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Review

Minimally invasive percutaneous nephrolithotomy versus retrograde intrarenal surgery in surgical management of upper urinary stones - A systematic review with meta-analysis

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ABSTRACT

Objective: The purpose of this study was to retrospectively assess the efficacy and safety of minimally invasive nephrolithotomy (MPCNL) versus retrograde intrarenal surgery (RIRS) in the management of upper urinary stones.

Methods: A comprehensive literature review of articles that investigated the efficacy and safety of MPCNL and RIRS was conducted by systematically searching PubMed, EMBASE, and Cochrane Library in March 2019. Two reviewers searched the literature, independently extracted the data and evaluated the quality of the data according to the inclusion and exclusion criteria. A meta-analysis was performed by using Review Manager 5.3 software.

Results: Eight randomized controlled trials (RCTs) involving 725 patients with upper urinary stones were analysed based on the inclusion criteria. While MPCNL has a better clinical efficacy than RIRS with respect to the stone-free rate (SFR) [RR = 1.11, 95% CI (1.05–1.17), $p = 0.0005$], MPCNL has a higher incidence of haematoma [RR = 3.09, 95% CI (1.44–6.66), $p = 0.004$] and longer hospitalization time [MD = 0.89 day, 95% CI (0.07–1.72), $p = 0.04$]. In addition, no significant difference in operative time [MD = 2.46 min, 95% CI (−17.99 to 22.92), $p = 0.81$] and postoperative pain score [MD = 0.74, 95% CI (−0.45 to 1.94), $p = 0.22$] were observed between the two methods. Overall, the evidence was insufficient to suggest a statistically significant difference in the adverse event profile for MPCNL compared with RIRS.

Conclusions: Our data suggest that MPCNL is an effective method for treating upper urinary stones, especially lower calyceal stones that are 1–2 cm in size. Compared to RIRS, MPCNL is associated with a longer hospital stay time and a higher incidence of haematoma. In addition, both methods have proven to be safe. Nevertheless, the findings should be further confirmed through well-designed prospective RCTs with a larger patient series.

1. Introduction

Globally, the incidence and prevalence of kidney stones are increasing [1,2]. Though kidney stones initially remain asymptomatic, the treatment is commonly performed to avoid future problems linked with the disease. Currently, the best treatment options include extracorporeal shock wave lithotripsy (ESWL), percutaneous nephrolithotomy (PCNL) and retrograde intrarenal surgery (RIRS). The shortcomings of ESWL are a lower stone free rate (SFR) and the need to repeat sessions, especially for stones located in the lower polar region or harder stones [3]. PCNL is currently considered the first line of treatment for larger renal stones (> 2 cm) [4,5]. Nevertheless, considering the complications associated with PCNL, which may include bleeding, pain, and urine leakage [6,7], alternative treatment methods,

Abbreviations: CI, Confidence interval; MD, Mean difference; PRISMA, Preferred Reporting Items for Systematic Reviews and Meta-analysis; RR, Risk ratio; RCT, Randomized controlled trial; SMD, Standardized mean difference; MPCNL, Minimally invasive percutaneous nephrolithotomy; PCNL, Standard percutaneous nephrolithotomy; RIRS, Retrograde intrarenal surgery

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e.g., minimally invasive procedures (MPCNL and RIRS) have been investigated [8,9]. MPCNL has a lower risk of surgical morbidities and requires a shorter hospital stay; nevertheless, it has a similar stone free rate when compared with conventional PCNL [7,10]. Meanwhile, improvements in endoscopy technology have made the RIRS an attractive treatment option for renal stones. Both ureteroscopy (URS) and percutaneous nephrolithotomy (PCNL) are minimally invasive procedures, that include a natural orifice and route or a tiny artificial tract to reach the renal stone [11]. In recent years, many studies have focused on investigating the effectiveness and safety of MPCNL versus RIRS in the management of upper urinary stones and reported different results. The meta-analysis performed by Jiang et al. [12] showed that MPCNL led to a higher SFR compared with RIRS. However, their study included some non-RCTs, which created some bias in the conclusion. Consequently, we conducted a new systematic review and meta-analysis of the relevant well-designed prospective RCTs published to date to evaluate the efficacy of MPCNL(Access sheath from 11 to 20 F)and RIRS.

2. Methods

2.1. Search strategy

A comprehensive literature review of articles that investigated the clinical efficacy and safety of the MPCNL and RIRS was performed. The relevant literature was obtained by systematically searching PubMed, EMBASE, and Cochrane Library in March 2019. The following key search terms and their potential combinations were used: (“mini percutaneous nephrolithotomy” or “minimally invasive PCNL” or “Mini-Perc” or “minimally invasive”) and (“retrograde intrarenal surgery” or “RIRS” or “flexible ureteroscopy” or “FURS”) and (“renal calculi” or “kidney stones” or “upper urinary stones” or “ureteral stones” or “urolithiasis”). The literature selection was performed following the search strategy promoted by the Preferred Reporting Items for Systematic Reviews and Meta-analysis (PRISMA) guidelines and the Assessing the Methodological Quality of Systematic Reviews (AMSTAR) Guidelines.

2.2. Inclusion and exclusion criteria

The included studies met the following criteria: (1) the study was a randomized controlled trial (RCT); (2) the study compared the efficacy and safety of MPCNL with RIRS; (3) the participants were adults and diagnosed with urolithiasis; (4) the study found no statistically significant differences in the basic characteristics of the participants; and (5) the study included at least one of the following outcomes: stone-free rate, surgery-related data, and postoperative complications. The studies were excluded based on the following criteria: (1) failure to meet the inclusion criteria; (2) a tract size of MPCNL > 20F or < 11F; (3) non-English literature; (4) renal abnormalities (horseshoe kidney or solitary kidney); and (5) publication type as conference articles, letters, comments and reviews.

2.3. Data extraction and quality assessment

According to the inclusion and exclusion criteria, two reviewers (B.J. and Z.L.) searched the literature, independently extracted the data and then cross-checked the data. The extracted data included first author, year of publication, country, study design, intervention, sample size, follow-up data, definition of stone-free, and relative outcomes (including operation duration, hospitalization time, and postoperative pain score) and overall complication. Relative disagreements were resolved through discussions among all the authors.

The levels of evidence for each selected article were evaluated based on the criteria recommended by the Oxford Centre for Evidence-based Medicine [13]. The quality of the randomized controlled trials (RCTs) was assessed using the Jadad scale (Table 1). The procedure was performed by two reviewers independently, and any disagreements were resolved through discussion.

2.4. Statistical analysis

The meta-analysis of comparable data was performed using Review Manager 5.3 software (Table 2). The continuous outcomes were evaluated using the mean difference (MD) or standardized mean difference (SMD). The results were expressed as a risk ratio (RR) with a 95% confidence interval (CI) for dichotomous variables. $\chi 2$ and I2 tests (I2 > 50% was regarded as substantial heterogeneity) were used to assess the data heterogeneity. Fixed-effects models were applied for the meta-analyses when the heterogeneity was low. Otherwise, a random effects model was used to reduce the effect of statistical heterogeneity. The pooled effects were determined by the z test, and a p value < 0.05 was considered statistically significant. Moreover, in the comparisons of MPCNL and RIRS, the relevant publications with appropriate data allowed us to perform subgroup analyses according to the device used. For several comparisons, sensitivity analyses were used. Publication bias was screened by using the funnel plot.

