

# Minimally invasive nephrolithotomy versus retrograde intrarenal surgery in surgical management of Lower calyceal stones: a systematic review with meta-analysis

Ming Liu, MD<sup>b</sup>, Jun Hou, MD<sup>a</sup>, FeiHong Xu, MD<sup>a</sup>, HuiFang Du, MD<sup>a</sup>, JingXuan Liu, MD<sup>a</sup>, Ning Li, PhD<sup>a,\*</sup>

**Objective:** The efficacy and safety of minimally invasive nephrolithotomy (MPCNL) versus retrograde intrarenal surgery (RIRS) was assessed for lower calyceal (LC) stones.

**Methods:** Our team conducted a systematic literature search up to December, 2022, using PUBMED, EMBASE and the Cochrane Library. The study was registered in PROSPERO, CRD 42021247197. Randomized controlled trials evaluating the efficacy and safety of MPCNL versus RIRS for LC stones were collected. Heterogeneity among the studies was assessed using the  $\chi^2$  test based on the Q and  $I^2$  tests. Pooled effect sizes were calculated using a fixed model if  $I^2$  is less than 50%; otherwise, a random-effects model was chosen. The primary outcomes were the 3-month stone-free rate (3SFR) and total complications, while the secondary outcomes were the operating time, hospital stay, haemoglobin reduction, bleeding, postoperative fever and complications with the Clavien–Dindo system. A subgroup analysis of 10–20 mm LC stones was also designed.

**Results:** A total of 7 peer-reviewed trials comprising 711 patients were identified. No statistical differences were observed in the heterogeneity results of the 3SFR or total complications (P > 0.1,  $I^2 < 50\%$ ). Compared with RIRS, MPCNL had an unfavourable safety profile, resulting in total complications [odds ratio (OR): 1.87 (95% CI: 1.05, 3.33); P = 0.03], haemoglobin reduction [OR: 0.81 (95% CI: 0.15, 1.47); P = 0.02] and complications with Grade I [OR: 5.52 (95% CI: 1.34, 22.83); P = 0.02] but an improved efficacy and 3SFR [OR: 2.43 (95% CI: 1.48, 3.97); P = 0.0004]. As for the 10–20 mm LC stones, compared with RIRS, MPCNL also had an unfavourable safety profile, resulting in total complications [OR: 2.47 (95% CI: 1.20, 5.07); P = 0.01], complications with Grade I [OR: 4.97 (95% CI: 0.99, 25.01); P = 0.05] and an increased hospital stay [OR: 2.46 (95% CI: 2.26, 2.66); P = 0.00001] but an improved efficacy and 3SFR {OR: 3.10 (95% CI: 1.61, 5.99); P = 0.0008]. The efficacy effect of MPCNL and safety effect of RIRS were nearly equal for both stones sized less than 20 mm (number needed to treat = 17, number needed to harm = 20) and stones sized 10–20 mm (number needed to treat = 20, number needed to harm = 13). No statistical difference was found between the MPCNL and RIRS groups for the rest of outcomes.

**Conclusion:** Both MPCNL and RIRS are safe and effective management methods. Moreover, compared with RIRS, MPCNL had an unfavourable safety profile but improved efficacy for LC stones of ≤20 mm or 10–20 mm, and the differences were statistically significant. The relative profit of efficacy of MPCNL was similar to the relative profit of safety of RIRS.

Keywords: meta-analysis, minimally invasive nephrolithotomy, retrograde intrarenal surgery, lower calyceal stones

Departments of <sup>a</sup>Urology and <sup>b</sup>Operations and Performance Management Office, Fourth Affiliated Hospital, China Medical University, Shenyang, Liaoning, China

M.L. and J.H. contributed equally to this paper.

Sponsorships or competing interests that may be relevant to content are disclosed at the end of this article.

\*Corresponding author. Address: Department of Urology, Fourth Affiliated Hospital of China Medical University, 4 Chongshan East Rd, Shenyang, Liaoning, China, 110032. Tel: 86-24-62042270. fax: 86-24-62571119. E-mail address: air-nick@hotmail.com (N. Li).

Copyright © 2023 The Author(s). Published by Wolters Kluwer Health, Inc. This is an open access article distributed under the terms of the Creative Commons Attribution-Non Commercial-No Derivatives License 4.0 (CCBY-NC-ND), where it is permissible to download and share the work provided it is properly cited. The work cannot be changed in any way or used commercially without permission from the journal.

International Journal of Surgery (2023) 109:1481-1488

Received 11 December 2022; Accepted 29 March 2023

Supplemental Digital Content is available for this article. Direct URL citations are provided in the HTML and PDF versions of this article on the journal's website, www. journal-surgery.net.

