery between PCNL and URL. Meta-analysis for F-SFR favored PCNL over URL (OR 10.35; 95% CI 5.26–20.35; $P < 0.00001$) without heterogeneity ($I^2 = 0\%$, $P = 1.0$) (Fig. 2b). In the subgroup analyses according to PCNL type, 1-month SFRs of either standard PCNL (OR 9.29; 95% CI 3.72–23.21; $P < 0.00001$) or mini-PCNL (OR 11.64; 95% CI 4.26–31.81; $P < 0.00001$) were significantly higher than URL. Subgroup analyses based on URL type also indicated that 1-month SFR of PCNL was significantly higher than both flexible-URL (F-URL) (OR 9.18; 95% CI: 3.83–22.03; $P < 0.00001$) and rigid-URL (R-URL) (OR 12.15; 95% CI 4.18–35.31; $P < 0.00001$). No publication bias was detected through either inverted funnel plot or Egger's test ($t = 1.00$, $P = 0.389$).

Two studies [3, 5] compared the F-SFR after 1 month between PCNL and LU. No significant difference existed between two groups (OR 0.25; 95% CI 0.03–2.26; $P = 0.22$) without heterogeneity ($I^2 = 0\%$, $P = 0.83$) (Fig. 3a).

Four studies [2, 3, 6, 22] compared the F-SFR between URL and LU, and our results favored LU over URL (OR 0.11; 95% CI 0.05–0.25; $P < 0.00001$) without heterogeneity ($I^2 = 2\%$, $P = 0.38$) (Fig. 3b). In subgroup analyses according to time points of F-SFR, LU provided a significantly higher F-SFR at the time of 1 month (OR 0.06; 95% CI 0.02–0.24; $P < 0.0001$) or more than 3 months (OR 0.16; 95% CI 0.06–0.46; $P = 0.0006$) after surgery compared with URL.

Three studies [7, 23, 24] compared the F-SFR between SWL and URL, and the result of meta-analysis favored URL over SWL (OR 0.54; 95% CI 0.31–0.95; $P = 0.03$) without heterogeneity ($I^2 = 0\%$, $P = 0.47$) (Fig. 3c). In subgroup analyses based on time points of F-SFR, three studies [7, 23, 24] reported the F-SFR at ≤ 1 month after surgery and indicated that URL had a significantly higher F-SFR than SWL (OR 0.41; 95% CI 0.23–0.72; $P = 0.002$). Only one study [7] compared the F-SFR at the time of ≥ 3 months after surgery; however, no significant difference was found between these two methods (OR 0.78; 95% CI 0.26–2.34; $P = 0.66$).