3. Results

3.1. Characteristics of selected studies

After searching and screening, eight relevant studies [14–21], including 725 patients, were selected for analysis. The selected or excluded literature at each stage is presented in a flowchart (Fig. 1). No differences were found in the basic physical conditions between the MPCNL group and RIRS group (Table 3). The outcome parameters of MPCNL and RIRS are shown in a table (Table 4).

3.2. Overall stone free rate

Eight studies were included to compare the stone free rates (SFRs) of MPCNL and RIRS. Due to no significant heterogeneity among these trials, the fixed-effects model was chosen to analyse the heterogeneity among these trials ($I^2 = 47\%$). The overall results showed that the stone free rates of MPCNL were significantly greater compared to the RIRS group [RR = 1.11, 95% CI (1.05–1.17), $p = 0.0005$] (Fig. 2A).In addition, we performed the subgroup analysis. The sensitivity analysis demonstrated the same results [RR = 1.13, 95% CI (1.07–1.21), $p < 0.0001$] (Fig. 2B), i.e., that MPCNL can lead to higher stone clearance in the 1–2 cm subgroups [RR = 1.14, 95% CI (1.07–1.22), $p < 0.0001$] (Fig. 3A). Moreover, no statistically significant difference was found in the > 2 cm subgroup [RR = 0.95, 95% CI (0.84–1.08), $p = 0.44$] (Fig. 3B). In terms of lower pole renal stones, pooled data from two studies showed a higher SFR in the MPCNL group [RR = 1.70, 95% CI (1.13–2.53), $p = 0.01$] (Fig. 3C) with no heterogeneity between the trials ($I^2 = 0\%$).

3.3. Operation duration

As shown in Fig. 4, among the seven trials that met the inclusion criteria, there was no significant difference [MD = 2.46 min, 95% CI (−17.99 to 22.92), $p = 0.81$] (Fig. 4), while high heterogeneity ($I^2 = 98\%$) was observed. To avoid biases, a sensitivity analysis and subgroup analysis were performed. The results showed that the differences between MPCNL and RIRS were not statistically significant.

3.4. Blood transfusion

Very few events of blood transfusion were reported in five studies that compared Mini-PCNL versus RIRS. Meta-analysis using a fixed-effects model ($I^2 = 0\%$) demonstrated that there was no remarkable difference between mini-PCNL and RIRS with respect to the blood transfusion [RR = 5.00, 95% CI (0.60–41.91), $p = 0.14$] (Fig. 5).

Table 1
Summary of comparative studies included in Meta-analysis.

Study	country	Study period	Study design	LE	Intervention		Sample size		Study quality
					Trial	Control	Trial	Control	
Demirbas 2016	Turkey	2015.3–2015.9	RCT	2a	MPCNL	RIRS	30	43	3*
Fayad 2016	Egypt	2012.7–2015.12	RCT	2a	MPCNL	RIRS	60	60	3*
Gu 2013	China	2010.9–2011.11	RCT	2a	MPCNL	RIRS	30	30	3*
Gucuk 2018	Turkey	2016.4–2017.5	RCT	2a	MPCNL	RIRS	30	30	3*
Kumar 2015	India	2012.1–2013.5	RCT	2a	MPCNL	RIRS	41	43	4*
Lee 2015	Korea	2014.6–2015.2	RCT	2a	MPCNL	RIRS	35	33	4*
Wang 2017	China	2012.1–2015.12	RCT	2a	MPCNL	RIRS	50	50	3*
Zeng 2018	China	2015.8–2017.7	RCT	2a	MPCNL	RIRS	80	80	4*

LE = level of evidence; * Using Jadad scale (score from 0 to 5); RCT = randomized controlled trial.

Table 2
Study outcomes comparing MPCNL and RIRS.

Outcomes	No.of studies	Sample size		Heterogeneity(Total)				MD/RR(95%CI)	*P* value(Total)
		MPCNL	RIRS	chi^2	df	I^2%	*P* value		
Overall SFR	8	351	355	13.27	7	47	0.07	1.11[1.05, 1.17]	$P = 0.0005$
SFR(sensitivity analysis)	7	316	322	4.12	6	0	0.66	1.13[1.07, 1.21]	$P < 0.0001$
SFR(stone < 2 cm)	6	286	292	3.56	5	0	0.61	1.14[1.07, 1.22]	$P < 0.0001$
SFR(stone > 2 cm)	2	65	63	1.62	1	38	0.20	0.95[0.84, 1.08]	$P = 0.44$
SFR(lower calices)	2	29	19	0.76	1	0	0.38	1.70[1.13, 2.53]	$P = 0.01$
Operation duration	7	326	339	397.87	6	98	< 0.00001	2.46 [-17.99, 22.92]	$p = 0.81$
Blood transfusion	5	250	249	0.15	1	0	0.70	5.00[0.60, 41.91]	$P = 0.14$
Hospitalization time	5	205	216	34.42	4	88	< 0.00001	0.89 [0.07, 1.72]	$P = 0.03$
Postoperative pain score	4	175	186	40.69	3	93	< 0.00001	0.74[-0.45, 1.94]	$P = 0.22$
Haematoma	3	151	152	0.10	2	0	0.95	3.09[1.44, 6.66]	$P = 0.004$
Postoperative fever	6	285	282	1.70	5	0	0.89	1.11[0.67, 1.85]	$P = 0.69$
Urinary perforation	4	175	172	2.15	3	0	0.54	0.56[0.17, 1.88]	$p = 0.35$
Urinary tract infection	3	126	126	1.37	2	0	0.50	1.87[0.52, 6.73]	$P = 0.34$
Complications(Grade I)	5	236	236	11.61	4	66	0.02	1.00[0.73, 1.37]	$P = 1.00$
Complications(Grade II)	5	236	236	3.98	4	0	0.41	0.85[0.40, 1.80]	$P = 0.67$
Complications(Grade III)	3	110	123	3.05	2	35	0.22	1.81 [0.67, 4.87]	$P = 0.24$

CI = confidence interval, MD = mean difference, RR = risk ratio.