Published online 11 April 2023

http://dx.doi.org/10.1097/JS9.0000000000000394

## **HIGHLIGHTS**

- Two most widely used surgical methods for lower calyceal stones were analyzed.
- This is the first meta-analysis which is based totally on randomized controlled trails (RCTs).
- Sub-analysis for lower calyceal stones 10–20 mm also was
- Remarkable difference was noticed in the main outcomes.
- The relative profit of efficacy for minimally invasive nephrolithotomy was similar to the relative profit of safety of retrograde intrarenal surgery.

## Introduction

Renal stones are one of the most common diseases, and their incidence is increasing across the world<sup>[1]</sup>. Lower calyceal (LC) stones account for ~35% of all cases of renal stones<sup>[2]</sup>. Extracorporeal shock wave lithotripsy, percutaneous nephrolithotomy (PCNL) and

retrograde intrarenal surgery (RIRS) are the active surgery options for LC stones. As a result of anatomical variations in LC, especially considering stone clearance, extracorporeal shock wave lithotripsy has usually failed. PCNL has been used as an effective, successful and easy approach to treating LC stones. However, the risks of complications and nephron loss are concerning<sup>[3]</sup>. In addition, in pace with the development of technology, the miniaturization of PCNL has also been carried out in order to reduce the incidence of various access-related complications<sup>[4]</sup>. Meanwhile, improvements in endoscopy technology have made RIRS an attractive treatment option for LC stones, but again, due to anatomical reasons and the durability of the instruments involved, it may not always be possible to perform RIRS for LC stones<sup>[5]</sup>. For the management of lower calyceal stones, minimally invasive nephrolithotomy (MPCNL) and RIRS are the currently available options, each with its own success rates and morbidities<sup>[1]</sup>. Previously, a similar meta-analysis published in 2020 compared MPCNL with RIRS for 10-20 mm LC stones<sup>[6]</sup>. However, there were only two randomized controlled trails (RCTs) and three case-controlled trials included in the study. Over time, more RCTs have been published. Therefore, it is necessary to conduct an RCT based meta-analysis.

With the publication of new RCTs, do we find a higher level of evidence for the treatment of LC stones? In the current study, a head-to-head meta-analysis was designed to comprehensively assess the efficacy and safety of MPCNL versus RIRS for LC stones. To our knowledge, this is the first meta-analysis which is based totally on RCTs.

## **Materials and methods**

## Search strategy

Cochrane Library, PubMed, and EMBASE were searched for RCTs (search performed on 3 JUNE 2020 with no date restrictions). The search terms that we used were "kidney stone", "lower" and "randomized controlled trials" (Supplementary

Tables 1-3, Supplemental Digital Content 1, http://links.lww.com/JS9/A296, Supplemental Digital Content 2, http://links.lww.com/JS9/A297, Supplemental Digital Content 3, http://links.lww.com/JS9/A298). We also reviewed the references of the relevant articles, and no additional papers were obtained. A study protocol was not prepared. The study was registered in PROSPERO, CRD42021228404 and is accessible at: https://www.crd.york.ac.uk/PROSPERO/display\_record.php?RecordID=247197.

Initially, following registration in PROSPERO, our team prepared to design a network meta-analysis to assess surgical options for lower calyceal stones sized 10–20 mm. However, owing to the lack of eligible randomized controlled trails, we eventually chose to conduct head-to-head meta-analysis. For the same reason, only MPCNL and RIRS, which are the most active surgical methods were analyzed.

Each article identified through the electronic search was screened by two reviewers for relevance, initially using the title and abstract and subsequently by reading the full text to select articles that met the inclusion criteria. The work is reported in line with the search strategy promoted by the Preferred Reporting Items for Systematic Reviews and Meta-analysis (PRISMA, Supplemental Digital Content 4, http://links.lww.com/JS9/A299, Supplemental Digital Content 5, http://links.lww.com/JS9/A300) guidelines<sup>[7]</sup>. Only peer-reviewed studies were investigated, we did not search for grey literature, non-English papers or studies in registries. Moreover, our self-evaluation of the quality of this work showed that it had a high level of compliance with the Assessing the Methodological Quality of Systematic Reviews (AMSTAR, Supplemental Digital Content 6, http://links.lww.com/JS9/A301) guidelines<sup>[8]</sup>.

Records of the selection process were retained and a PRISMA flowchart was generated (Fig. 1) Supplemental Digital Content 4, http://links.lww.com/JS9/A299. Originally, four articles containing four RCTs were included. A latter search was performed on 2 March 2022, and two new articles [9,10] were included, while a more recent search was performed on 9 December 2022, and

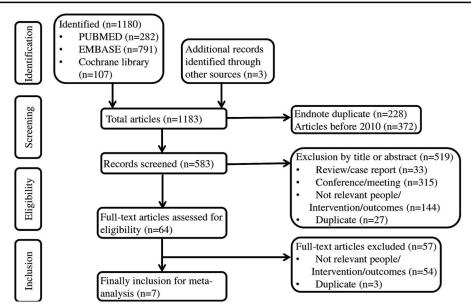


Figure 1. PRISMA flow diagram showing study selection process and rationale for exclusions. EMBASE, Excerpta Medica database; PRISMA, preferred reporting items for systematic reviews and meta-analyses.