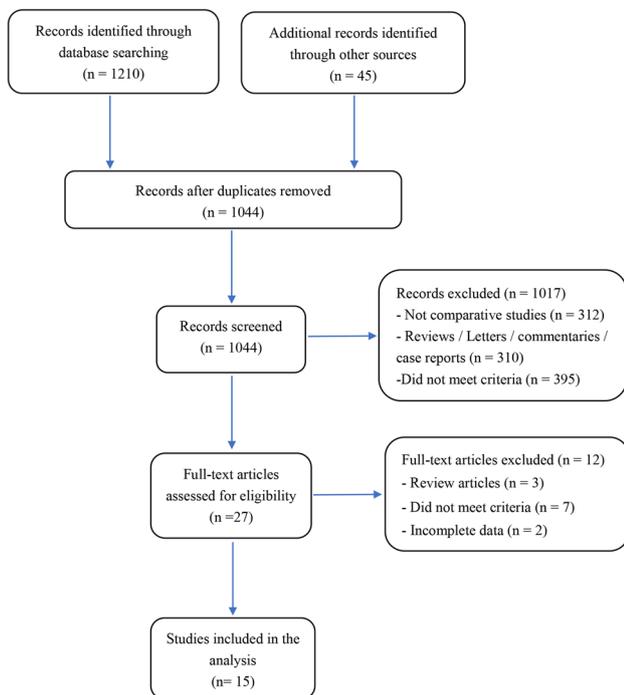


Fig. 1 Flow diagram of study selection

Table 1 Baseline characteristics of included studies

Comparisons	References	Country	Study period	Study design	LOE	Treatment	Cases, n	Mean age \pm SD (years)	Gender (male/female)	Unilateral/bilateral	Stone size	Follow-up time (mons)	Quality score
PCNL vs. URL vs. LU	Wang [2]	China	2012–2015	RCT	2a	R-URL	50	42 \pm 14	28/22	Unilateral	16.8 \pm 2.1 mm	12	6 ^b
						Mini-PCNL	50	41 \pm 15	31/19		19.3 \pm 1.8 mm		
						RPLU	50	44 \pm 11	29/21		18.8 \pm 1.4 mm		
PCNL vs. URL	Liu [3]	China	2011–2013	RCT	2a	R-URL	45	43.41 \pm 10.17	25/22	Unilateral	148.13 \pm 27.52 mm ³	1	5 ^b
						Mini-PCNL	45	46.35 \pm 10.31	23/22		146.85 \pm 30.36 mm ³		
						RPLU	45	44.73 \pm 10.56	26/19		149.16 \pm 32.15 mm ³		
PCNL vs. URL	Qi [4]	China	2010–2013	RCT	2a	F-URL	52	42.5 \pm 10.3	31/21	Unilateral	19.8 \pm 4.3 mm	1	6 ^b
						Standard-PCNL	52	41.1 \pm 12.4	30/22		20.3 \pm 3.6 mm		
						F-URL	29	44.22 \pm 13.0	18/11	Unilateral	16.23 mm	3	5 ^b
PCNL vs. URL	Gu [16]	China	2010–2011	RCT	2a	F-URL	30	42.5 \pm 10.1	17/13	Unilateral	17.27 mm	18	7 ^a
						Mini-PCNL	91	45.35 \pm 12.51	44/47	Unilateral	20.61 \pm 4.26 mm		
						F-URL	83	44.12 \pm 11.56	46/37	Unilateral	20.0 \pm 4.44 mm		
PCNL vs. URL	Moufid [18]	Morocco	2007–2011	RCCS	3	F-URL	30	43.10 \pm 11.67	30/7	Unilateral	29.3 \pm 1.8 mm	2	6 ^a
						Standard-PCNL	22	41.18 \pm 14	22/6		34 \pm 1.2 mm		
						R-URL	91	46.4 \pm 15.1	54/37	Unilateral	134.2 \pm 83.3 mm ²	12	6 ^b
PCNL vs. URL	Yang [19]	China	2012	RCT	2a	Mini-PCNL	91	45.2 \pm 14.7	53/38	Unilateral	158.7 \pm 96.8 mm ²	1	6 ^a
						F-URL	31	48.9 \pm 12.5	23/8	Unilateral	18.6 \pm 6.3 mm		
						Standard-PCNL	22	48.2 \pm 11.2	16/6		20.1 \pm 5.4 mm		
PCNL vs. URL	Sun [21]	China	2004–2006	RCT	2a	R-URL	47	39.6 \pm 7.3	31/16	Unilateral	14.6 \pm 1.8 mm	2	5 ^b
						Mini-PCNL	44	40.4 \pm 8.4	30/14	Unilateral	14.7 \pm 2.0 mm	1	7 ^a
						PCNL	37	48	22/15	Unilateral	105.3 \pm 77.6 mm ²		
PCNL vs. URL	Topaloglu [5]	Turkey	2007–2014	RCCS	3	RPLU	21	49	13/8	Unilateral	117.4 \pm 83.4 mm ²	41	7 ^a
						R-URL	108	51	87/21	Unilateral	10.4 \pm 1.6 mm		
						RPLU	81	53	61/20	Unilateral	16.1 \pm 1.4 mm		
PCNL vs. URL	Jiang [22]	China	2007–2014	RCCS	3	F-URL	139	41	90/49	Unilateral	13.6 \pm 1.4 mm	66	5 ^b
						RPLU	136	40	92/44	Unilateral	13.8 \pm 1.9 mm		
						F-URL	139	41	90/49	Unilateral	13.6 \pm 1.4 mm		
PCNL vs. URL	Shao [6]	China	2009–2013	RCT	2a	RPLU	136	40	92/44	Unilateral	13.8 \pm 1.9 mm	66	5 ^b
						F-URL	139	41	90/49	Unilateral	13.6 \pm 1.4 mm		
						RPLU	136	40	92/44	Unilateral	13.8 \pm 1.9 mm		

Table 1 (continued)

Comparisons	References	Country	Study period	Study design	LOE	Treatment	Cases, n	Mean age ±SD (years)	Gender (male/female)	Unilateral/bilateral	Stone size	Follow-up time (mons)	Quality score
URL vs. ESWL	Khalil [7]	Kuwait	2007–2011	PCS	2b	SWL	37	37.1 ± 8.8	31/6	Unilateral	13.2 ± 2.9 mm	3	7 ^a
	Ziaee [23]	Iran	2002–2004	PCS	2b	F-URL	45	35.2 ± 10.4	37/8	Unilateral	13.4 ± 2.7 mm	3	7 ^a
	Wu [24]	China	2002–2003	PCS	2b	F-URL	54	44.96 ± 12	37/17	No record	7.6 ± 1.9 mm	1	6 ^a
						SWL	41	51	34/7		7.5 ± 2.4 mm		
						F-URL	39	51	34/5		1.28 ± 0.04 cm		
											1.51 ± 0.05 cm		

LOE level of evidence, PCNL percutaneous nephrolithotomy, PCS prospective cohort study, RCCS retrospective case-control study, RCT randomized controlled trial, RPLU retroperitoneal laparoscopic ureterolithotomy, SWL extracorporeal shock wave lithotripsy, URL ureteroscopy lithotripsy

^aUsing the Newcastle–Ottawa Scale (score from 0 to 9)

^bUsing the Cochrane risk of bias tool (score from 0 to 7)

In summary, among four managements included in this analysis, PCNL and LU offered a relatively higher SFR compared with URL, while URL has a higher SFR than SWL.

Complications

Comparisons of overall complications were available in three studies [2, 3, 5] between PCNL and LU, four studies [2, 3, 6, 22] between URL and LU, and two studies [7, 23] between SWL and URL, respectively. Results of meta-analyses indicated that no significant differences could be detected in overall complications among all of them (PCNL vs. LU: OR 1.02, 95% CI 0.52–2.01, P=0.95; URL vs. LU: OR 1.24, 95% CI 0.36–4.27; P=0.73; SWL vs. URL: OR 0.46, 95% CI 0.03–7.2; P=0.58) (Fig. 4).

Eight studies [2–4, 16–20] compared the postoperative fever between PCNL and URL. Slight heterogeneity appeared among them (I² = 61%, P = 0.01) and our results indicated no significant difference in postoperative fever between these two groups (OR 1.48; 95% CI 0.66–3.31; P = 0.35) (Fig. 5a). No obvious publication bias was reached through the inverted funnel plot.

Five studies [2–4, 16, 17] compared the ureteral injury rates between PCNL and URL. Meta-analysis by a fixed-effect model showed that PCNL had a significantly lower ureteral injury rate compared with URL (OR 0.15; 95% CI 0.04–0.52; P = 0.003) (Fig. 5b). No obvious publication bias was found through the inverted funnel plot.

Three studies [2, 17, 20] compared the blood transfusion rates between PCNL and URL. Our results demonstrated that URL had a significantly lower blood transfusion rate compared with PCNL (OR 7.47; 95% CI 1.30–42.85; P = 0.02) (Fig. 5c). However, no significant difference was observed in the subgroup analyses based on PCNL type.

To sum up, SWL, URL, PCNL and LU all turned out to be safe alternative treatments for PIUS. In addition, URL was associated with a lower blood transfusion rate at the expense of a higher ureteral injury rate compared to PCNL.