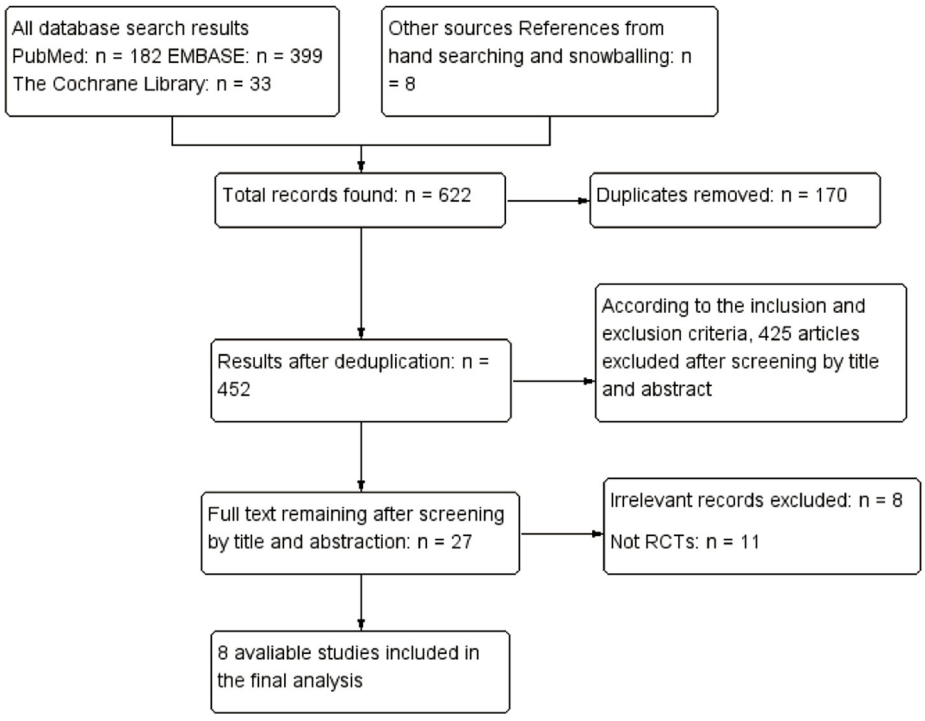

Fig. 1. PRISMA flowchart.

Table 3
Baseline characteristics of included studies.

Study	Treatments	Stone size	Access sheath size	Dilator	Nephoscopy size	Lithotripsy	Tools for evaluating the stone-free status	Definition of stone free rate	Follow-up (SFR)
Demirbas 2016	MPCNL	185.86 ± 88.29 mm^2	14F	Amplatz dilators	6/7.5F	Laser	CT	no stone ≥ 3 mm	1 month
	RIRS	181.70 ± 114.18 mm^2	9.5/11.5F	UAS	7.5F	Laser			
Fayad 2016	MPCNL	1.47(0.3; 0.8–2.0)cm	16F	Alkan dilators	10F	Laser	X-ray and CT	no stone ≥ 2 mm	1 month
	RIRS	1.41(0.3; 0.8–20)cm	12/14F	UAS	7.5F	Laser			
Gu 2013	MPCNL	17.27(15–25)mm	12–18F	FD	8.5/9.8F	Laser	X-ray and US	no stone ≥ 4 mm	3 months
	RIRS	16.23(15–25) mm	N/A	UAS	8.5/9.8F	Laser			
Guc uk 2018	MPCNL	275.5 ± 75.1 mm^2	16.5F	One step dilator	12F	Laser	CT	no residual stones	3 months
	RIRS	259.1 ± 65.2 mm^2	9.5/11.5 F	UAS	7.5F	Laser			
Kumar 2015	MPCNL	13.3 ± 1.3 mm	18F	N/A	15F	Pneumatic	CT and US	no stone ≥ 4 mm	3 months
	RIRS	13.1 ± 1.1 mm	12F	UAS	8/9.8F	Laser			
Lee 2015	MPCNL	39.1 ± 30.7 mm	18F	Balloon dilator	15F	Laser	CT	no stone ≥ 2 mm	3 months
	RIRS	28.9 ± 17.5 mm	12/14/16F	UAS	7.5F	Laser			
Wang 2017	MPCNL	19.3 ± 1.8 mm	18F	FD	N/A	Pneumatic–ultrasonic	X-ray	no stone ≥ 4 mm	1 month
	RIRS	16.8 ± 2.1 mm	N/A	N/A	8–9.8 F	Laser			
Zeng 2018	MPCNL	1.50(0.29)cm	14F	FD	N/A	Laser	CT	N/A	3 months
	RIRS	1.43(0.34)cm	12/14F	UAS	N/A	Laser			

MPCNL = minimally invasive percutaneous nephrolithotomy, RIRS = retrograde intrarenal surgery, FD fascial dilators,; UAS ureteral access sheath placement, N/A not available CT = computed tomography, US = ultrasound.

3.5. Hospitalization time

Regarding the length of in-patient stay, five studies were included in this meta-analysis. When pooled, the results showed that the MPCNL group had a longer hospitalization time [MD = 0.89 day, 95% CI (0.07–1.72), $p = 0.03$] (Fig. 6).

3.6. Postoperative pain score

Four studies provided data on the postoperative pain score, which were analysed by random effect model. The meta-analysis showed no difference between the MPCNL and RIRS [MD = 0.74, 95% CI (−0.45 to 1.94), $p = 0.22$] (Fig. 7), with high heterogeneity between the trials ($I^2 = 93\%$). The sensitivity analysis suggested the same results.

3.7. Haematoma

Three studies, that reported the outcomes of comparing MPCNL against RIRS were evaluated in the meta-analysis with a random-effects model. The results showed that the incidence of haematoma in MPCNL group was higher against RIRS [RR = 3.09, 95% CI (1.44–6.66), $p = 0.004$] (Fig. 8).

3.8. Complications

Postoperative complications, including postoperative fever, urinary perforation and urinary tract infection were analysed. The overall results showed no significant difference between MPCNL and RIRS. [RR = 1.11, 95% CI (0.67–1.85), $p = 0.69$] (Fig. 9A), [RR = 0.56, 95% CI (0.17–1.88), $p = 0.35$] (Fig. 9B), [RR = 1.87, 95% CI (0.52–6.73), $p = 0.34$] (Fig. 9C). With the aim of detecting the assessment of the complications based on the Clavien–Dindo grade, five studies were used for the statistical analysis. The incidence of Clavien–Dindo grade I complications was not significantly different between groups [RR = 1.00,95% CI (0.73–1.37), $p = 1.00$], and there was no remarkable difference in terms of the incidence of Clavien–Dindo grade II complications [RR = 0.85,95% CI(0.40 to 1.80), $p = 0.67$]. In addition, the incidence of Clavien–Dindo grade III complications was not significantly different between groups [RR = 1.81, 95% CI(0.67 to 4.87), $p = 0.24$] (Fig. 10).

3.9. Publication bias

A funnel plot was performed to assess publication bias (Fig. 11). The result showed no apparent asymmetry, which indicated no obvious publication bias.

4. Discussion

According to the European Association of Urology guidelines on urolithiasis, SWL, PNL and URS are available treatment options for the management of upper urinary stones [5]. The drawbacks of ESWL are relatively lower stone clearance rates and high rates of re-treatment [3]. PCNL is considered the first treatment option for large burden (> 2 cm) renal stones [5]. However, although PCNL has high SFR, it is associated with significant complications and morbidity. Since most of the morbidities associated with PCNL are related to the size of tract, a reduction in tract size can minimize the complications of PCNL [22]. Minimally invasive PCNL is a modified PCNL technique that is performed using miniaturized scope through a smaller (20F or less) nephrostomy tract [23], which allows high clearance with little trauma. Moreover, improvements in endoscopy technology have made the flexible scopes an appealing treatment option for the majority of renal stones [24]. MPCNL and RIRS are also considered as attractive treatment modalities for renal stones. The purpose of this meta-analysis was to evaluate and compare the efficacy and safety of MPCNL and RIRS for the treatment

Table 4
Outcome parameters of MPCNL and RIRS.