Table 1

### Assessment of basic characteristic.

Study	Trial design	Number/groups	Diagnosis	Stone size (mm)	Number	SFR (month)	Population
Coskun <i>et al.</i> <sup>[9]</sup>	RCT	25/MPCNL, 25/RIRS	CT	10–20	50	3	LC, 18–65 years
Fayad et al.[12]	RCT	55/MPCNL, 51/RIRS	CT	≤20	106	3	LC, 18-75 years
Jiang <i>et al</i> . <sup>[13]</sup>	RCT	58/MPCNL, 58/RIRS	CT	≤20	116	3	LC, $\geq$ 18 years
Jin <i>et al</i> . <sup>[14]</sup>	RCT	106/MPCNL, 110/RIRS	CT	10-20	216	3	LC, average 52.3 years
Kumar <i>et al.</i> <sup>[15]</sup>	RCT	41/MPCNL, 43/RIRS	CT	10-20	84	3	LC, $\geq$ 15 years
Perri et al.[11]	RCT	36/MPCNL, 36/RIRS	CT	10-20	72	3	LC, 18-75 years
Yavuz <i>et al.</i> [10]	RCT	34/MPCNL, 33/RIRS	CT	10-20	67	3	LC, 18-75 years
Total	_	319/MPCNL, 320/RIRS			639	_	_

CT, computerized tomography; LC, stones located in lower calyceal; MPCNL, minimally invasive nephrolithotomy; RCT, randomized controlled trial; RIRS, retrograde intrarenal surgery; SFR, stone-free rate.

one new article<sup>[11]</sup> was included. The baseline characteristics of these seven studies are summarized in Table 1. All disputes arising during the systematic literature review process were resolved by a third reviewer.

#### Inclusion and exclusion criteria

RCTs from the last 10 years were included if the patients with LC stones were treated by MPCNL or RIRS with follow-up of the stone-free rate for 3 months (3SFR) after the procedure. Patients with urinary stones in other locations, non-English articles, conference papers, case reports and case series were excluded.

## Assessment of quality and baseline characteristics

All seven RCTs<sup>[9–15]</sup> were randomized studies. The baseline characteristics are presented in Table 1. The quality of evidence for the retrieved references was determined using the Cochrane risk of bias tool<sup>[16]</sup>. ①Was randomization carried out appropriately? ②Were the baselines between groups comparable? ③Was the concealment of treatment allocation adequate? ④Were the care providers, participants and outcome assessors blind to the treatment allocation? ⑤Were the lost visit and specific number of missing data reported? ⑥Was there any evidence to suggest that the authors measured more outcomes than they reported? ⑦Did the analysis include an intention to treat analysis? The assessments of the quality are presented in Table 2. No significant differences were found from in the quality evaluations of the six RCTs<sup>[9,10,12–15]</sup>.

## Data analysis

The data were analyzed using RevMan v5.3.0 (Cochrane Collaboration). The odds ratio (OR) was employed to assess dichotomous and continuous data, and the risk difference was

employed to calculate the number needed to treat (NNT) and number needed to harm (NNH). We analyzed comparable data using 95% CIs and P values. Heterogeneity among the studies was assessed using the  $\chi^2$  test based on the Q and  $I^2$  tests ( $I^2 > 50\%$  is considered of substantial heterogeneity; a P value of Q test less than 0.1 will be considered statistically significant). An individual study was characterized as a fixed model if P is greater than 0.1 and  $I^2$  less than 50%; otherwise, a random-effects model was chosen.

## **Results**

# Heterogeneity

Only seven RCTs were included; therefore, it seemed meaningless to assess them for publication bias. Nevertheless, a funnel plot was drawn and showed that all the studies presented a symmetric distribution, which proved that nearly no publication bias existed (Supplementary Fig. 1, Supplemental Digital Content 7, http://links.lww.com/JS9/A302), Supplemental Digital Content 11, http://links.lww.com/JS9/A306.

# The 3-month stone-free rate

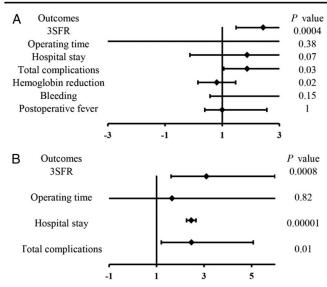
A total of seven RCTs<sup>[9–15]</sup> involving 711 participants (355 in the MPCNL group and 356 in the RIRS group) contained data on the 3SFR. No obvious between-study heterogeneity (P=0.46, I<sup>2</sup> = 0%) was found. Using a fixed-effects model for the 3SFR [OR: 2.43 (95% CI: 1.48, 3.97); P=0.0004 < 0.05]; (Fig. 2A or Table 3 or Supplementary Fig. 2A, Supplemental Digital Content 8, http://links.lww.com/JS9/A303), Supplemental Digital Content 11, http://links.lww.com/JS9/A306, we showed significant differences between MPCNL and RIRS.