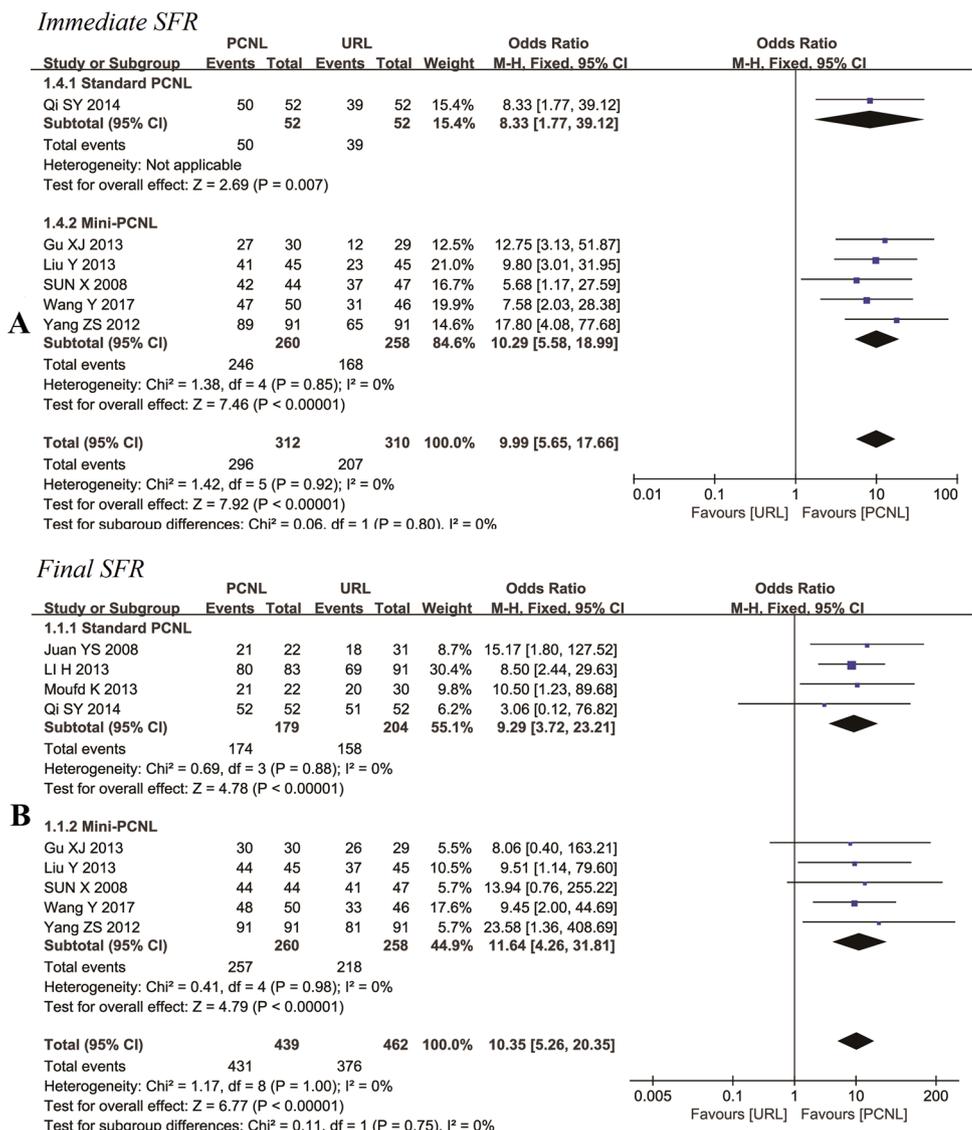
Secondary outcomes

Operation time

Eight studies [2–4, 17–21] compared the operation time between PCNL and URL. Significant heterogeneity existed (I² = 100%, P < 0.00001) and no significant difference was found between two groups (WMD = 18.27 min; 95% CI – 6.66 to 43.21; P = 0.15) (Fig. 6a). The inverted funnel plot did not find any publication bias among the included studies.

Three studies [2, 3, 5] compared the operation time between PCNL and LU, and no significant difference was found (WMD = – 7.54 min; 95% CI – 49.09 to 34.02; P = 0.72) (Fig. 6b). Comparisons of operation time between

Fig. 2 Comparisons of immediate SFR (a) and final SFR (b) between PCNL and URL



URL and LU were available in four studies [2, 3, 6, 22]. Results of our meta-analysis provided the information that URL shared significantly shorter operation time than LU (WMD = - 32.13 min; 95% CI - 47.53 to - 16.73; P < 0.0001) (Fig. 6c).

Hospitalization time

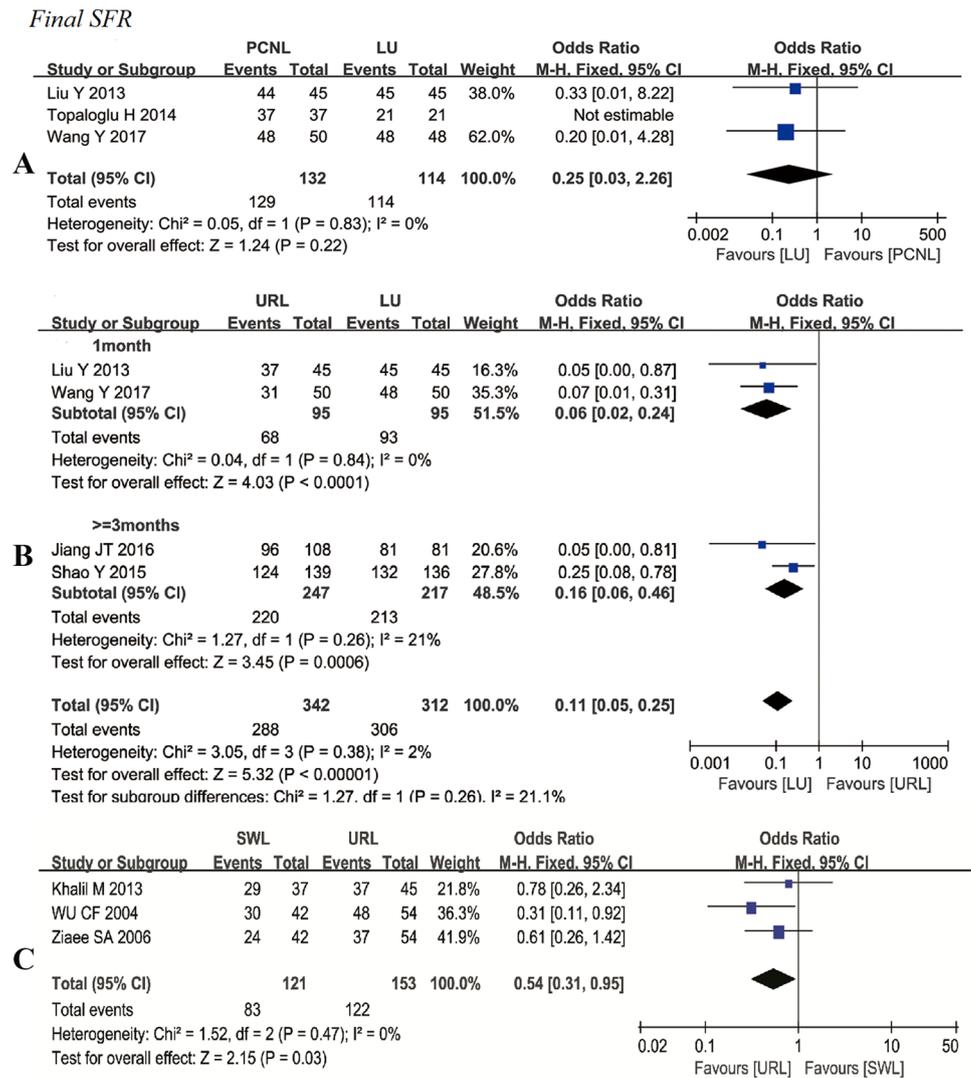
Comparisons of hospitalization time between PCNL and URL were available in eight studies [2–4, 16–18, 20, 21] with significant heterogeneity (I² = 98%, P < 0.00001). We found that patients receiving PCNL had significantly longer hospitalization time than those receiving URL (WMD = 2.75 days; 95% CI 1.59–3.91; P < 0.00001) (Fig. 7a). No obvious publication bias was detected through the inverted funnel plot.