Study	Surgery	SFR	Operation	Hospitalization	Postoperative	Complications(%)		
		(%)	duration(min)	time(day)	pain score	Grade I	Grade II	Grade III
Demirbas 2016	MPCNL	80	54.53 ± 23.09	2.46 ± 3.02	4.73 ± 1.25	N*	N*	16.7
	RIRS	74.4	59.41 ± 15.78	1.37 ± 1.48	2.30 ± 1.12	N*	N*	7
Fayad 2016	MPCNL	92.72	71.66 ± 10.36	–	–		5#	
	RIRS	84.31	109.66 ± 20.75	–	–		3.33#	
Gu 2013	MPCNL	100	50–135 (96.2)	4.6 ± 1.8	–		N*	
	RIRS	89.7	45–100 (66.8)	1.9 ± 1.3	–		N*	
Gucuk 2018	MPCNL	86.7	98.3 ± 18.8	2.1 ± 2.03	3.1 ± 1.4	30	10	0
	RIRS	83.3	109.0 ± 33.8	1.6 ± 1.34	3.0 ± 1.4	20	3.3	6.6
Kumar 2015	MPCNL	95.1	61.1 ± 1.3	3.1	–	20	4.9	N
	RIRS	86.1	47.5 ± 1.1	1.3	–	4.7	4.7	N
Lee 2015	MPCNL	85.7	76.1 ± 70.6	1.6 ± 1.1	2.7 ± 2.1	45.7	11.4	0
	RIRS	97.0	99.6 ± 60.8	1.5 ± 0.9	3.1 ± 2.0	78.8	9.1	0
Wang 2017.	MPCNL	96	125.6 ± 41.2	6.8 ± 2.6	–	24	2	6
	RIRS	72	55.7 ± 23.9	2.5 ± 1.3	–	20	12	0
Zeng 2018	MPCNL	93.8	58.6 ± 21.6	2.5 ± 1.1	2.7 ± 1.7	6.25	2.25	N
	RIRS	82.5	52.3 ± 22.4	2.2 ± 1.1	2.0 ± 1.5	6.25	2.25	N

MPCNL = minimally invasive percutaneous nephrolithotomy, RIRS = retrograde intrarenal surgery, * Insufficient Information Provided, # Overall complication rate.

of upper urinary stones.

SFR is the most important parameter for estimating the clinical efficacy of surgical methods. In our study, we found that MPCNL has significantly higher SFR for treating 1–2 cm lower pole renal stones compared to RIRS, which is consistent with the study results published by Knoll et al. [25]. In contrast, De et al. [26] obtained different results, which indicated that RIRS provided a higher SFR than MPCNL [OR = 1.70, 95% CI (1.07–2.70), p = 0.03]. The difference in results may be associated with the following reasons: first, we noted a variety of definitions and imaging modalities among the eight studies that evaluated SFR. For example, some studies adopted the non-contrast computed tomography (CT) which is a more accurate imaging approach for assessing residual fragments compared to the plain-film X-ray and/or ultrasonography. Notably, in this study, stone-free fragments were defined as residual fragments ranging from 0 to 4 mm. Stone-free rates are correlated with the lithotripsy and the location or size of stones. Liu et al. [27] reported that laser can achieve a better early and delayed stone-free rate than pneumatic lithotripsy. Pneumatics have a better release of energy in calculi and stronger crushing ability compared to laser. Furthermore, Tepeler et al. [28] concluded that MPCNL might

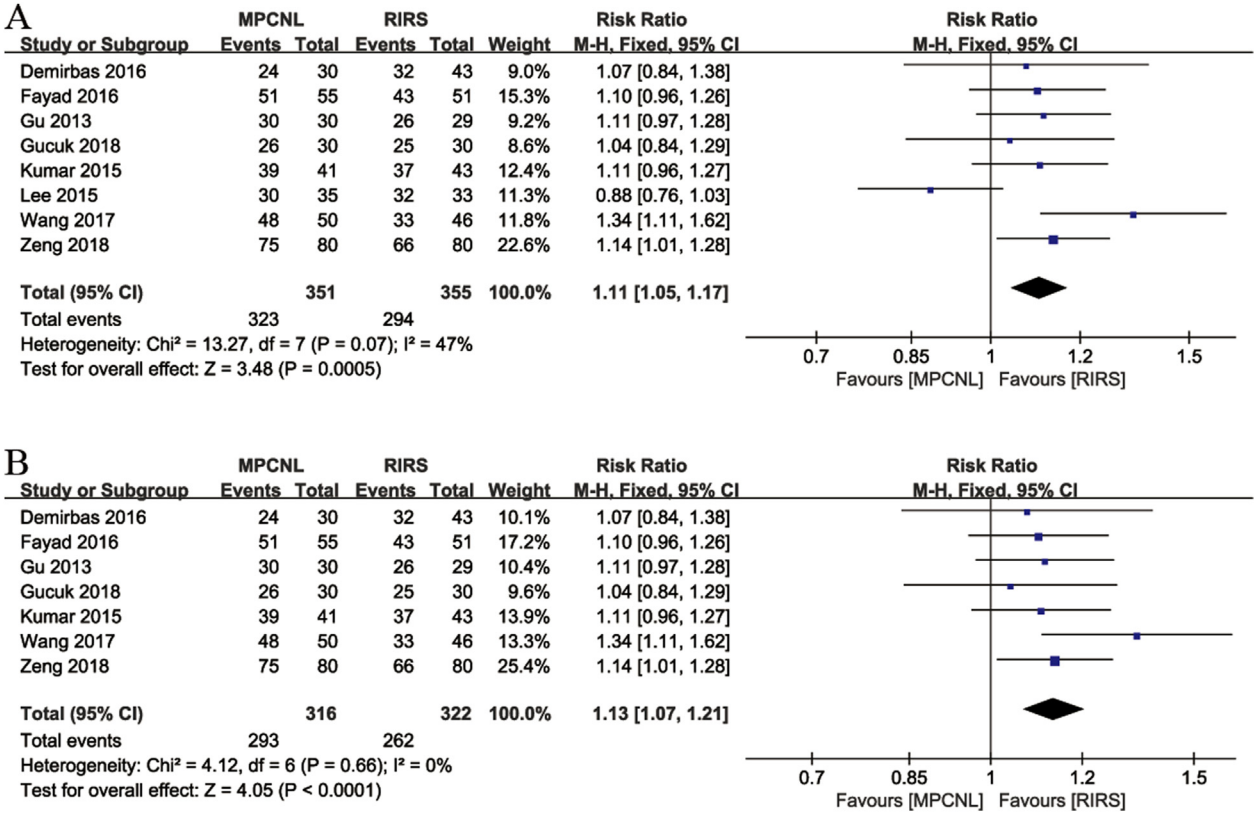

Fig. 2. Forest plots and meta-analyses. **A:** Overall SFR; **B:** SFR (sensitivity analysis); [95% CI: 95% confidence intervals, df: degrees of freedom, Fixed: fixed effects model, M − H, SD: standard deviation].