100			
	101	1=1	$\sim$

## Assessment of quality.

Study	Randomization	Alloca ted	Blinding	Baseline	Loss of follow-up	Selective report results	ITT
Coskun et al.[9]	Unclear	No	No	Comparable	Yes (n=0)	Unclear	Yes
Fayad <i>et al.</i> <sup>[12]</sup>	Unclear	No	Unclear	Comparable	Yes $(n = 14)$	Unclear	Unclear
Jiang <i>et al</i> . <sup>[13]</sup>	Unclear	No	Unclear	Comparable	Yes $(n=3)$	Unclear	Unclear
Jin <i>et al</i> . <sup>[14]</sup>	Simple random sampling	No	Unblinded	Comparable	Yes $(n=0)$	Unclear	Yes
Kumar <i>et al</i> . <sup>[15]</sup>	Computer generated	Yes	Unclear	Comparable	Yes $(N = 23)$	Unclear	Unclear
Perri <i>et al.</i> <sup>[11]</sup>	Randomization software	Yes	Unclear	Comparable	Yes $(n=0)$	Unclear	Unclear
Yavuz <i>et al.</i> <sup>[10]</sup>	Computer generated	No	Unclear	Comparable	Yes $(n=7)$	Unclear	Unclear

ITT, intention to treat.



**Figure 2.** Forest plots and meta-analyses. (A) 3SFR, total complications, operating time, hospital stay, haemoglobin reduction, bleeding, postoperative fever. (B) subgroup analysis for 3SFR, total complications, operating time, hospital stay. 3SFR, 3-month stone-free rate; df, degrees of freedom; Fixed, fixed-effects model; M-H, Mantel-Haenszel.

## Total complications

A total of five RCTs<sup>[10,12–15]</sup> involving 589 participants (294 in the MPCNL group and 295 in the RIRS group) contained data on the total complications. No obvious between-study heterogeneity (P = 0.53,  $I^2 = 0\%$ ) was found. Using a fixed-effects model, for total complications [OR: 1.87 (95% CI: 1.05, 3.33); P = 0.03 < 0.05]; (Fig. 2A or Table 3 or Supplementary Fig. 2E, Supplemental Digital Content 8, http://links.lww.com/JS9/A303), Supplemental Digital Content 11, http://links.lww.com/JS9/A306, we showed significant differences between MPCNL and RIRS.

# Other five outcomes

A total of two RCTs<sup>[13,14]</sup> involving 332 participants (164 in the MPCNL group and 168 in the RIRS group) contained data on haemoglobin reduction. No obvious between-study heterogeneity (P = 0.37,  $I^2 = 0\%$ ) was found. Using a fixed-effects

model for haemoglobin reduction [OR: 0.81 (95% CI: 0.15, 1.47); P = 0.02], showing the significant differences between MPCNL and RIRS. The results for the operating time, hospital stay, bleeding and postoperative fever, showed no significant differences, respectively (Fig. 2A or Table 3 or Supplementary Fig. 2, Supplemental Digital Content 8, http://links.lww.com/JS9/A303, Supplemental Digital Content 11, http://links.lww.com/JS9/A306 -3, Supplemental Digital Content 9, http://links.lww.com/JS9/A304), Supplemental Digital Content 11, http://links.lww.com/JS9/A306.

## Results of subgroup analyses for 10-20 mm LC stones

For the 3SFR [OR: 3.10 (95% CI: 1.61, 5.99); P = 0.0008] (Fig. 2B or Table 3 or Supplementary Fig. 3B, Supplemental Digital Content 9, http://links.lww.com/JS9/A304), Supplemental Digital Content 11, http://links.lww.com/JS9/A306, significant differences between MPCNL and RIRS were observed. For the total complications [OR: 2.47 (95% CI: 1.20, 5.07); P = 0.01] (Fig. 2B or Table 3 or Supplementary Fig. 3C, Supplemental Digital Content 9, http://links.lww.com/JS9/A304), Supplemental Digital Content 11, http://links.lww.com/JS9/A306, significant differences between MPCNL and RIRS were observed. For the operating time [OR: 1.65 (95% CI: -12.25, 15.55); P = 0.82] (Fig. 2B or Table 3), no significant differences between MPCNL and RIRS were observed. For the hospital stay [OR: 2.46 (95%) CI: 2.26, 2.66); P = 0.00001] (Fig. 2B or Table 3 or Supplementary Fig. 3D, Supplemental Digital Content 9, http:// links.lww.com/JS9/A304), Supplemental Digital Content 11, http://links.lww.com/JS9/A306, significant differences between MPCNL and RIRS were observed. The result for the operating time showed no significant difference (Fig. 2B or Table 3 or Supplementary Fig. 3E, Supplemental Digital Content 9, http:// links.lww.com/JS9/A304), Supplemental Digital Content 11, http://links.lww.com/JS9/A306.

