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Minimally invasive percutaneous nephrolithotomy compared with retrograde intrarenal surgery: a meta-analysis.

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Abstract

Percutaneous Nephrolithotomy (PCNL) and Retrograde Intrarenal Surgery (RIRS) are widely used in the management of kidney stones. But the safety and efficiency between these two technologies is still a mystery. This meta-analysis was performed to compare the efficacy as well as safety of Minimally Invasive Percutaneous Procedures (MIPPs) including ultra mini-PCNL, mini-PCNL, and micro-PCNL with RIRS. PubMed, Embase and Scopus were searched, and twelve studies included data on 1207 cases (613 for MIPPs and 594 for RIRS) satisfied the inclusion criteria and were included in this research finally. MIPPs were found to be associated with higher stone-free rate but longer hospital stays, and a larger drop in hemoglobin levels. Difference between MIPPs and RIRS in complication rate, operative time, and total cost were not notable. Given no obvious difference in the complication rate and higher efficacy, our findings suggest that mini-PCNL should be recommended over RIRS for stones>2 cm, and that for stones<2 cm any of MIPPs or RIRS are reasonable.

Keywords: Percutaneous nephrolithotomy, Retrograde intrarenal surgery, Kidney stones, Meta-analysis.

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Introduction

Kidney stones, is the existence of renal calculi that resulted from a disruption in the balance between precipitation and solubility of salts [1]. Kidney stone is a common disease which affects at least 10% of people. And almost 70% of people who suffer kidney stone will have kidney stones recurred [2].

The 2016 guidelines (http://uroweb.org/guideline/urolithiasis/) made by European Association of Urology (EAU) indicates that PCNL should be used as first-line treatment of kidney stones that larger than 2.0 cm, in case PCNL is not an option, RIRS should be used. And for stones smaller than 2.0 cm, PCNL and RIRS are both recommended.

There has been a dramatic shift in indications for Percutaneous Nephrolithotomy (PCNL) over the last decade. Some studies indicated that through reducing the tract size, complications associated with percutaneous surgery might be reduced [3]. Miniaturized instruments, including mini-PCNL, micro-PCNL and ultra mini-PCNL, have removed the need to dilate the tract over 20 Fr. In this research, we collectively refer to these miniaturized technologies as Minimally Invasive Percutaneous Procedures (MIPPs).

Retrograde Intrarenal Surgery (RIRS) has become increasingly widely used with the advent of technical developments including endoscope miniaturization, enhanced optical quality and tools, improved deflection mechanisms, and the introduction of disposable instruments [4-6].

The EUA guidelines also play emphasis on the appearance of MIPPs, but which technology is better still stay as mystery. The objective of this article was to compare the efficacy as well as safety of MIPPs with RIRS in the therapy of kidney stones through meta-analysis, so that we could provide more supplement materials for the guidelines.

Materials and Methods

Literature search

Relevant articles were searched in October 2016 and updated in February 2017 using PubMed, Scopus, and Embase without limitation of publication types, regions, or languages. MeSH terms and their related words were also used when searched. The search strategy of PubMed is following: ((((Retrograde Intrarenal Surgery (Title/Abstract)) OR Flexible ureteroscopy (Title/ Abstract)) OR retrograde nephrolithotripsy (Title/

Abstract))) AND (((((ultra mini-PCNL (Title/Abstract)) OR mini-PCNL (Title/Abstract)) OR micro-PCNL (Title/Abstract)) OR minimally percutaneous nephrolithotomy (Title/Abstract)) OR micro percutaneous nephrolithotomy (Title/ Abstract)). Related articles were also searched from the reference lists. The complete or the most recent report was used when several passages describing the same population [7].

Inclusion and exclusion criteria

Preferred Reporting Items for systematic reviews and meta-analysis criteria [8] was used to guide the article selection. Detailed inclusion criteria included: (1) Participants: single or multiple renal stones. (2) Interventions: MIPPs or RIRS for renal stones. (3) Comparisons: compared MIPPs and RIRS at the same time. (4) Outcomes: the primary outcomes were stone-free rate and complications (Clavien-Dindo grading system [9] was used to classify the complications). The secondary outcomes were operative time, hemoglobin levels, hospital stays, and total cost. (5) Study design: RCT, retrospective and prospective studies. Exclusion criteria: Studies that only described one of the interventions, animal experimental studies, letters to editor, editorials, reviews, and case reports [10]. Studies involved patients with abnormal renal anatomy (horseshoe, pelvic, and malrotated kidneys, bifid pelvis, ectopic pelvic fusion anomaly) or involved patients with non-opaque stones, and pediatric patients were excluded. Two reviewers (M.Z.L. and H.F.Z.) completed this process, and all disagreement was judged by a senior author (Y.Q.F.).