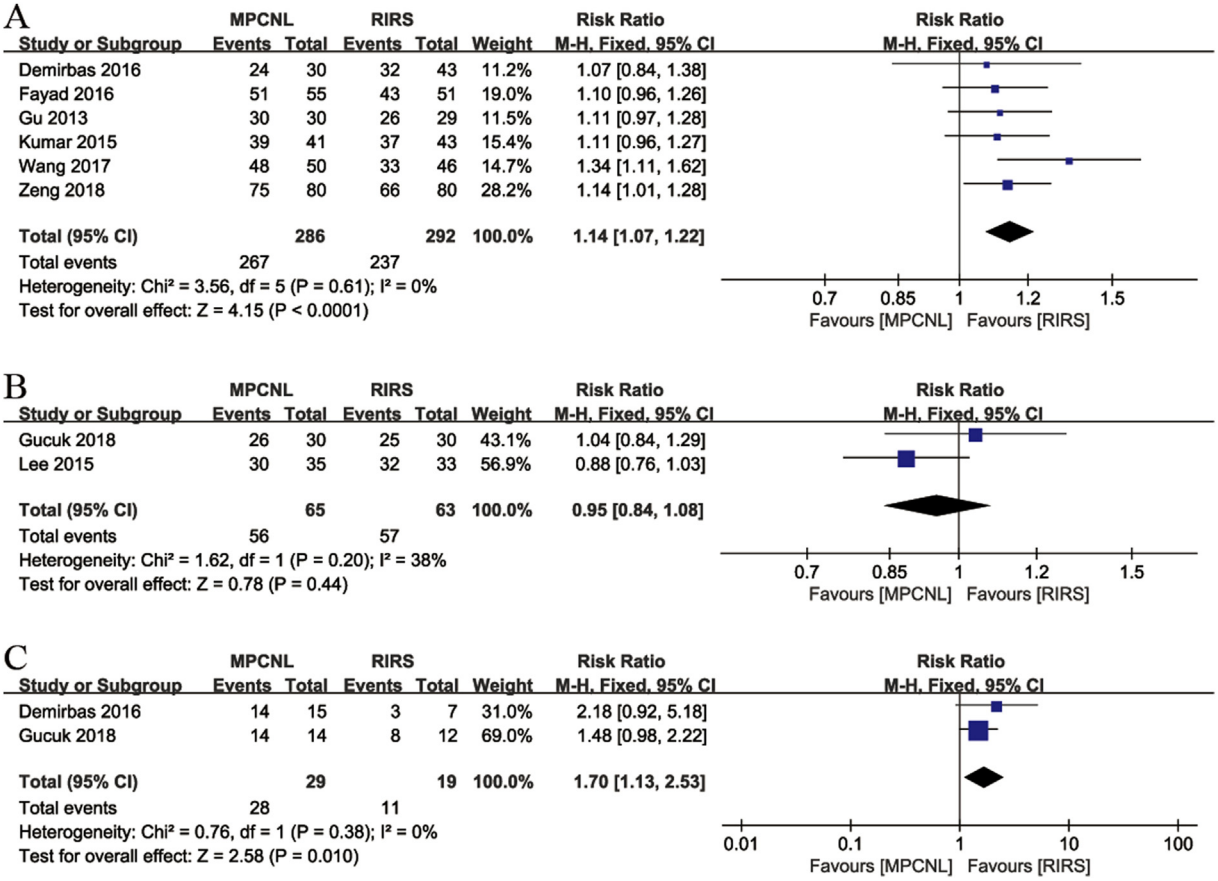

Fig. 3. Forest plots and meta-analyses. **A:** SFR(stone < 2 cm); **B:** SFR(stone > 2 cm); **C:** SFR(lower calices) [95% CI: 95% confidence intervals, df: degrees of freedom, Fixed: fixed effects model, M − H, SD: standard deviation].

take part in SWL and RIRS failures or as an alternative to percutaneous nephrolithotomy or RIRS in the management of symptomatic lower pole renal calculi. The accessibility of RIRS in the lower pole will be limited by the anatomy type of the collecting system [29]. The unfavourable anatomy of the kidney, which includes the infundibulopelvic angle, the infundibular width, and the infundibular length, might be related to the SFR of the lower pole stones [30]. The subgroup analysis of lower pole renal stones showed that MPCNL had obvious advantages. Nevertheless, thus far, only 2 studies [18,21] were included [MPCNL14/14 (100%): RIRS8/12 (66.7%), $p < 0.05$], [MPCNL14/15 (93.3%): RIRS 3/7 (42.9%), $p < 0.05$]. Therefore the obtained results should be further confirmed by well-designed prospective RCTs with larger cohorts. Our subgroup analysis suggested no remarkable difference between the two groups when stones were larger than 2 cm. In addition, we found that MPCNL could lead to higher stone clearance in the 1–2 cm subgroup. Nevertheless, Zeng and his team [31] have demonstrated that the MPCNL group has a higher SFR than the RIRS group when managing stones that are larger than 2 cm [MPCNL 38/53 (71.70%): RIRS 23/53 (43.40%), $p < 0.05$]. In addition, the existing literature [11,32] revealed no significant differences between groups when stones were smaller than 2 cm [MPCNL25/30 (84%): RIRS 26/30 (87%), $p > 0.05$], [MPCNL34/35 (97.1%): RIRS 33/35 (94.3%), $p > 0.05$]. Currently, there are no uniform standards for the definition and tract of MPCNL. The diversity in definition may lead to outcome differences between the current meta-analysis and the previous study. Accordingly, more studies are needed to obtain more reliable outcomes.

Furthermore, we found no differences in operative time between MPCNL and RIRS. Nevertheless, some studies [8,20] have suggested that the mean operation time was significantly longer in the RIRS group compared with the MPCNL group operation time (min) (MPCNL − 9.0 ± 12.6: RIRS −3.6 ± 8.5 $p < 0.05$), (MPCNL − 9.0 ± 12.6: RIRS −3.6 ± 8.5 $p < 0.05$). This observation might be due to the following reasons: the placement of the ureteral

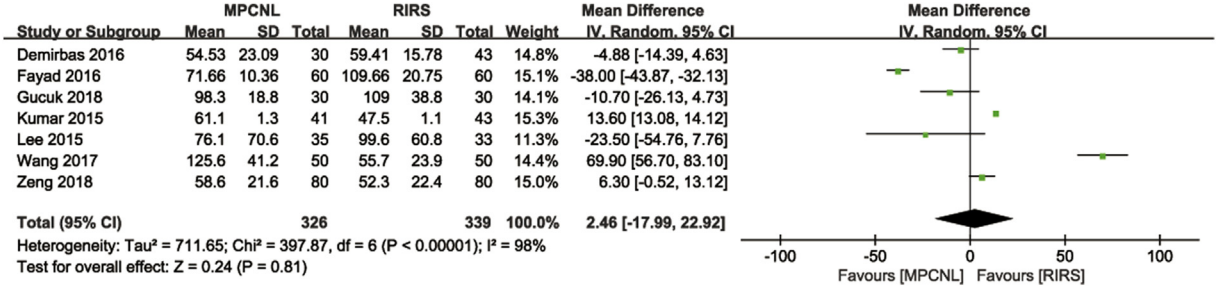

Fig. 4. Forest plot of the operation duration. [95% CI: 95% confidence intervals, df: degrees of freedom, Random: random effects model, IV: inverse variance, SD: standard deviation].