Three studies [2, 3, 5] compared the hospitalization time between PCNL and LU. Summarized results proved that PCNL also shared significantly longer hospitalization time than LU (WMD = 1.64 days; 95% CI 1.06–2.22; P < 0.00001) (Fig. 7b).

Similar comparisons between URL and LU were reported in four studies [2, 3, 6, 22] and no significant difference was found in hospitalization time between these two groups (WMD = - 1.54 days; 95% CI - 3.15 to 0.07; P = 0.06) (Fig. 7c).

In total, LU was associated with the longest operation time and PCNL had the longest hospitalization time among these four managements.

Fig. 3 Comparisons of final SFR between PCNL and LU (a), URL and LU (b) and SWL and URL (c)



Stone-retropulsion rate

Comparisons of stone-retropulsion rates were only available between PCNL and URL in three studies [16, 17, 20]. Our results from combined data showed that PCNL provided a significantly lower stone-retropulsion rate compared with URL (OR 0.03; 95% CI 0.01–0.15; $P < 0.0001$) without heterogeneity ($I^2 = 0\%$, $P = 0.81$) (Fig. 8a).

Auxiliary procedures

Six studies [2–4, 16, 17, 19] compared the requirements of auxiliary procedures after PCNL and URL, and no significant difference was found between them (OR 0.66; 95% CI 0.08–5.58; $P = 0.71$) (Fig. 8b). No obvious publication bias was detected through the inverted funnel plot.

Two studies [2, 3] compared this point between PCNL and LU, and also no significant difference was concluded between two groups (OR 7.47; 95% CI 0.9–61.91; $P = 0.06$).

Treatment costs

Differences in treatment costs between PCNL and URL were available in three studies [4, 18, 19]. Meta-analysis by a random-effect model indicated that the fee of PCNL was significantly higher than URL (SMD = 2.71; 95% CI 0.71–4.70; $P = 0.008$) (Fig. 8c). In the subgroup analyses, we discovered that PCNL was significantly more expensive than R-URL (SMD = 3.69; 95% CI 3.21–4.17; $P < 0.00001$) but similar with F-URL (SMD = 2.21; 95% CI – 0.82 to 5.25; $P = 0.15$); on the other hand, the costs of URL were found similar with standard PCNL (SMD = 2.21; 95% CI – 0.82