Quality assessment

The Oxford Centre for Evidence-based Medicine (http://www.cebm.net/index.aspx?o=5653) was used to judge the level of evidence (LE) for included studies. RCTs were assessed by the modified Jadad scale [11]. Retrospective studies and prospective studies was judged by the adjusted Newcastle-Ottawa Scale (NOS) [12]. Scores range from 0 to 9 for Non RCTs. And non RCTs that achieving six or more points as well as RCTs were thought to be of high quality.

Statistical analysis

Review Manager 5.3 (Cochrane Collaboration, Oxford, UK) was assigned to perform the analysis. Weighted Mean Difference (WMD) was used for analysis continuous parameters, and Odds Ratio (OR) was used for binary Variables. If the continuous data presented as range and means, the methodology described by Hozo [13] would be used to calculate standard deviations. We used the chi-square test to assess the statistical heterogeneity between studies with significance set at $p<0.10$, and the I^2 statistic was used to assess heterogeneity. Of course, $I^2=0$ means no heterogeneity. $I^2<30\%$ means low heterogeneity, $30\% \leq I2 \leq 50\%$ means mediate heterogeneity and $I^2>50\%$ means high heterogeneity. The random-effects model (DerSimonian-Laird method) worked when there the heterogeneity between articles was obvious (usually we choose random-effects model when $I^2>50\%$), otherwise, the fixed-effects (Mantel-Haenszel method) worked. The z-test was used to determine the pooled effects and $p<0.05$ was considered statistically significant.

Analyses in the subgroup were also performed to compare difference PCNL techniques and stone sizes on stone-free rate, operative time, and complication rate. Different grade of complications was also taken into considerations. Sensitivity analyses and publication bias analysis were also performed.

Results

Evidence synthesis

Twelve studies including 1207 patients (613 patients for MIPPs and 594 patients for RIRS) meet the inclusion criteria we mentioned above and were included (Figure 1). All studies included were full-text articles. Among all the studies, RIRS was compared with mini-PCNL in six studies [14-19], micro-PCNL in three studies [20-22], ultra-mini PCNL in two studies [23,24], and mixture of mini and micro PCNL in one study [25]. Agreement between the two reviewers was 91.67% for quality assessment of articles. As for the study that both compared micro-PCNL and mini-PCNL with RIRS, we only take it into the overall and stone sizes subgroup analysis, but not for the PCNL devices subgroups (Supplementary Table S1).

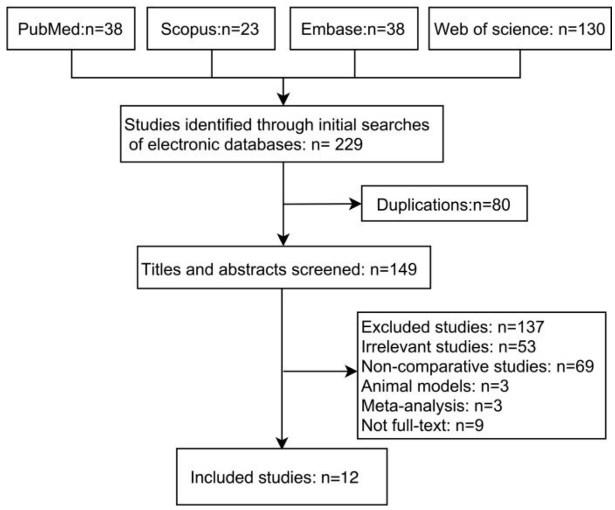

Figure 1. *Flow diagram of studies identified, included, and excluded.*

Characteristics of eligible studies

Characteristics of trails included in this research are shown in Table 1. All studies excluded Kiremit's [25] take age, gender, and stone sizes into considerations, and there is no signification difference between each group. During our research, there were only two small sampled RCTs [16,22] (level of evidence: 2b); eight retrospective studies [14,15,17,19,20,23-25] discussed contemporary series of patients (LE: 3b); three were two prospective studies [18,21], and one of them was matched-pair study [18] (LE: 2b), and the rest [21] was prospective data collection (LE: 3b). As for surgical indications, six studies were about mini-PCNL, three studies about micro-PCNL, two about ultra-mini PCNL, and one study discuss mini-PCNL and micro-PCNL at the same time. Among all the studies, five studies aimed at stones that less than two centimeters, two were more than two centimeter, and the rest were mixture of stone sizes.