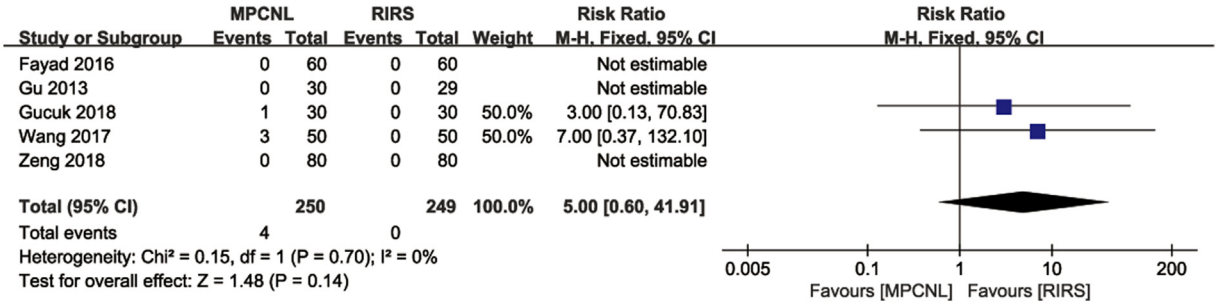

Fig. 5. Forest plot of the blood transfusion. [95% CI: 95% confidence intervals, df: degrees of freedom, Fixed: fixed effects model, M − H, SD: standard deviation].

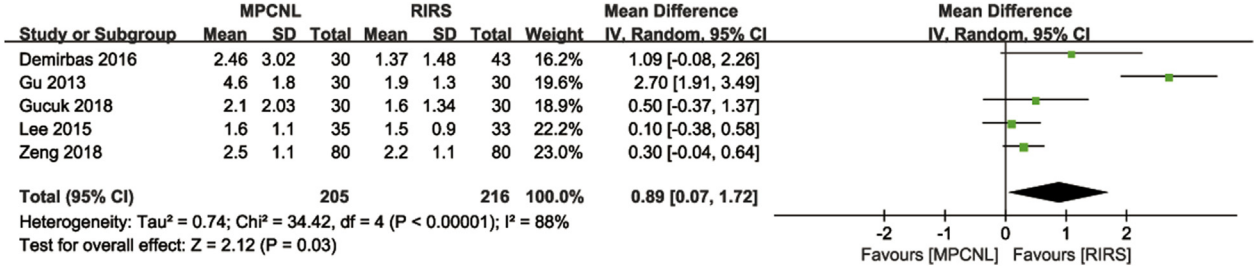

Fig. 6. Forest plot of the hospitalization time [95% CI: 95% confidence intervals, df: degrees of freedom, Random: random effects model, IV: inverse variance, SD: standard deviation].

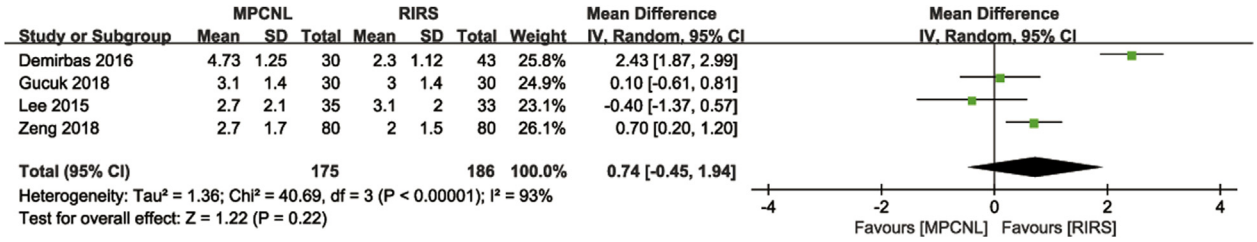

Fig. 7. Forest plot of the postoperative pain score [95% CI: 95% confidence intervals, df: degrees of freedom, Random: random effects model, IV: inverse variance, SD: standard deviation].

access sheath before the procedure, which is an important factor [33]; and the time-consuming manoeuvring, such as placement of the stones in a favourable calyx to avoid strain on the deflection mechanism and risk of the laser fibre damaging the scope required in RIRS for stone fragmentation. In addition, a high stone burden always contributes to a longer operative time and a longer crushing time and implies a significant amount of stone dust and debris that limits visibility [34]. However, certain factors have been identified as the reasons why MPCNL had a longer operative time compared with RIRS [35,36]. Furthermore, placement of the nephrostomy tube in the mini-perc group and the need to switch the patient's position from the lithotomy position to the prone position are also associated with a long operative time in the mini-perc group. According to our clinical experiences, the operative time might be associated with the surgeon's experience and the patients' baseline basic characteristics. Additionally, the operative time in obese patients is longer than in average weight patients [37].The method used to evaluate operative time also has an important role in the reported results. The operative time in different studies was calculated using different criteria, most of which were not clearly defined. This factor was the most important source of high heterogeneity and published bias. In the current study, the meta-analysis on operative time had a high heterogeneity (I^2 = 98%), and the sensitivity analysis and subgroup analysis also showed no statistical significance between the two groups. Our findings on the operative time were somewhat consistent with the existing literature [32,38]. We evaluated eight RCTs, and future high quality RCTs could be used to reduce bias.

Our pooled data indicated that MPCNL had a longer hospital stay (0.89 day) than RIRS, and the observed difference was statistically significant. We assume that the use of a nephrostomy tube for drainage is an important factor affecting the length of the hospital stay. A shorter

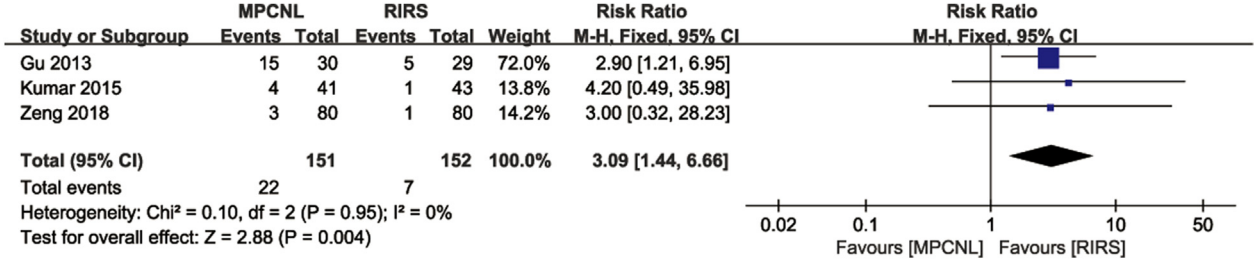

Fig. 8. Forest plot of the haematoma [95% CI: 95% confidence intervals, df: degrees of freedom, Fixed: fixed effects model, M − H, SD: standard deviation].