# Results of subgroup analyses of the complications with Clavien–Dindo classification

With regard to LC stones sized less than 20 mm, for complications with Grade I [OR: 5.52 (95% CI: 1.34, 22.83); P = 0.02]; (Fig. 3), we showed the significant differences between MPCNL and RIRS; for complications with Grade II [OR: 0.87 (95% CI: 0.29, 2.62); P = 0.80] (Fig. 3), we showed no significant differences between MPCNL and RIRS.

	Table 3
--	---------

## Results of meta-analysis.

Stone size (mm)	Outcomes	Trials	Total	Model	<i>f</i> ² (%)	95% CI	OR	P
<u>≤20</u>	3SFR	7	711	Fixed	0	[1.48, 3.97]	2.43	0.0004
	Total complications	5	589	Fixed	0	[1.05, 3.33]	1.87	0.03
	Operating time	6	639	Random	99	[-20.89,8.05]	-6.42	0.38
	Hospital stay	3	382	Random	99	[-0.13, 3.87]	1.87	0.07
	Haemoglobin reduction	2	332	Fixed	0	[0.15, 1.47]	0.81	0.02
	Bleeding	2	222	Fixed	0	[0.57, 43.43]	4.99	0.15
		[0.39, 2.56]	1.00	1.00				
10-20	3SFR	5	489	Fixed	4	[1.61, 5.99]	3.10	0.0008
	Total complications	3	367	Fixed         14         [0.39, 2.56]         1.00           Fixed         4         [1.61, 5.99]         3.10           Fixed         0         [1.20, 5.07]         2.47	0.01			
	Operating time	4	417	Random	98	[-12.25, 15.55]	1.65	0.82
	Hospital stay	2	266	Fixed	44	[2.26, 2.66]	2.46	0.00001

3SFR, 3-month stone-free rate; Fixed, fixed-effects model; f, f tests; OR, odds ratio; Random, random-effects model.

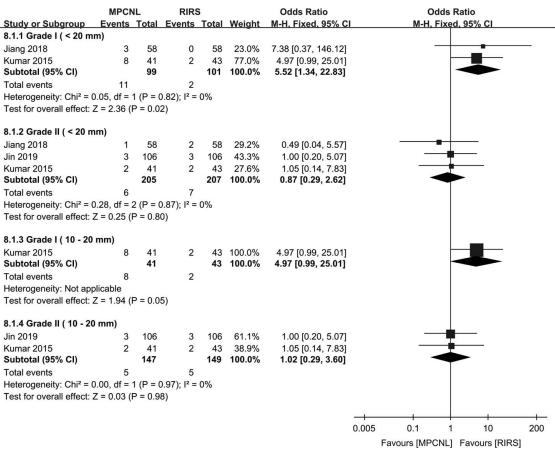


Figure 3. Forest plots for sub-analyses of complications with Clavien–Dindo system. df, degrees of freedom; Fixed, fixed-effects model; MPCNL, minimally invasive nephrolithotomy; M-H, Mantel-Haenszel; RIRS, retrograde intrarenal surgery.

With regard to LC stones sized 10–20 mm, for complications with Grade I [OR: 4.97 (95% CI: 0.99, 25.01) P = 0.05] (Fig. 3), we showed the significant differences between MPCNL and RIRS. For complications with Grade II [OR: 1.02 (95% CI: 0.29, 3.60) P = 0.98] (Fig. 3), we showed no significant differences between MPCNL and RIRS.

## Risk difference (RD) and NNT/NNH.

With regard to LC stones sized less than 20 mm, for the 3SFR, RD: 0.06 [95% CI: 0.01, 0.10]; P=0.01, NNT = 17 (Table 4 or Supplementary Fig. 4, Supplemental Digital Content 10, http://links.lww.com/JS9/A305), Supplemental Digital Content 11, http://links.lww.com/JS9/A306; for total complications, RD: 0.05 [95% CI: 0.01, 0.10]; P=0.03, NNH = 20 (Table 4 or Supplementary Fig. 4, Supplemental Digital Content 10, http://links.lww.com/JS9/A305), Supplemental Digital Content 11, http://links.lww.com/JS9/A306.

With regard to LC stones sized 10–20 mm, for the 3SFR, RD: 0.05 [95% CI: 1.61, 5.99]; P=0.04, NNT = 20 (Table 4 or Supplementary Fig. 4, Supplemental Digital Content 10, http://links.lww.com/JS9/A305), Supplemental Digital Content 11, http://links.lww.com/JS9/A306; for total complications, RD: 0.08 [95% CI: 0.12, 0.14]; P=0.01, NNH = 13 (Table 4 or Supplementary Fig. 4, Supplemental Digital Content 10, http://

links.lww.com/JS9/A305), Supplemental Digital Content 11, http://links.lww.com/JS9/A306.