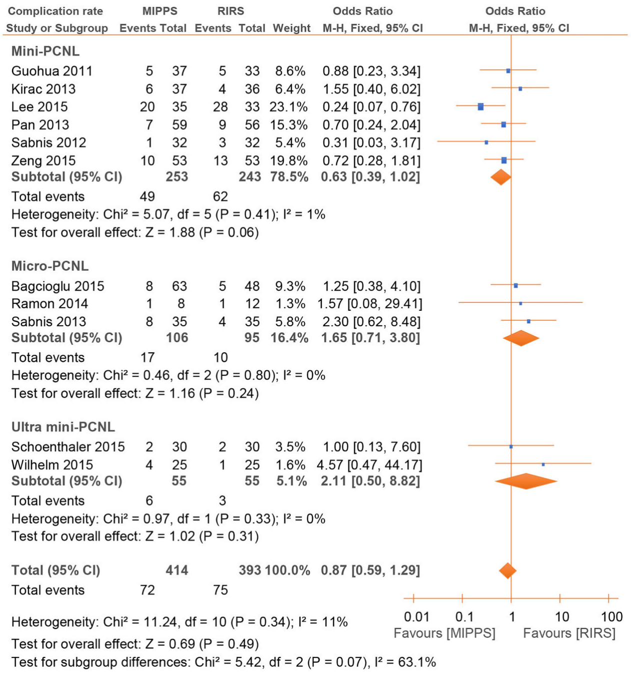

***Figure** 2. Forest plot and meta-analysis of complication rate (classified by instrument of percutaneous procedures). MIPPS: Minimally Invasive Percutaneous Procedures; RIRS: Retrograde Intrarenal Surgery; M-H: Mantel-Haenszel Method; CI: Confidence Interval.*

Quality of included studies

Nine of nonrandomized articles [14,15,17-21,23,24] (NOS: 6 or more of 9 points) were thought to be of high quality, the rest one [25] was low (NOS: 3 of 9 points) (Supplementary Table S2), and two RCTs were also high quality (Supplementary Table S3). None of the included trails discussed about allocation concealment. Matching criteria in trails were variable expect for one study [25], which had no declarations. Ten studies [14-22,24] talked about the detail length of follow-up. Methods for handling missing data were declared in the majority, but not for intention-to-treat.

Overall analysis

The results of overall analysis were summarized in Table 2. As for the analysis of different grade of complications, difference between MIPPs and RIRS in Grade I or II (OR: 0.79; 95% CI, 0.50, 1.24; P=0.30), and III or senior grades (OR: 0.97; 95% CI, 0.39, 2.41; P=0.95) were no significant (Supplementary Figure S1). No obvious difference was found between MIPPs and RIRS relate to operative time (WMD: -1.97 min; 95% CI, -13.00, 9.06; P=0.73), complication rates (OR: 1.22; 95% CI, 0.62, 2.37; P=0.57) ((Supplementary Figure S2) and total cost (WMD: -$75.89; 95% CI, -209.71, 57.93; P=0.27) (Supplementary Figure S3) and secondary operations (OR: 0.53; 95% CI, 0.27, 1.06; P=0.07) (Supplementary Figure S4); MIPPs was associated with higher stone-free rate (OR: 1.70; 95% CI, 1.23, 2.34; P=0.001), greater drop in hemoglobin levels (WMD: 0.48 g/dl; 95% CI, 0.28, 0.67; p<0.00001) (Supplementary Figure S5), and longer hospital stays (WMD: 0.71 days (d); 95% CI, 0.21, 1.21; p<0.00001) (Supplementary Figure S6).