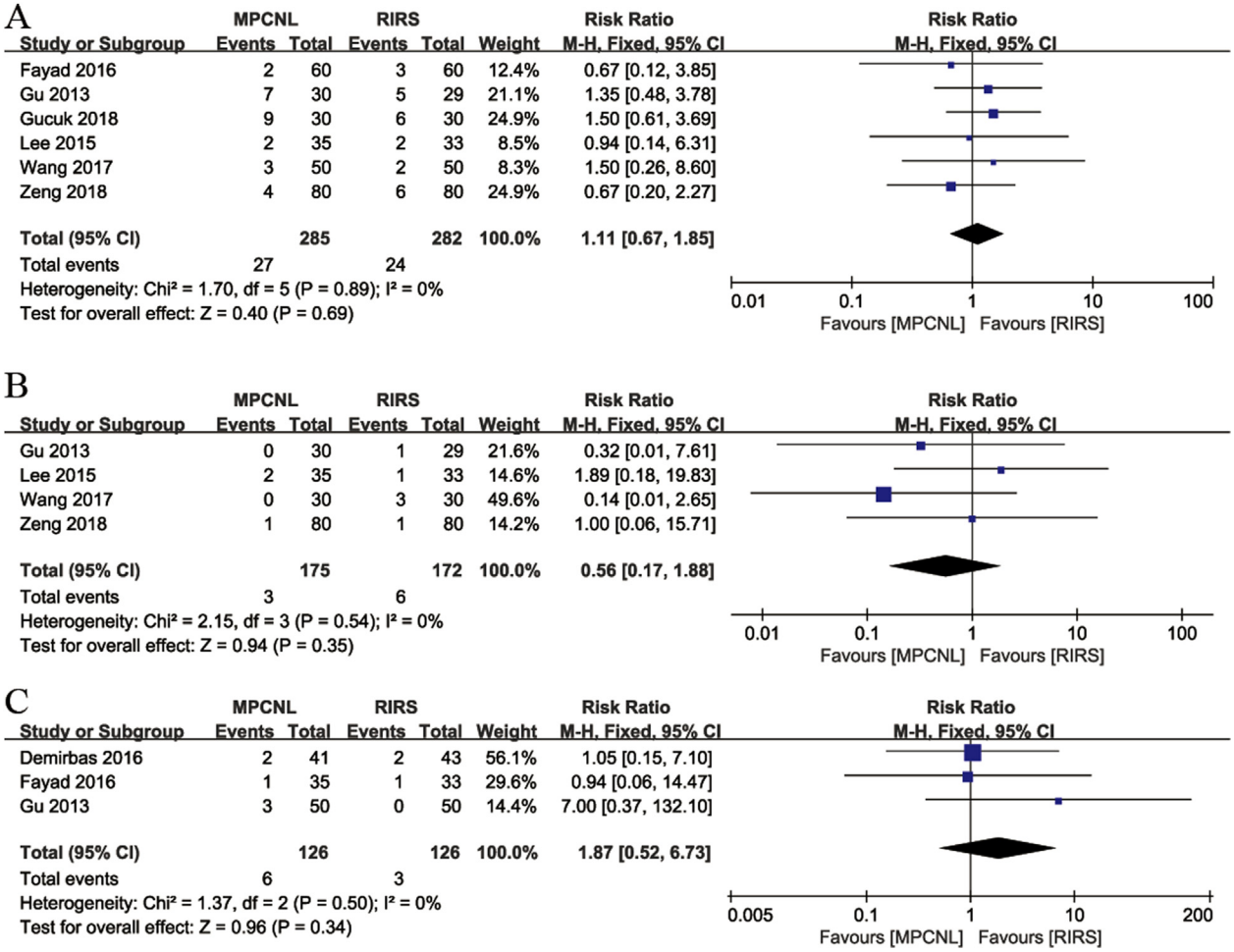

Fig. 9. Forest plots and meta-analyses. **A:** postoperative fever; **B:** urinary perforation; **C:** urinary tract infection [95% CI: 95% confidence intervals, df: degrees of freedom, Fixed: fixed effects model, M − H, SD: standard deviation].

hospital stay, less operative pain and faster recovery were found for RIRS compared to MPCNL. Patients could benefit from the observed differences since these factors could reduce their financial costs.

There was no remarkable difference in the incidence of Clavien–Dindo grade I, II and III complications among the mini-PCNL and RIRS groups. In addition, the incidence of postoperative fever, urinary perforation and urinary tract infection were not significantly different between both groups.

Major procedure-related complications of PCNL included significant bleeding (7.8%), renal pelvis perforation (3.4%), hydrothorax (1.8%) and blood transfusion (5.7%) [39]. With reference to haematoma, mini-PCNL had a significantly higher rate than RIRS according to our meta-analysis. Therefore, the most common complication of MPCNL was renal haemorrhage. Haemorrhage is generally associated with the initial puncture and injury of renal blood vessels and the surrounding organs [40]. The size of the tract is one key factor for blood loss during endourology surgery. A larger tract in PCNL may increase the risk of injury to major blood vessels. The idea behind the use of miniaturized instruments was based on the assumption that the smaller tract diameter could decrease the risk of morbidity resulting in less renal trauma [25]. Compared with standard PCNL, the amount of blood loss was lower in MPCNL. Although the reduced diameter of tract dilation during MPCNL reduces the potential for damage to the renal vasculature and infundibular calyceal tear [41], it can also cause bleeding during the operation. A haemoglobin drop is efficient in expressing the blood loss. The limitation of this study is that we did not perform a meta-analysis on blood loss. Of the eight included studies, only one study [16] reported blood loss data, Hb change (g/dL) (MPCNL0.69 ± 0.98: RIRS 0.38 ± 0.97 $p > 0.05$). Other meta-analyses [38,42] have reported that RIRS leads to a lower Hb drop than MPCNL. Sakr et al. [43] concluded that RIRS is safer than mini-PCNL with respect to blood loss. Furthermore, Hu et al. [44] showed that the drop in Hb was significantly different between MPCNL and RIRS, Hb change (g/dL) (MPCNL − 9.0 ± 12.6: RIRS −3.6 ± 8.5 $p < 0.05$). In contrast to MPCNL, RIRS is an endoscopic surgery that is performed through the natural tract. Therefore, it may cause less trauma to the renal parenchyma and less blood loss during the surgical procedure. Meta-analysis by the fixed-effects model ($I^2 = 0\%$) demonstrated that there was no remarkable difference between mini-PCNL and RIRS with respect to blood transfusion. This finding was because the proper perioperative management would reduce the incidence of severe blood loss. Integrating existing data, RIRS will be a better choice for those patients whose blood loss needs to be taken into consideration. Due to the limited number of studies and the relatively small sample size, subgroup analysis based on MPCNL tract size could not be performed. To determine whether a smaller tract MPCNL would reduce the haematoma rate and transfusion rate to non-significance compared with RIRS, more related studies should include more reliable results. On the other hand, the major complication of RIRS is ureteral avulsion or perforation [8]. A ureteral access sheath was used during RIRS sometimes, which may cause ureteral wall injuries [45]. Nevertheless, in this study, no significant differences were observed with respect to ureteral avulsion or perforation and postoperative fever, which was consistent with other studies [25].

