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Research Article

Percutaneous Nephrolithotomy or Retrograde Intrarenal Surgery with Flexible Ureteroscopes? A Systematic Review and Meta-Analysis of The Management of Renal Stones Larger Than 2 cm

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Abstract

Objective: The purpose of this study was to review systematically the efficacy and safety of percutaneous nephrolithotomy (PCNL) and retrograde intrarenal surgery (RIRS) for the treatment of renal stones larger than 2 cm.

Methods: Electronic databases such as the Cochrane Library, PubMed, Embase, and Wanfang Data were searched for studies that compared PCNL versus RIRS for treating renal stones larger than 2 cm from January 1, 2010, to December 1, 2022. Using inclusion and exclusion criteria, relevant literature was strictly screened. RevMan 5.4 software was used to perform a meta-analysis of the data.

Results: A total of 4 randomized controlled studies and 17 nonrandomized controlled studies, with a total of 3231 patients (1839 in the PCNL group and 1392 in the RIRS group) were included in this study. The initial stone clearance rate (odds ratio (OR) = 0.31; 95% CI [0.20, 0.47]; $P < 0.00001$) and final stone clearance rate (OR = 0.32; 95% CI [0.26, 0.41]; $P < 0.00001$) were significantly better in the PCNL group than in the RIRS group. Hemoglobin drop (WMD = -0.78; 95% CI [-1.03, -0.53]; $P < 0.00001$) and length of hospital stay (WMD = -2.22; 95% CI [-2.77], -1.68]; $P < 0.00001$) were significantly better in the RIRS group than in the PCNL group. The incidence of postoperative complications in both groups (OR=0.91; 95%CI [0.75, 1.11]; P =0.35) had no statistical significance.

Conclusion: PCNL and RIRS are both safe and effective surgical methods for the treatment of renal stones larger than 2 cm. PCNL is superior to RIRS in stone clearance rate, which supports PCNL as the preferred treatment. RIRS has fewer severe complications and faster postoperative recovery. RIRS can also achieve satisfactory stone clearance rate through auxiliary or staged procedure. Therefore, RIRS can be used as an alternative treatment for PCNL.

Keywords: Percutaneous nephrolithotomy; retrograde intrarenal surgery; flexible ureteroscopy; renal stones; meta-analysis; systematic review

Introduction

Renal stones are common diseases of the urinary system, with an annual incidence of approximately 8 in 1,000 [1]. The European Association of Urology (EAU) and American Urological Association (AUA) recommend PCNL as the preferred method for the treatment of renal stones larger than 2 cm, and RIRS using a flexible ureteroscope (FURS) is recommended as a second-line treatment after PCNL [2,3]. Although the success rate of PCNL exceeds 95%, it is an invasive approach, and there are obvious complications, including urinary extravasation (7.2%), bleeding requiring blood transfusion (11.2-17.5%), postoperative fever (21-32.1%), sepsis (0.3-4.7%), colon injury (0.2-0.8%) and pleural injury (0.0-3.1%), etc.

Due to advances in the design and fabrication of modern flexible ureteroscopes, for example, reduced diameter, increased resolution, improved light diffusion, and expanded field of view, RIRS has been widely considered a promising alternative to PCNL for larger renal stones [4-7]. Therefore, the efficacy and safety of PCNL and RIRS for the treatment of larger renal stones (>2 cm) are important issues that need to be evaluated and discussed. The purpose of this study was to conduct a meta-analysis of relevant published articles, update the efficacy and safety of PCNL and RIRS for the treatment of renal stones larger than 2 cm, and compare and analyze the respective advantages of the 2 treatment methods to provide more objective evidence for clinical treatment.

Materials and Methods

Search Strategy

For this meta-analysis, electronic databases such as the Cochrane Library, PubMed, Embase, Springer, CNKI, and Wanfang Data were searched. The retrieval and publication period were from January 1, 2010, to December 1, 2022. The Chinese key words for the searches were "percutaneous nephrolithotomy", "flexible ureteroscopy", "upper urinary tract calculi", "nephrolithiasis," etc., and the English key words for the searches were "percutaneous nephrolithotomy", "PCNL", "flexible ureteroscopy", "FURS", "retrograde intrarenal surgery", "RIRS", "renal", "pelvis", "upper ureter", "kidney", "calculus", "stone" and related synonyms and variants.

Inclusion and Exclusion Criteria

The inclusion criteria were as follows:

a) Research subjects – patients diagnosed with upper urinary tract calculi (kidney, renal pelvis and calyces, and upper ureter) by imaging examinations such as ultrasound, kidneys, ureters, and bladder (KUB), intravenous pyelography (IVP), computed tomography (CT), with the diameter of the calculi > 2 cm.

b) Study type – randomized controlled trials (RCTs) and nonrandomized controlled studies (case-control studies, cohort studies) of RIRS and PCNL for the treatment of renal stones larger than 2 cm.

c) Outcome indicators – final stone clearance rate (SFR), complication rate, operation time, hemoglobin decline, length of hospital stay, etc.

The exclusion criteria were as follows:

a) Studies not belonging to controlled clinical trials.

b) Conference abstracts, reviews, case reports and meta-analyses.

c) Incomplete or vague literature data and unextractable corresponding data and results.

d) Studies related to stones < 2cm.

e) Research subjects/object are pregnant women, horseshoe kidney, patients with severe cardiopulmonary Insufficiency or with contraindications to surgery, etc.

f) Language other than Chinese or English.

g) Original text could not be obtained.