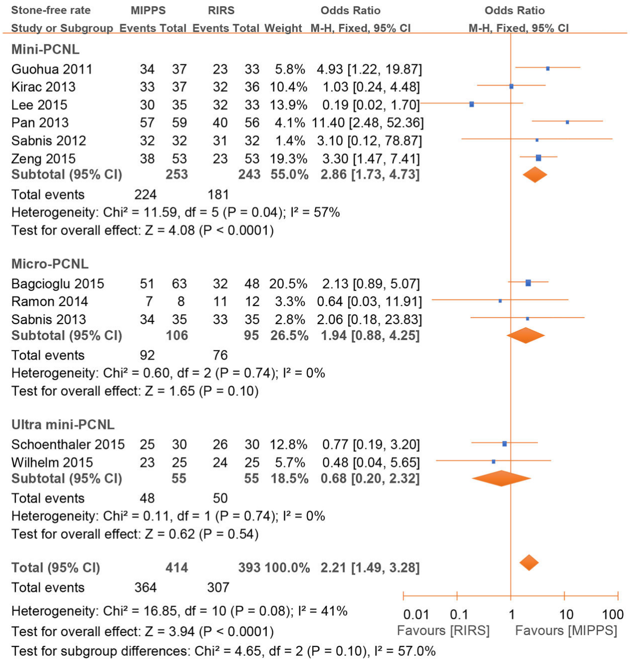

***Figure** 3. Forest plot and meta-analysis of stone-free rate (classified by instrument of percutaneous procedures). MIPPS: Minimally Invasive Percutaneous Procedures; RIRS: Retrograde Intrarenal Surgery; M-H: Mantel-Haenszel Method; CI: Confidence Interval.*

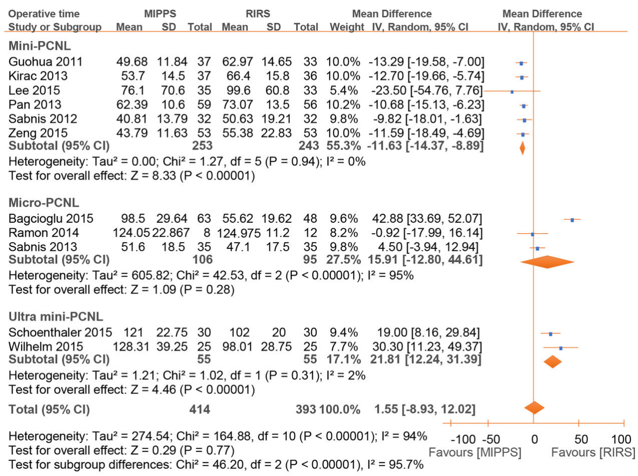

***Figure** 4. Forest plot and meta-analysis of operative time (classified by instruments of percutaneous procedures). MIPPS: Minimally Invasive Percutaneous Procedures; RIRS: Retrograde Intrarenal Surgery; SD; Standard Deviation; IV: Inverse Variance Method; CI: Confidence Interval.*

Subgroup analysis

In the stone sizes subgroup, as for the stone-free rate, difference between MIPPs and RIRS for stones smaller than 2.0 cm was no notable difference (OR: 1.02; 95% CI, 0.64, 1.65; P=0.92) (Supplementary Figure S7). But as for stones bigger than 2.0 cm, MIPPs provide a higher stone-free rate (OR: 4.73; 95% CI, 2.36, 9.47; p<0.0001). As for the operative time, there was no obvious difference between each other (WMD: -7.68 min; 95% CI, -24.81, 9.46, P=0.38) for stones smaller than 2.0 cm (Supplementary Figure S8). And for stones bigger than 2.0 cm, there was significant difference between the two technologies. MIPPs provided a shorter time (WMD: -10.95 min; 95% CI, -14.69, -7.21; p<0.00001).

In the PCNL devices subgroups, result for complication rates seemed the same as the overall analysis (Figure 2). Mini-PCNL seemed have a significant higher stone-free rate when (OR: 2.86; 95% CI, 1.73, 4.73; p<0.0001); while micro-PCNL and ultra mini-PCNL had no significant different compared with RIRS for stone-free rate (Figure 3). As for the operative time, mini-PCNL also provided a shorter operative time (WMD: -11.63 min; 95% CI, -14.37, -8.89, p<0.00001) related to RIRS. Ultra mini-PCNL needed a longer operative time (WMD: 21.81 min; 95% CI, 12.24, 31.39, p<0.00001) compared with RIRS. But as for operation time, there was no significant difference (WMD: 15.91 min; 95% CI, -12.80, 44.61, P=0.28) (Figure 4).

Sensitivity analysis

Nine nonrandomized and two RCTs trails were included when we performed sensitivity analysis (Table 3). In the present study, no obvious difference was found after sensitivity analysis. The heterogeneity between studies remained obvious.