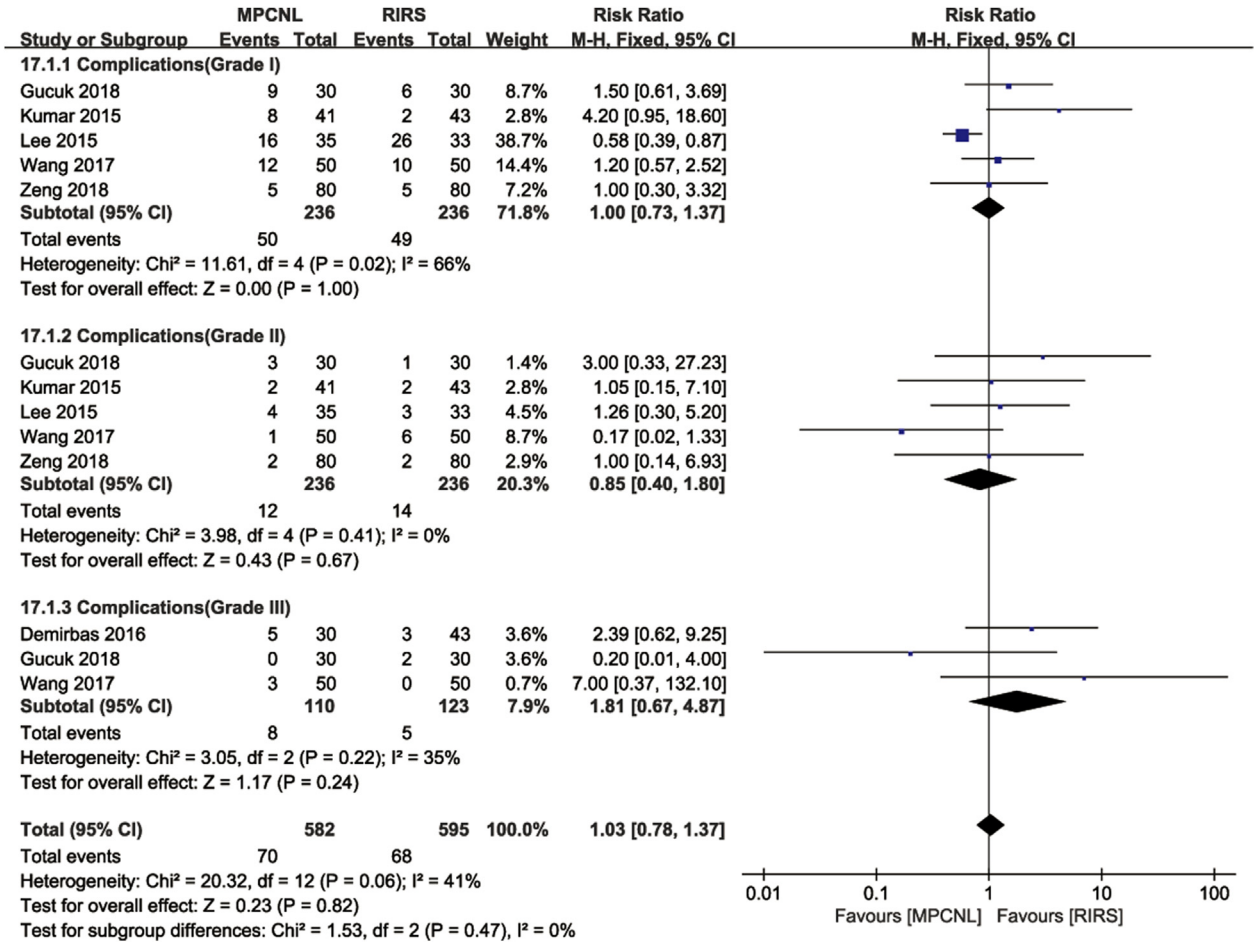

Fig. 10. Forest plot of Clavien–Dindo grade complications for patients undergoing MPCNL and RIRS [95% CI: 95% confidence intervals, df: degrees of freedom, Random: random effects model, Fixed: fixed effects model, M − H, SD: standard deviation].

This study has some limitations. First, the sample size and number of included studies were small, and some relative subgroup analyses could not be performed due to these limitations. Second, some of the included trials failed to describe the blinding methods and detailed randomization concealment, which in turn might lead to conclusion bias. In addition, the definitions of the outcome definitions and measurement were different among the studies included in this meta-analysis, which may explain why heterogeneity among these trials was high with respect to several parameters. Finally, diverse stone size and location may lead to heterogeneities among the included studies. Our findings should be interpreted with caution due to these heterogeneities.

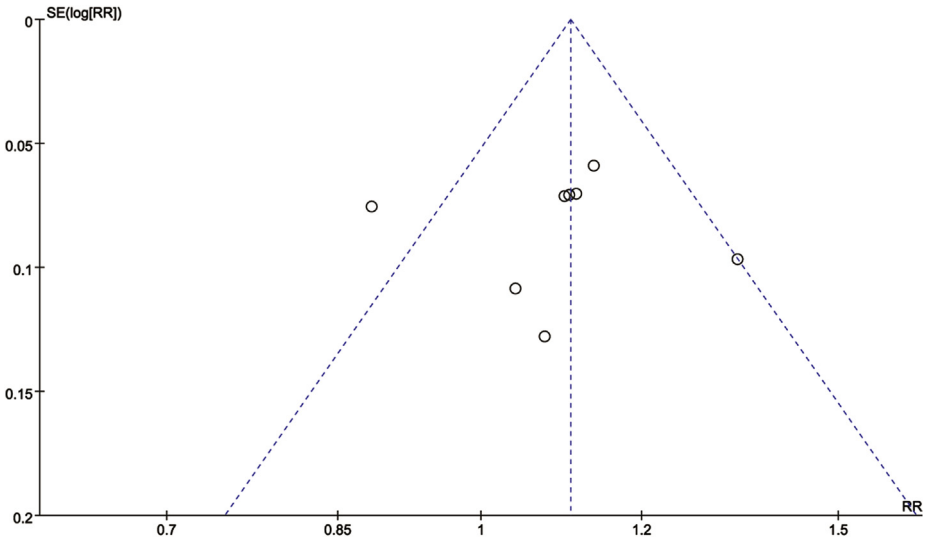

Fig. 11. Funnel plot of stone-free rate for publication bias.

5. Conclusions

This meta-analysis suggests that MPCNL is an effective method for treating upper urinary stones, especially lower calyceal stones that are 1–2 cm in size. Compared to RIRS, MPCNL is associated with a longer hospital stay time and a higher incidence of haematoma. In addition, both methods have proven to be safe. These results should be interpreted with caution since they are based on a mixed group of patients. We hope that the findings of this study will be further confirmed by well-designed prospective RCTs with a larger patient series.

Conflicts of interest

The authors declared that no conflicts of interest exit.

Sources of funding

There was no sources of funding for this meta-analyses.

Ethical approval

Among all of the included 8 studies, 8 studies mentioned the Approval of Institutional Review Board.

Research registration unique identifying number (UIN)

Registration: reviewregistry662.
https://www.researchregistry.com/browse-the-registry#registryofsystematicreviewsmeta-analyses/registryofsystematicreviewsmeta-analysesdetails/5c43fd11bf8eab1113980dbb/

Author contribution

Contribution: (I)study design: Guan Zhang, Binbin Jiao, Zhenkai Luo; (II)data collection: Binbin Jiao, Zhenkai Luo; (III)data analysis and interpretation: Binbin Jiao, Zhenkai Luo, Xin Xu, Meng Zhang; (IV) Manuscript writing: Binbin Jiao, Zhenkai Luo.

Guarantor

In this meta-analysis, the guarantors are Guan Zhang, Binbin Jiao, Zhenkai Luo.

Potential reviewers

The data used in this meta could be available together with the published article if required.

Provenance and peer review

Not commissioned, externally peer-reviewed.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.ijsu.2019.09.005.

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