Overall complications

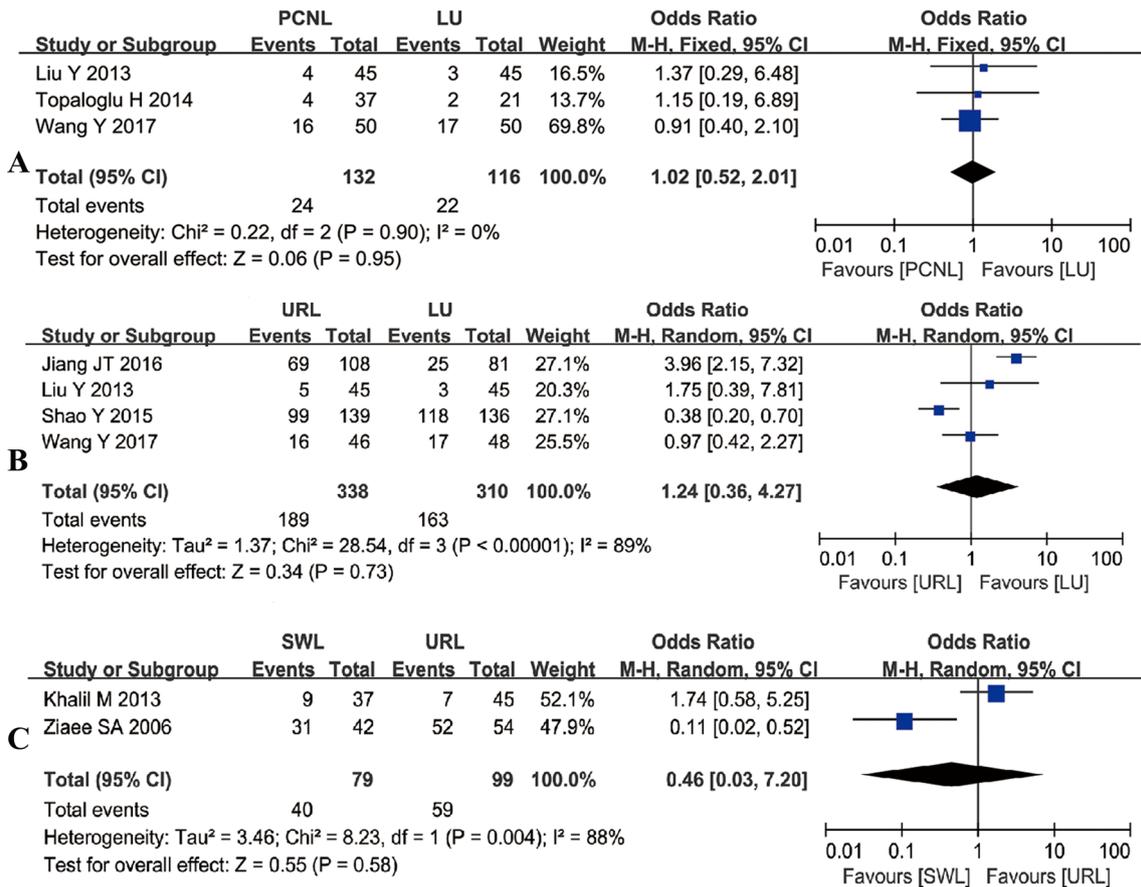


Fig. 4 Comparisons of overall complications between PCNL and LU (a), URL and LU (b), and SWL and URL (c)

to 5.25; $P=0.15$) but significantly lower than mini-PCNL (SMD = 3.69; 95% CI 3.21–4.17; $P < 0.00001$).

Sensitivity analyses

Sensitivity analyses were performed in RCTs comparing PCNL with URL, and no changes in terms of the significance were necessary for all outcomes (Table 2). Between-study heterogeneity was significantly reduced in the outcome of treatment costs, while heterogeneity remained statistically significant in outcomes of postoperative fever, operation time, hospitalization time, and auxiliary procedures.

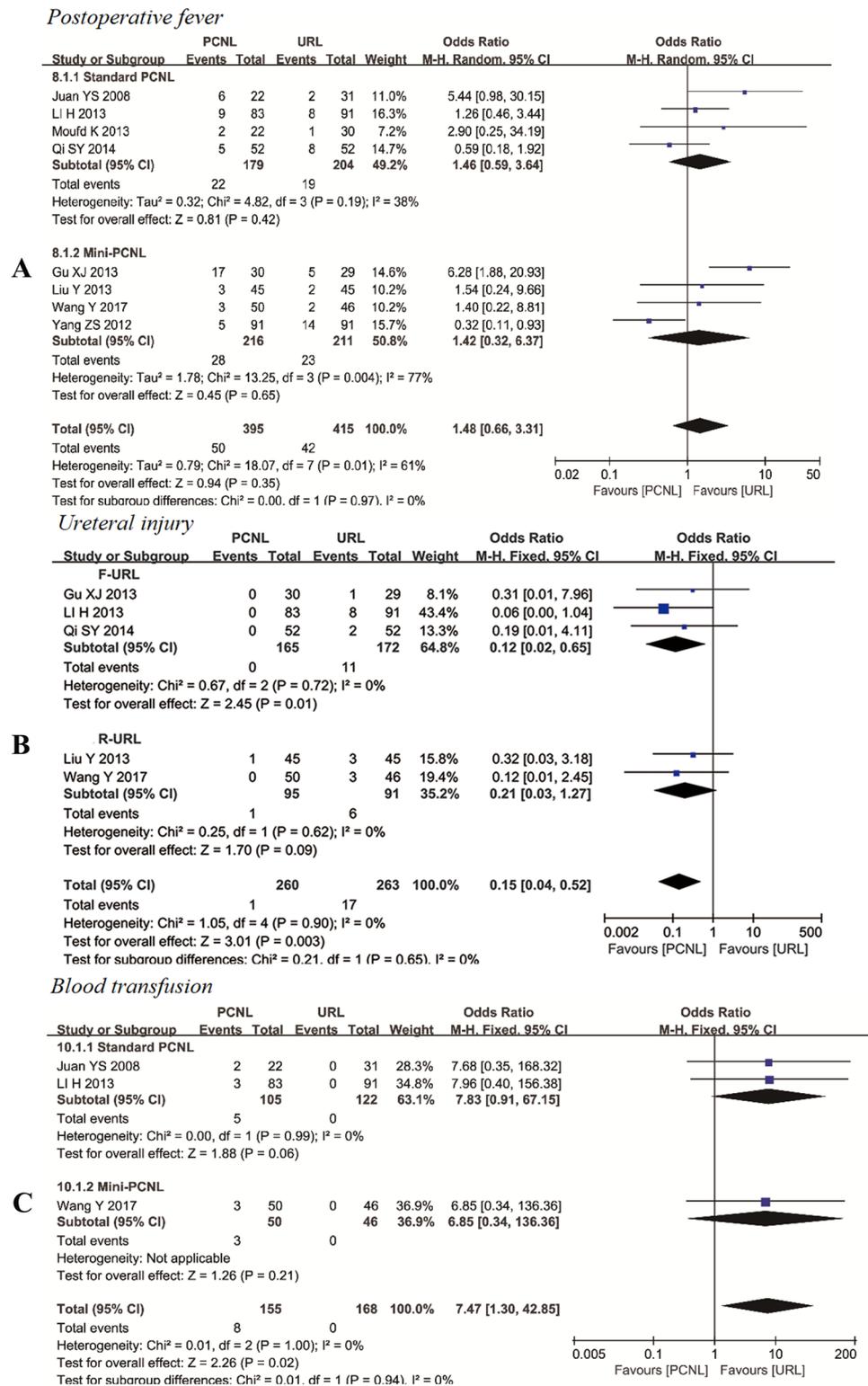
Discussion

After combining data from original articles comparing the operation methods on PIUS, our systematic review and meta-analysis finally concluded that PCNL and LU had a higher SFR than URL, while the SFR of SWL was the lowest among these four managements. All of them brought few

complications to PIUS patients. PCNL had a relative higher rate of blood transfusion. Stone retropulsion and ureteral injury seemed more frequent in URL, but it cost patients less compared with PCNL. Additionally, LU had the longest operation time and PCNL required the longest hospitalization time among the four methods (Table 3).