Publication bias

Figure 5 indicates a funnel plot of the selected studies in this research which reported the stone-free rate. Two studies lie outside the 95% CIs. Other articles lie inside the 95% confidence interval, with an unsymmetrical distribution around the vertical, indication potential publication bias.

Table 1. *MIPPS versus RIRS: summary of comparative studies.*

Study	Level evidence	Study period	Design	Inclusion criteria	Patients no.		Type of PCNL technique	Study quality
					MIPPS	RIRS		
Bagciogle et al. [20]	3b	2013/8-2015/1	R	1.0-3.0 cm	63	48	Micro-PCNL	7'
Guohua et al. [14]	3b	2005/5-2010/5	R	Larger than 1.0 cm	37	33	Mini-PCNL	6'
Kirac et al. [15]	3b	2009/12-2012/7	R	Smaller than 1.5 cm	37	36	Mini-PCNL	6'
Kiremit et al. [25]	3b	2012/7-2014/3	R	1.0-2.0 cm	199	201	Mini-PCNL	3'
Lee et al. [16]	2b	2014/6-2015/2	RCT	Larger than 1.0 cm	35	33	Mini-PCNL	6'
Pan et al. [17]	3b	2005/5-2011/2	R	2.0-3.0 cm	59	56	Mini-PCNL	7'
Ramon et al. [21]	3b	2013/9-2013/12	RP	1.0-3.0 cm	8	12	Micro-PCNL	6'
Sabnis et al. [22]	2b	2011/2-2012/8	RCT	Less than 1.5 cm	35	35	Micro-PCNL	6'
Sabnis et al. [18]	2b	2009/3-2011/4	RP	1.0-2.0 cm	32	32	Mini-PCNL	6'
Schoenthaler et al. [23]	3b	2013/4-2014/3	R	1.0-2.0 cm	30	30	Ultra mini-PCNL	6'
Wilhelm et al. [24]	3b	2013/4-2014/4	R	1.0-3.5 cm	25	25	Ultra mini-PCNL	6'
Zeng et al. [19]	3b	2012/12-2014/3	R	Larger than 2.0 cm	53	53	Mini-PCNL	8'

MIPPS: Minimally Invasive Percutaneous Procedures; RIRS: Retrograde Intrarenal Surgery; PCNL: Percutaneous Nephrolithotomy; R: Retrospective; RP: Retrospective Design, Prospective Data Collection; RCT: Randomized Controlled Trail.

Table 2. *Results of meta-analysis comparison of MIPPS and RIRS.*

Outcomes of interest	Studies, no.	MIPPS patients, no.	RIRS patients, no.	WMD/OR* (95% CI)	P value	Study heterogeneity			P value
						χ^2	df	I^2, %	
Overall analysis									
Operative time, min	12	613	594	-1.97 (-13.00 to 9.06)	0.73	222.95	11	95	<0.00001
Stone free-rate, %	12	613	594	1.70 (1.23 to 2.34)	0.001	21.69	11	49	0.03