## **Discussion**

According to the European Association of Urology (EAU) guidelines, for LC stones, in the case of unfavourable conditions for extracorporeal shock wave lithotripsy, endourological interventions such as PCNL or RIRS are advised as the first choices<sup>[1]</sup>. PCNL is considered as the first treatment option for large LC stones sized greater than 20 mm<sup>[1,17]</sup>. MPCNL is a modified PCNL technique that is performed using a miniaturized scope through a smaller (20F or less) nephrostomy tract<sup>[18]</sup>, which enables high clearance with minimal trauma. The stone location has an undisputed impact on the effectiveness regarding the outcomes, mostly observed between lower-pole and non-lowerpole stones<sup>[19]</sup>. The treatment of lower-pole stones with RIRS might be challenging due to steep infundibulopelvic angles<sup>[20]</sup>, and PCNL has been proved to be more effective<sup>[21]</sup>. Moreover, improvements in endoscopy technology have made flexible scopes an appealing treatment option for the majority of renal stones<sup>[22]</sup>. In other words, with the development of laser systems, RIRS has become available for bigger stones<sup>[23–25]</sup>. Both MPCNL and RIRS are considered as attractive treatment modalities for renal stones<sup>[26]</sup>. The purpose of this meta-analysis was to evaluate

Table 4
Results of meta-analysis based on RD.

Stone size(mm)	Outcomes	Trials	Total	Model	<i>f</i> <sup>2</sup> (%)	95% CI	RD	P	NNT/NNH
≤20	3SFR	6	639	Fixed	16	[0.01, 0.10]	0.06	0.01	17
	Total complications	5	589	Fixed	0	[0.01, 0.10]	0.05	0.03	20
10-20	3SFR	4	417	Fixed	37	[1.61, 5.99]	0.05	0.04	20
	Total complications	3	367	Fixed	0	[0.12, 0.14]	0.08	0.01	13

3SFR, 3-month stone-free rate; Fixed, fixed-effects model;  $\mathring{F}$ ,  $\mathring{F}$  tests; NNH, number needed to harm; NNT, number needed to treat; RD, risk difference.

and compare the efficacy and safety of MPCNL and RIRS for the treatment of LC stones.

The 3SFR is the most important parameter for estimating the clinical efficacy of surgical methods. According to the present study, in terms of the 3SFR, MPCNL was significantly superior to RIRS treatment (P < 0.05, Fig. 2A or Table 3). This result was inconsistent with six of the original articles [9,10,12–15] and consistent with one of the original articles [11]. This difference might be associated with the small number of samples in the original RCT, which reflects the value of the current study. As for 10–20 mm LC stones, MPCNL was also significantly superior to RIRS treatment (P < 0.05, Fig. 2B or Table 3). RCTs with larger sample sizes are recommended to strengthen the credibility of the conclusions of this analysis.

For the total complications, based on the results of the current study, MPCNL was significantly inferior to RIRS treatment (P < 0.05, Fig. 2A or Table 3). Similarly, this result was inconsistent with other five of the original articles<sup>[10,12–15]</sup>. As for 10–20 mm LC stones, MPCNL was also significantly inferior to RIRS treatment (P < 0.05, Fig. 2B or Table 3). Once again, RCTs with larger sample sizes are recommended. This result also showed that the current meta-analysis was necessary.

No significant difference was observed between MPCNL and RIRS, regarding the operating time, hospital stay, haemoglobin reduction, bleeding or postoperative fever, respectively. As for 10–20 mm LC stones, MPCNL was also significantly superior to RIRS treatment in terms of the hospital stay (P < 0.001, Fig. 2B or Table 3), while no significant difference between MPCNL and RIRS was observed for the operating time. However, limited by the small number of RCTs and their sample sizes, these results might differ from the actual results. In spite of this, we still only screened articles from the last 10 years for potential differences, yielded by the high-speed advance of science and technology.

No severe complications were observed in six of the original articles<sup>[9,10,12–15]</sup>, with the exception of the study of Coskun *et al.*<sup>[9]</sup> whose total complications were 100% for both MPCNL and RIRS. The authors briefly reported that six patients had Grade III complications and three patients had life-threatening Grade IV complications in the MPCNL group. Moreover, we conducted a sub-analysis of complications with the Clavien–Dindo system and only found significant differences in Grade I complications for LC stones sized less than 20 mm and 10–20 mm. The definition of Grade I is any deviation from the normal postoperative course not requiring surgical, endoscopic or radiological intervention<sup>[27]</sup>. These results indicated that the minor-risk events<sup>[27]</sup> were different between MPCNL and RIRS for LC stones sized less than 20 mm and 10–20 mm.

NNT/NNH was also employed to conduct a quantitative assessment, and we found that NNT and NNH were similar

between MPCNL and RIRS for LC stones sized less than 20 mm (NNT = 17, NNH = 20) and 10–20 mm (NNT = 20, NNH = 13). This meant that the efficacy effect of MPCNL and safety effect of RIRS were nearly equal.