For a variety of urinary stones, the AUA guidelines do not recommend any kind of open surgery as the first-line treatment [10]. Impacted stones are regarded as those remaining in the original position for at least 2 months and the rest part of ureter below them cannot be visualized on the intravenous urography even 3 h after the contrast being injected. Since the largest transverse diameter of the impacted stone is wider than that of the ureter, mucosa inflammation often occurs, followed by enfolding ureteral polyps and stricture [25, 26]. Handling the impacted stones still leaves great difficulties for doctors. SWL is the least invasive method; however, it is hard to clear the large, obstructed or impacted stones because no adequate stone-water interface exists for stones to be diluted [27, 28]. It is also tough to localize them accurately, especially for enfolding ones [5]. Increasing the

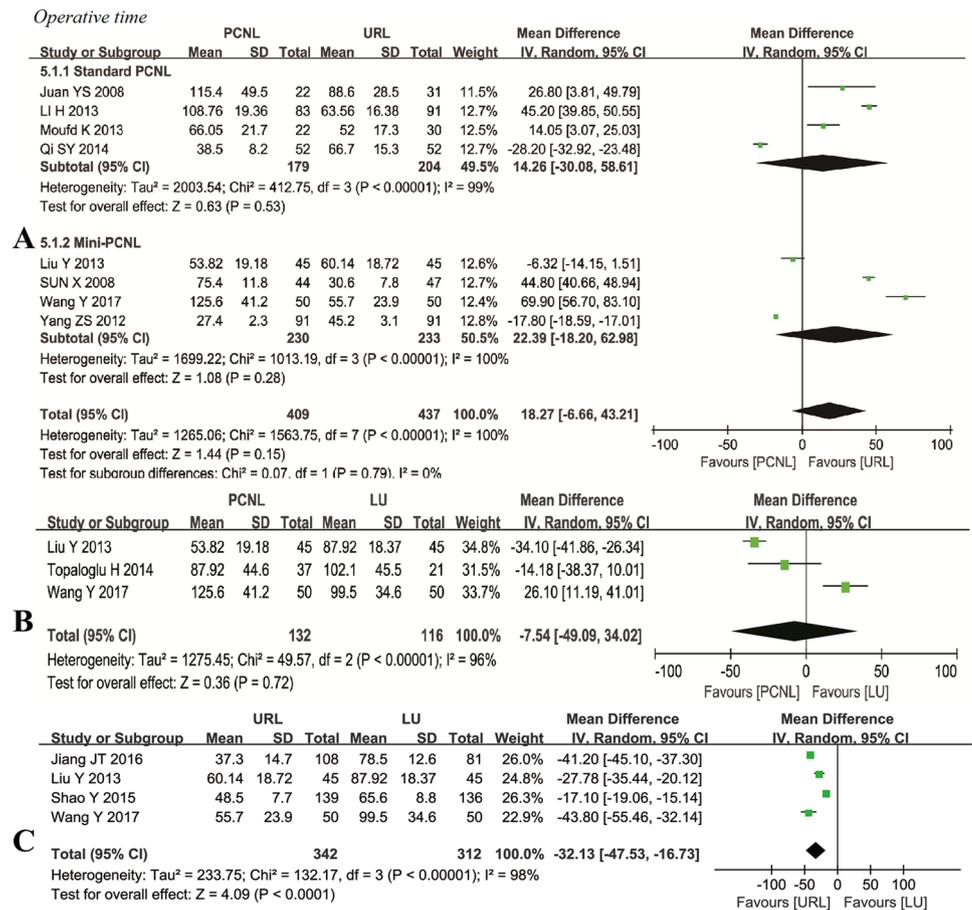
Fig. 5 Comparisons of postoperative fever (a), ureteral injury (b) and blood transfusion (c) between PCNL and URL



power of SWL may cause more complications, such as colic pain, hematuria and fever [29]. Since URL was invented, its technique has developed a lot. AUA and EAU recommend URL to be a choice of first-line treatments for urinary

stones [9, 10]. Although safe and effective, URL tends to introduce the broken stones back to the kidney, bringing more problems and extra surgical procedures [3]. Ureteral injury or perforation is one major severe complication of

Fig. 6 Comparisons of operation time between PCNL and URL (a), PCNL and LU (b), and URL and LU (c)



URL, but it can be solved to some degree with the rapid refreshments of URL instruments and technologies [30]. In our results, we found that URL had a higher SFR than SWL, which was similar to Ziaee et al.'s study [23]. The published articles reported no differences in the complications after comparing URL and SWL [7, 23]. Above all, as less invasive methods, URL is superior to SWL in treating PIUS with few complications.

PCNL is more direct and accurate to stones by penetrating into the kidney, especially for very large stones (> 15 mm) or stones in the upper position, which are not accessible for URL [31]. Combined kidney stones can be removed in the meantime by PCNL [20]. Although open surgery is seldom applied, LU, sharing similar surgical procedures, sometimes plays an important role to deal with the proximal, hard or large stones [31]. LU avoids injuries of nephron probably existing in PCNL [32], but it is relative more complicated and only skilled surgeons can perform it. Our results demonstrated that both PCNL and LU were more effective than URL in eliminating stones. Juan et al. [20], Moufid et al. [18] and Jiang et al. [22] also drew the same conclusions with ours. Although PCNL might cause hemorrhage on patients, it can easily be solved by blood transfusion compared with ureteral injury or perforation in

URL [33]. Recently, Legemate et al. conducted a worldwide prospective study with 2650 cases, indicating that URL had a relative lower stone-free rate and higher risk of intraoperative complication [34], further proving some limitations of URL on PIUS. Above all, PCNL acquires more operation time, longer hospital stays and higher cost, but its safety and efficacy on PIUS cannot be replaced by URL.

Meanwhile, as the development of mini-PCNL, smaller access sheaths have become well populated among patients. Mini-PCNL causes less bleeding, requiring shorter hospital stays and lower requirements of analgesia [35]. In a meta-analysis conducted by our team comparing mini- with standard PCNL, we found that mini-PCNL was associated with less blood transfusion and pain [36]. In this way, the advanced techniques compensate some shortcomings in conventional operative method, so PCNL can be applied more widely on PIUS patients. We also performed subgroup analysis based on PCNL type. Although no significant differences were found between mini- and standard PCNL in above outcomes, the number of studies in each subgroup was small and these results should be regarded cautiously.