Complication rate, %	12	613	594	1.22 (0.62 to 2.37)	0.57	28.05	11	61	0.003
Hemoglobin drop, g/dl	8	351	326	0.48 (0.28 to 0.67)	<0.00001	24.77	7	72	0.0008
Hospital stay, day	11	414	393	0.71 (0.21 to 1.21)	0.006	116.38	10	91	<0.00001
Total cost, $	3	159	137	-75.89 (-209.71 to 57.93)	0.27	7.11	2	72	0.03
PCNL subgroup analysis									
Operative time, min									
Using mini-PCNL	6	253	243	-11.63 (-14.37 to -8.89)	<0.00001	1.27	5	0	0.94
Using micro-PCNL	3	106	95	15.91 (-12.80 to 44.61)	0.28	42.53	2	95	<0.00001
Using ultra mini-PCNL	2	55	55	21.81 (12.24 to 31.39)	<0.00001	1.02	1	2	0.31
Total	11	414	393	1.55 (-8.94 to 12.02)	0.77	164.88	10	94	<0.00001
Stone free-rate, %									
Using mini-PCNL	6	253	243	2.86 (1.73 to 4.73)	<0.0001	11.59	5	57	0.04
Using micro-PCNL	3	106	95	1.94 (0.88 to 4.25)	0.1	0.6	2	0	0.74
Using ultra mini-PCNL	2	55	55	0.68 (0.20 to 2.32)	0.54	0.11	1	0	0.74
Total	11	414	393	2.21 (1.49 to 3.28)	<0.0001	16.85	10	41	0.08
Complication rate, %									
Using mini-PCNL	6	253	243	0.63 (0.39 to 1.02)	0.06	5.07	5	1	0.41
Using micro-PCNL	3	106	95	1.65 (0.71 to 3.80)	0.24	0.46	2	0	0.8
Using ultra mini-PCNL	2	55	55	2.11 (0.50 to 8.82)	0.31	0.97	1	0	0.33
Total	11	414	393	0.87 (0.59 to 1.29)	0.49	11.24	10	11	0.34
Stone sizes subgroup analysis									
Stone free-rate, %									
Smaller than 2.0 cm	5	333	334	1.02 (0.64 to 1.65)	0.92	0.93	4	0	0.92
Bigger than 2.0 cm	2	112	109	4.73 (2.36 to 9.47)	<0.00001	2.04	1	51	0.15
Stone mixture	5	168	151	1.62 (0.89 to 2.96)	0.12	7.82	4	49	0.1
Total	12	613	594	1.70 (1.23 to 2.34)	0.001	21.69	11	49	0.03
Operative time, min									
Smaller than 2.0 cm	5	333	334	-7.68 (-24.81 to 9.46)	0.38	82.82	4	95	<0.00001
Bigger than 2.0 cm	2	112	109	-10.95 (-14.69 to -7.21)	<0.00001	0.05	1	0	0.83
Stone mixture	5	168	151	7.98 (-21.31 to 37.28)	0.59	108.24	4	96	<0.00001
Total	12	613	594	-1.97 (-13.00 to 9.06)	0.73	222.95	11	95	<0.00001

MIPPS: Minimally Invasive Percutaneous Procedures; RIRS: Retrograde Intrarenal Surgery; PCNL: Percutaneous Nephrolithotomy; WMD/OR: Weighted Mean Difference/Odds Ratio; df: Degrees of Freedom; CI: Confidence Interval.

***Table 3.** Result of sensitivity analysis comparison of MIPPS and RIRS.*

Outcomes of interest	Studies, no.	MIPPs patients, no.	RIRS patients, no.	WMD/OR* (95% CI)	P value	Study heterogeneity			P value
						χ^2	df	I^2, %	
Overall analysis									

Operative time, min	11	414	393	1.55 (-8.93 to 12.02)	0.77	164.88	10	94	<0.00001
Stone free-rate, %	11	414	393	2.21 (1.49 to 3.28)	<0.0001	16.85	10	41	0.08
Complication rate, %	11	414	393	0.87 (0.59 to 1.29)	0.49	11.24	10	11	0.34
Hemoglobin drop, g/dl	8	351	326	0.48 (0.28 to 0.67)	<0.00001	24.77	7	72	0.0008
Hospital stay, day	11	414	393	0.71 (0.21 to 1.21)	0.006	116.38	10	91	<0.00001
Total cost, $	4	189	167	-75.89 (-209.71 to 57.93)	0.27	7.11	2	72	0.03
PCNL subgroup analysis									
Operative time, min									
Using mini-PCNL	6	253	243	-11.63 (-14.37 to -8.89)	<0.00001	1.27	5	0	0.94
Using micro-PCNL	3	106	95	15.91 (-12.80 to 44.61)	0.28	42.53	2	95	<0.00001
Using ultra mini-PCNL	2	55	55	21.81 (12.24 to 31.39)	<0.00001	1.02	1	2	0.31
Total	11	414	393	1.55 (-8.94 to 12.02)	0.77	164.88	10	94	<0.00001
Stone free-rate, %									
Using mini-PCNL	6	253	243	2.86 (1.73 to 4.73)	<0.0001	11.59	5	57	0.04
Using micro-PCNL	3	106	95	1.94 (0.88 to 4.25)	0.1	0.6	2	0	0.74
Using ultra mini-PCNL	2	55	55	0.68 (0.20 to 2.32)	0.54	0.11	1	0	0.74
Total	11	414	393	2.21 (1.49 to 3.28)	<0.0001	16.85	10	41	0.08
Complication rate, %									
Using mini-PCNL	6	253	243	0.63 (0.39 to 1.02)	0.06	5.07	5	1	0.41
Using micro-PCNL	3	106	95	1.65 (0.71 to 3.80)	0.24	0.46	2	0	0.8
Using ultra mini-PCNL	2	55	55	2.11 (0.50 to 8.82)	0.31	0.97	1	0	0.33
Total	11	414	393	0.87 (0.59 to 1.29)	0.49	11.24	10	11	0.34
Stone sizes subgroup analysis									
Stone free-rate, %									
Smaller than 2.0 cm	4	134	133	1.12 (0.46 to 2.72)	0.8	0.9	3	0	0.83
Bigger than 2.0 cm	2	112	109	4.73 (2.36 to 9.47)	<0.00001	2.04	1	51	0.15
Stone mixture	5	168	151	1.62 (0.89 to 2.96)	0.12	7.82	4	49	0.1
Total	11	414	393	2.21 (1.49 to 3.28)	<0.0001	16.85	10	41	0.08