Previously, a similar meta-analysis published in 2020 compared MPCNL with RIRS for 10–20 mm LC stones<sup>[6]</sup>. However, there were only two RCTs and three case-control trials included in the study. The outcomes assessed were the success rate, complication rates, operative times, fluoroscopy times and length of hospital stay. MPCNL was significantly superior to RIRS in terms of efficacy (P = 0.05), while the other outcomes were similar between MPCNL and RIRS (P > 0.05). These results differ from ours which might be due to the fact that different studies were included.

With the progress of surgical methods, needle-perc using a 4.2-Fr needle has already been independently and successfully applied in the clinical treatment of five patients<sup>[28]</sup>. However, urologists seem to lack motivation to conduct RCTs to compare the surgical methods. To update the guidelines and spread advanced technology in a timely manner, it is important to accelerate the transmutation of clinical practice to theoretical research. More RCTs of a high quality are urgently needed.

During the current study, we identified some improvements primarily associated with complications in the included RCTs. First, bleeding, infection and severe pain are the important complications which should be mentioned. Second, it is inadequate to merely list numbers of complications with the Clavien–Dindo system. Third, severe complications should be characterized at length.

There are some certain merits of our study. First, it was shown that head-to-head meta-analysis is more reliable than network meta-analysis. Second, the results of the present study provide a reference for clinical practice, showing that both MPCNL and RIRS are safe and effective methods. However, compared with RIRS, MPCNL showed more complications but an improved efficacy. Third, more outcomes were analyzed in our study than in previous meta-analyses, thus enhancing the power of the present study. We found that MPCNL is nearly as safe as RIRS. Fourth, no significant heterogeneity was observed in the major results (3SFR and total complications), indicating that the results are highly credible. However, some limitations of our report should be taken into consideration. First, only seven RCTs were included, and 711 patients were assessed, therefore, the results of the study might differ from the actual results. Second, no other subgroup analyses were designed, meaning that the results might be not applicable to patients with different characteristics. More RCTs with larger sample sizes are recommended to strengthen the credibility of the conclusions of this analysis.

## Conclusion

Both MPCNL and RIRS are safe and effective management methods. Moreover, compared with RIRS, MPCNL had an unfavourable safety profile but improved efficacy for LC stones of less than or equal to 20 mm or 10–20 mm, and the differences were statistically significant. The relative profit of efficacy of MPCNL was similar to the relative profit of safety of RIRS.

## **Ethical approval**

Not applicable.

## Consent

Not applicable.

## Source of funding

The research was supported by the educational department of Liaoning Province No.: QN2019018 grant to Ning Li.

### **Author contributions**

M.L., J.H., H.X., F.D., X.L., and N.L. conceived and designed the studies; M.L., J.H., H.X., X.L., and F.D. performed the studies; M.L., J.H., H.X., X.L., and F.D. reviewed the literatures and analyzed the data; N.L. contributed technical and material support; M.L., J.H., and N.L. wrote the paper.

## **Conflicts of interest disclosure**

The authors declare that they have no conflict of interest that might bias this work.

## Guarantor

Ning Li.

# Research involving human participants and / or animals

This article does not contain any studies with human participants or animals performed by any of the authors.

## Availability of data, code, and other materials

Not applicable.

## References

- [1] Türk C, Petřík A, Sarica K, et al. EAU Guidelines on Interventional Treatment for Urolithiasis. Eur Urol 2016;69:475–82.
- [2] Cass AS, Grine WB, Jenkins JM, et al. The incidence of lower-pole nephrolithiasis—increasing or not? Br J Urol 1998;82:12–5.
- [3] Moore SL, Bres-Niewada E, Cook P, et al. Optimal management of lower pole stones: the direction of future travel. Cent Eur J Urol 2016;69:274–9.