Gao et al. performed a meta-analysis on the safety and efficacy of PCNL among five perspective studies [8]. They also found that PCNL had a better SFR compared with

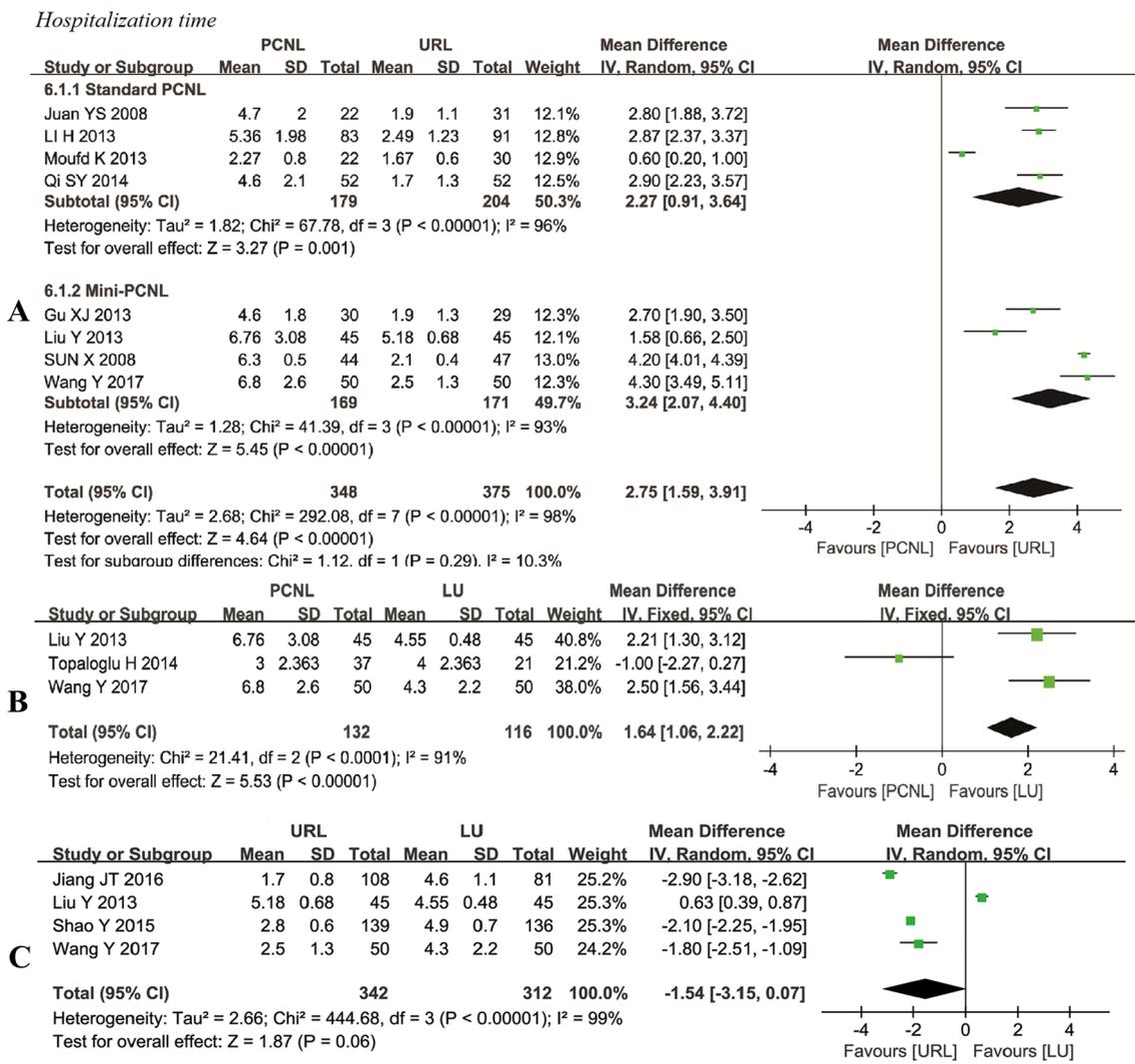


Fig. 7 Comparisons of hospitalization time between PCNL versus URL (a), PCNL versus LU (b) and URL versus LU (c)

URL and SWL. Postoperative SWL was needed less than URL. No significant differences existed in the occurrence of complications, except for hematuria. We extended these comparisons to four kinds of surgical methods including data from LU. 15 studies containing 1780 patients were included, so our results were relatively more valid and convincing. No heterogeneity existed in our primary outcomes, but significant heterogeneity was reached in operation time, hospitalization time, postoperative fever and auxiliary procedures. Because we included studies in different countries or regions whose economies and lifestyles varied, some above outcomes depended a lot on patients' income levels and pre/postoperative health status.

When choosing the proper surgery for PIUS, ureteral wall thickness (UWT) is a key factor for predicting the success rate which has been studied in many researches [37–39]. Patients with impacted stones tend to have thicker ureteral

walls, because of the ureteral edema and polyps, resulting from the inflammation, interstitial fibrosis and urothelial hypertrophy [7, 40]. The thickening ureteral walls then in turn increase the severity of impaction. In Sarica et al.'s study, UWT at the impacted site was the only independent predicting factor for the success rate of SWL [37]. Yoshida and colleagues found that high UWTs resulted in a lower SFR by URL compared with lower UWTs [38]. For smaller stones treated by non-invasive method, including SWL, medical expulsive therapy and spontaneous passage, UWT is a better predictive parameter, which is taken into great consideration by clinicians [41–43].

Our analysis had several limitations. First, the published dates of included studies were from 2004 to 2017, during which the surgical preferences changed a lot from open surgeries to minimal invasive methods. Doctors change their choices with the development of operative

Fig. 8 Comparisons of stone retropulsion (a), auxiliary procedure (b) and treatment costs (c) between PCNL and URL