Operative time, min									
Smaller than 2.0 cm	4	134	133	-0.18 (-13.31 to 12.95)	0.98	28.97	3	90	<0.00001
Bigger than 2.0 cm	2	112	109	-10.95 (-14.69 to -7.21)	<0.00001	0.05	1	0	0.83
Stone mixture	5	168	151	7.98 (-21.31 to 37.28)	0.59	108.24	4	96	<0.00001
Total	11	414	393	1.55 (-8.94 to 12.02)	0.77	164.88	10	94	<0.00001

MIPPS: Minimally Invasive Percutaneous Procedures; RIRS: Retrograde Intrarenal Surgery; PCNL: Percutaneous Nephrolithotomy; WMD/OR: Weighted Mean Difference/Odds Ratio; df: Degrees of Freedom; CI: Confidence Interval.

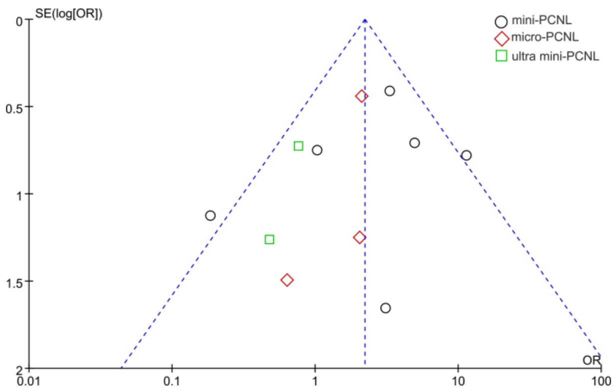

Figure 5. *Funnel plots illustrating meta-analysis of stone-free rate. SE: Standard Error; OR: Odds Ratio.*

Discussion

This meta-analysis made up of 10 non-randomized and 2 RCTs articles comparing the efficacy and safety of MIPPs with RIRS included data from 1209 patients. It was shown that MIPPs were more effective than RIRS, with a higher stone-free rate. However, RIRS was safer, with lower decreases in hemoglobin levels and shorter hospital stays. No obvious difference was found in complication rates, total cost, and operative time between the two technologies.

Mini-PCNL with ureteroscopy was first described [26], with the standard mini-PCNL technique being first described [27]. This was followed by the description of micro-PCNL by Bader et al. [28] and ultra mini-PCNL by Desai et al. [29]. The most important change in these instruments is the size of the sheath, but it must be noted that the scale of the procedure may have some limitations on the surgeon's performance.

The overall analysis showed that MIPPs resulted in a higher stone-free rate related to RIRS, a finding that differs from that of a previous meta-analysis [30]. When MIPPs were analysed according to technology type, pooled data showed that mini-PCNL was superior to RIRS, while ultra mini-PCNL and micro-PCNL were not significantly different compared with RIRS. Reasons for this observation may be the experience of the surgeons and the technique itself, whereby stone-free rates may improve with increasing surgeon`s skill and the length of time a technology has been established. However, sheath sizes, stone sizes, surgeon's habits, work conditions, and tools used may have limitations on the stone-free rate.

It is important to consider the complications caused by surgery, and complication rates were compared among pooled studies. In the overall analysis difference between MIPPs and RIRS was no significant, even when analysed by grade of complications and type of MIPPs. And this is quite different from the previous meta-analysis [30]. We could easily find in the Figure 2 that in most micro-PCNL studies, the complication rates were lower than RIRS. While in micro-PCNL group and ultra mini-PCNL groups, it was opposite. This may be because of poor experience of using ultra mini-PCNL and micro-PCNL, alongside the limitation of the sheath size itself. Stone sizes and surgeon's working conditions may have also contributed to this finding. All in all, the development of PCNL instruments as well as the improvement of hospital care may play important roles in this problem.