- [4] Ghani KR, Andonian S, Bultitude M, et al. Percutaneous nephrolithotomy: update, trends, and future directions. Eur Urol 2016;70: 382–96.
- [5] Monga M, Best S, Venkatesh R, *et al.* Durability of flexible ureteroscopes: a randomized, prospective study. J Urol 2006;176:137–41.
- [6] Cabrera JD, Manzo BO, Torres JE, et al. Mini-percutaneous nephrolithotomy versus retrograde intrarenal surgery for the treatment of 10-20 mm lower pole renal stones: a systematic review and meta-analysis. World J Urol 2020;38:2621–8.
- [7] Page MJ, McKenzie JE, Bossuyt PM, et al. The PRISMA 2020 statement: An updated guideline for reporting systematic reviews. Int J Surg (London, England) 2021;88:105906.
- [8] Shea BJ, Reeves BC, Wells G, et al. AMSTAR 2: a critical appraisal tool for systematic reviews that include randomised or non-randomised studies of healthcare interventions, or both. BMJ (Clinical research ed) 2017;358:j4008.
- [9] Coskun A, Eryildirim B, Sarica K, et al. Comparison of mini percutaneous nephrolithotomy (mini PCNL) and retrograde intrarenal surgery (RIRS) for the minimal invasive management of lower caliceal stones. Urol J 2021;18:485–90.
- [10] Yavuz A, Kilinc MF, Bayar G. Outcomes of different minimally invasive techniques in lower calyceal stones of 1 to 2 centimeters: a prospective, randomized study. Arch Esp Urol 2020;73:307–15.
- [11] Perri D, Berti L, Pacchetti A, et al. A comparison among RIRS and MiniPerc for renal stones between 10 and 20 mm using thulium fiber laser (Fiber Dust): a randomized controlled trial. World J Urol 2022;40: 2555–60.
- [12] Fayad AS, Elsheikh MG, Ghoneima W. Tubeless mini-percutaneous nephrolithotomy versus retrograde intrarenal surgery for lower calyceal stones of ≤2 cm: a prospective randomised controlled study. Arab J Urol 2017;15:36–41.
- [13] Jiang K, Chen H, Yu X, et al. The "all-seeing needle" micro-PCNL versus flexible ureterorenoscopy for lower calyceal stones of ≤2 cm. Urolithiasis 2018:1–6.
- [14] Jin L, Yang B, Zhou Z, et al. Comparative efficacy on flexible ureteroscopy lithotripsy and miniaturized percutaneous nephrolithotomy for the treatment of medium-sized lower-pole renal calculi. J Endourol 2019;33: 914–9.
- [15] Kumar A, Kumar N, Vasudeva P, et al. A prospective, randomized comparison of shock wave lithotripsy, retrograde intrarenal surgery and miniperc for treatment of 1 to 2 cm radiolucent lower calyceal renal calculi: a single center experience. J Urol 2015;193:160–4.
- [16] Higgins JP, Altman DG, Gøtzsche PC, et al. The Cochrane Collaboration's tool for assessing risk of bias in randomised trials. BMJ (Clinical research ed) 2011;343:d5928.
- [17] Assimos D, Krambeck A, Miller NL, et al. Surgical Management of Stones: American Urological Association/Endourological Society Guideline, PART I. J Urol 2016;196:1153–60.
- [18] Ganpule AP, Bhattu AS, Desai M. PCNL in the twenty-first century: role of Microperc, Miniperc, and Ultraminiperc. World J Urol 2015;33: 235–40.
- [19] Perlmutter AE, Talug C, Tarry WF, et al. Impact of stone location on success rates of endoscopic lithotripsy for nephrolithiasis. Urology 2008;71:214–7.
- [20] Karim SS, Hanna L, Geraghty R, et al. Role of pelvicalyceal anatomy in the outcomes of retrograde intrarenal surgery (RIRS) for lower pole stones: outcomes with a systematic review of literature. Urolithiasis Jun 2020;48:263–70.
- [21] Zhang W, Zhou T, Wu T, et al. Retrograde intrarenal surgery versus percutaneous nephrolithotomy versus extracorporeal shockwave lithotripsy for treatment of lower pole renal stones: a meta-analysis and systematic review. J Endourol 2015;29:745–59.
- [22] Pan J, Chen Q, Xue W, et al. RIRS versus mPCNL for single renal stone of 2-3 cm: clinical outcome and cost-effective analysis in Chinese medical setting. Urolithiasis 2013;41:73–8.
- [23] Schmidt S, Miernik A. Extracorporeal shock wave lithotripsy (ESWL) versus percutaneous nephrolithotomy (PCNL) or retrograde intrarenal surgery (RIRS) for kidney stones. (Extrakorporale Stoßwellenlithotripsie (ESWL) vs. perkutane Nephrolithotomie (PCNL) oder retrograde intrarenale Chirurgie (RIRS) bei Harnsteinen). Urologe A 2015;54: 1283–6.
- [24] Basulto-Martínez M, Proietti S, Yeow Y, et al. Holmium laser for RIRS. Watts are we doing? (Laser holmium para ureteroscopia flexible retrograda. ¿Qué estamos haciendo?). Arch Esp Urol 2020;73:735–44.

- [25] Giusti G, Proietti S, Peschechera R, et al. Sky is no limit for ureteroscopy: extending the indications and special circumstances. World J Urol 2015;33:257–73.
- [26] Knoll T, Jessen JP, Honeck P, et al. Flexible ureterorenoscopy versus miniaturized PNL for solitary renal calculi of 10-30 mm size. World J Urol 2011;29:755–9.
- [27] Dindo D, Demartines N, Clavien PA. Classification of surgical complications: a new proposal with evaluation in a cohort of 6336 patients and results of a survey. Ann Surg 2004;240:205–13.
- [28] Xiao B, Diao X, Jin S, *et al.* A novel surgical technique for treatment of renal stones in preschool-aged patients: initial experience with needleperc. Urology 2020;146:211–5.