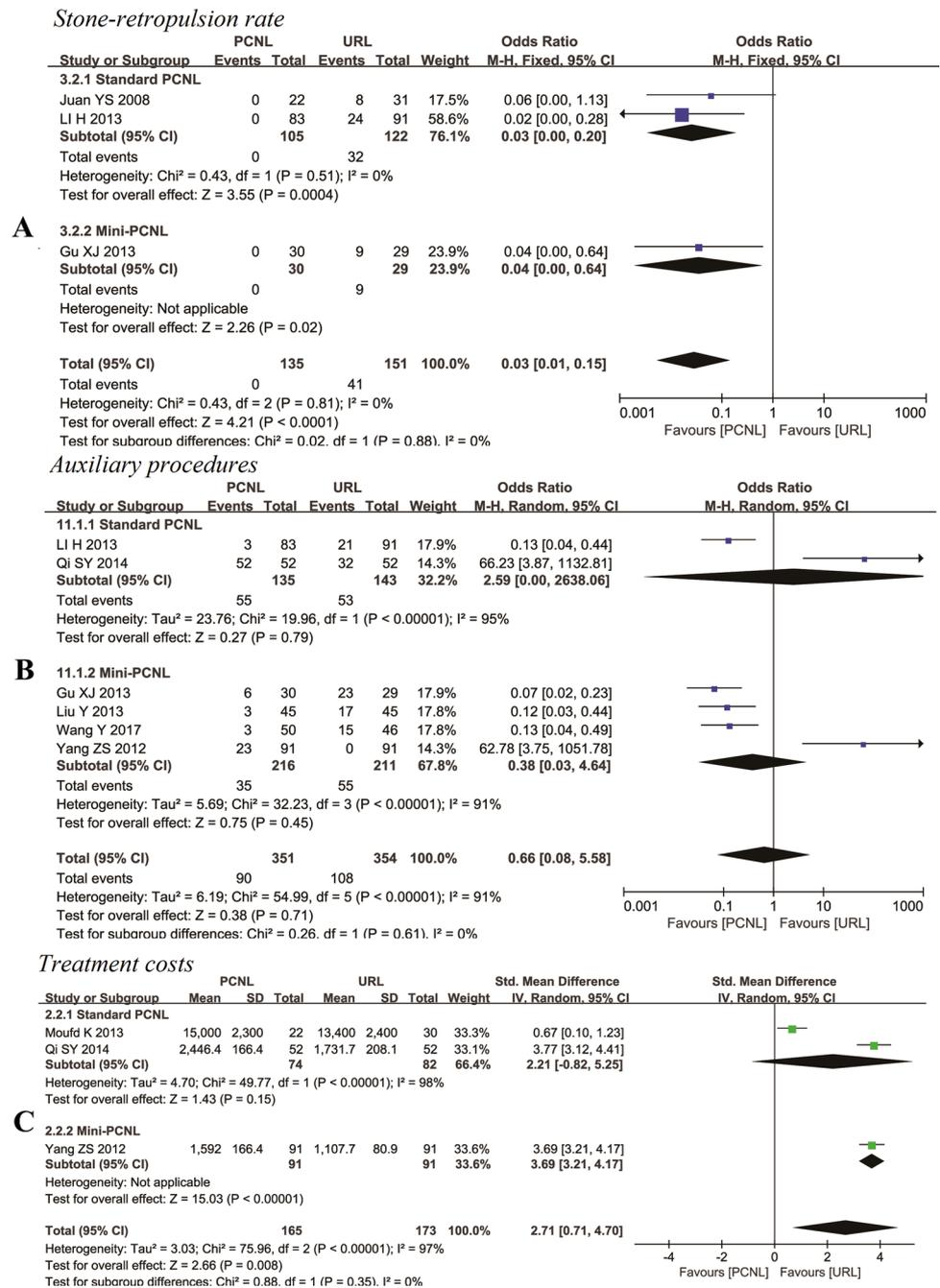


Table 2 Sensitivity analyses according to RCTs comparing PCNL and URL

Outcomes	Number of studies	Heterogeneity		WMD/SMD/OR (95% CI)	P value
		I²	P value		
Final SFR	6	0%	0.96	10.6 (4.09, 27.49)	<0.00001
Postoperative fever	5	72%	0.006	1.16 (0.36, 3.71)	0.8
Ureteral injury	4	0%	0.96	0.22 (0.05, 0.89)	0.03
Operation time	5	100%	<0.00001	12.1 (– 17.6, 41.8)	0.42
Hospitalization time	5	92%	<0.00001	3.18 (2.21, 4.14)	<0.00001
Auxiliary procedures	5	92%	<0.00001	1.03 (0.07, 15.65)	0.98
Treatment costs	2	0%	0.85	3.71 (3.33, 4.1)	<0.00001

CI confidence interval, OR odds ratio, SMD standard mean difference, WMD weighted mean difference

Table 3 Overall comparisons of four procedures

Comparisons	Immediate SFR	Final SFR	Complications		Ureteral injury	Blood transfusion	Operation time	Hospitalization time	Stone-retropulsion	Auxiliary procedures	Treatment costs
			Overall	Postoperative fever							
PCNL vs. URL	PCNL > URL	PCNL > URL	NA	NSD	PCNL < URL	URL < PCNL	NSD	URL < PCNL	PCNL < URL	NSD	URL < PCNL
PCNL vs. LU	NA	NSD	NSD	NA	NA	NA	NSD	LU < PCNL	NA	NA	NA
URL vs. LU	NA	LU > URL	NSD	NA	NA	NA	URL < LU	NSD	NA	NA	NA
SWL vs. URL	NA	URL > SWL	NSD	NA	NA	NA	NA	NA	NA	NA	NA

NA not available, NSD no significant difference, PCNL percutaneous nephrolithotomy, LU laparoscopic ureterolithotomy, SWL extracorporeal shock wave lithotripsy, URL ureteroscopy lithotripsy

techniques, which bring some biases to our results. Second, as to the study design, only 7 of the 15 studies were RCTs. Doctors and patients’ decisions undoubtedly affect the randomization when choosing the methods in non-RCTs. Third, some factors such as access sheath and laser used in URL, rigid or flexible scopes used in PCNL and CT values of stones may also have impacts on the outcomes; however, due to the lack of detailed information from original studies, related subgroup analyses were unable to conduct. At last, most of the eligible studies were conducted in China, which may potentially influence the applications of our results on other regions. The above shortcomings limit the validity and application of our results on all kinds of occasions.

Conclusion

Our analysis confirmed that SWL, URL, PCNL and LU all turned out to be safe and feasible alternative managements for PIUS. However, considering the major goal of treating PIUS is achieving high SFR and low complications, PCNL might be the best option owing to its higher successful rate, and its complications such as hemorrhage could be decreased by the application on mini-PCNL. In addition, clinicians should also adjust the managements according to the individual specificities of patients, and perfume suitable following strategies based on different managements.

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Compliance with ethical standards

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

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

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