Operative time is also an important factor for surgeons. Although difference between MIPPs and RIRS in the overall analysis was no significant, we found the time taken to perform mini-PCNL was less than that for RIRS in the subgroup analysis. However, ultra mini-PCNL took longer, and the difference in operative time between micro-PCNL and RIRS was no significant. In the subgroup analysis by stone sizes, we found that MIPPs had a shorter operative time than RIRS for stones>2.0 cm. This may be because larger stones are fragmented to the required size for spontaneous passage rather than removal of fragments by basket catheter. The reasons for this may be the same as those underlying the findings for complication rates.

The pooled analysis of the effect on hemoglobin levels showed that RIRS resulted in a lower reduction in hemoglobin levels compared with MIPPs, an observation that was consistent across almost all the studies analysed. This may because of the non-invasive nature of RIRS, whereby the surface and inner normal kidney tissues are undamaged, compared with the more invasive MIPPs techniques.

Shorter hospital stays are an advantage of RIRS. All studies expect Wilhelm [24] indicated that RIRS resulted in shorter hospital stays compared with MIPPs. Again, reasons underlying this may be similar to those proposed for the analysis of hemoglobin levels.

Cost of surgery is an important aspect to consider. Only three studies compared costs between the two techniques [14,17,20], and among these studies, no significant difference was found between MIPPs and RIRS. This may be because of medical policies in each country. We also compared the need for secondary operations between MIPPs and RIRS, which might have great influence on the cost of surgery. And we found no significant different between each other. But when we taking stone-free rate into consideration we could find that MIPPs provided higher stone-free rate than RIRS, which means RIRS may have more opportunity for a secondary operation. And this might cost more as the previous study said [17]. All in all, more studies should be performed for detail information.

Regarding the stone-free rate, we found the surprising result that difference between the two technologies for stone sizes<2.0 cm was no significant. In practice this may mean that when dealing with stones<2.0 cm, the use of RIRS warrants attention because of its similar efficacy but lower decrease in hemoglobin levels and shorter hospital stays compared with MIPPs.

The findings observed in the subgroup analysis of stone sizes support the European Association of Urology guidelines. Although we did not compare traditional PCNL with MIPPs in this study, we observed a great improvement with MIPPs, in contrast to the findings of the previous meta-analysis [30]. Not only the type of PCNL instruments, but also the improvement of hospital care, the surgeons' skills may have important influence on the results. Taking hemoglobin levels, hospital stays, and other important factors into consideration, it is possible that MIPPs is superior to traditional PCNL, and should be recommended first in patients with kidney stones.

To judge the potential influence of study quality on the outcomes, a sensitivity analysis was performed, and only studies of high quality were included. But it seemed little difference was found compared with the overall analysis. Although a research including only RCTs would provide a stronger level of evidence, the very limited number of random control trials stopped us from attaining any firmly conclusions. It is difficult to perform RCTs comparing MIPPs and RIRS because of patient expectations and ethical concerns, that`s why meta-analysis was needed.

Between-study heterogeneity was not notable for stone-free rate but was notable for most continuous variable. This may be resulted from the difference in outcome definitions, follow-up imaging, surgical practices, and so on. Using the random-effects model may have some ability to lessen the influence of heterogeneity, but does not eliminate it.

This meta-analysis has some limitations maybe that ought to be considerate. One thing we could not ignore is that the number and sample sizes of RCTs were small. And inadequate random sequence generation increases the risk of bias. So further comparative studies, particularly RCTs are necessary to make definitive recommendations, as most of the included studies had relatively small sample sizes, and the inclusion criteria as well as some definitions of outcomes for these trials were different. Furthermore, the included studies involved surgeons with different levels of surgical expertise, which may have influenced the outcomes. And only a limited number of studies examined ultra-mini-PCNL and micro-PCNL. Devices used at each medical center may vary, including the possibility that they were all referred to as RIRS or MIPPs. Differences in the sizes of instruments may also vary, further affecting our findings.

In conclusion, this research shows that MIPPs may be linked with higher stone-free rates, but that RIRS may be associated with a shorter hospital stays and lower decreases in hemoglobin levels. Given the higher efficacy and no notable difference in complication rates, our findings suggest that mini-PCNL should be recommended over RIRS for stones>2 cm, and that for stones<2 cm any of MIPPs or RIRS are reasonable. And in future more RCTs are needed to further explore the results of this research.

Disclosure of Conflict of Interest

None

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