Research Methods

Two authors independently read and organized the literature, screened eligible literature using the inclusion and exclusion criteria, and conducted full-text readings, quality risk assessments and data extraction of the included literature. In case of inconsistent results after cross-referencing, agreement was reached through third-party discussions. The following data were extracted in this study: name of the first author, publication time, type of study design, number of enrolled subjects, intervention measures, outcome indicators, and literature quality scores.

Quality Evaluation and Bias Analysis

This study divided the included literature into 2 categories: experimental research and observational research. The level of evidence of each included study was rated using the Oxford Centre for Evidence-Based Medicine criteria [8]. For experimental studies (RCTs), the Cochrane collaboration's tool for assessing risk of bias was used. The results of the literature evaluation were divided into 3 types: "high risk of bias," "low risk of bias" and "uncertain risk of bias." The quality of the literature was assessed using the modified Jadad scale [9,10], with a total score of 7 points; 4-7 points were considered high-quality experiments. For observational studies (such as case-ontrol studies), the Newcastle-Ottawa Scale (NOS) was used [11]; the total evaluation score was 9 points, with 5-9 points indicating higher quality experiments.

Statistical Methods

RevMan 5.4 software was used for the meta-analysis. A heterogeneity test was carried out for each study statistic. The test level was set to $P \geq 0.1$, and when $I2 < 50\%$ (there was homogeneity among studies), a fixed effect model was used to calculate the combined statistic; otherwise, a random effect model was used. The odds ratio (OR) and weighted mean (WMD) were used to calculate summary statistics for dichotomous variables and continuous variables, respectively, and 95% confidence intervals (CIs) are reported for ORs and WMDs. The probability P value of the pooled effect statistic was determined using the Z test, and statistical significance was defined as $P < 0.05$. A funnel plot was used to detect potential publication bias.

Results

Basic Characteristics and Quality Evaluation of The Literature Included in The Analyses

A total of 580 documents were retrieved from the relevant databases using the described search strategy, and 55 duplicate documents were excluded. After reading the titles and abstracts, 457 documents that did not meet the inclusion criteria were excluded. After reading the full text of the remaining 68 papers, some papers were excluded using the exclusion criteria, e.g., incomplete literature data, index that could not be included or wrong data, leaving 21 eligible papers [12-28] (Table 1, Figure 1). Four were RCTs with a level of evidence of 2b. The risk of bias was assessed for each RCT using the Cochrane risk of bias. The risk assessments included "high risk," "unclear" and "low risk" (Figure 2). The quality of the literature was scored using the modified Jadad scale (4-6 points). The 17 other publications were observational studies (case-control studies and cohort studies), and the level of evidence was 3b. The NOS score for literature quality was 5-8 points (Table 1). In the included studies, there were 1839 patients in the PCNL group and 1392 in the RIRS group (Table 2).

Table 1: General characteristics of the included studies.

First author, year	Country	Study period	Study design	Level of evidence	Inclusion criteria	Study quality
Ibis MA, et al. 2022[12]	Turkey	2019-2021	Retrospective	3b	2-3 cm, single or multiple stones	6
Atis G, et al. 2017[13]	Turkey	Not provide	Retrospective	3b	2-4 cm, single or multiple stones	5
Bai Y, et al. 2017[14]	China	2010-2015	Retrospective	3b	>2 cm, single or multiple stones	8
Ucer O, et al. 2022[15]	Turkey	2016-2018	Prospective	3b	2-4cm, single or multiple stones	6
Erkoc M, et al. 2021[16]	Turkey	2016-2020	Retrospective	3b	2-3cm, renal pelvic stones	5
Lv G, et al. 2022[17]	China	2016-2021	Retrospective, PSM	3b	>2 cm, single or multiple stones	8
Karakoyunlu AN, et al. 2019[18]	Turkey	2011-2015	Retrospective	3b	≥4 cm · single or multiple stones	7
Saad KS, et al. 2015[19]	Egypt	2011-2014	Randomized clinical trial	2b	>2 cm, single or multiple stones	4
Deng YQ. 2021[21]	China	2018-2020	Prospective	3b	2-4cm, single or multiple stones	5
Li JW, et al. 2016[20]	China	2013-2015	Randomized clinical trial	2b	2-4cm, single or multiple stones	6
Akman T, et al. 2012[4]	Turkey	2008-2011	Matched pair analysis	3b	2-4cm, single or multiple stones	6
Pan J, et al. 2013[23]	China	2005-2011	Prospective	3b	2-3cm, single stone	6
Bryniarski P, et al. 2012[5]	Poland	2008-2010	Randomized clinical trial	2b	>2 cm, single stone	5
Zeng G, et al. 2014[25]	China	2012-2014	Matched pair analysis	3b	>2 cm, single stone, solitary kidney	7
Karakoç O, et al. 2015[6]	Turkey	2009-2013	Retrospective	3b	>2 cm, single or multiple stones	6
Karakoyunlu N, et al. 2015[22]	Turkey	2013-2014	Randomized clinical trial	2b	>2 cm, single stone	5
Zengin K, et al. 2015[26]	Turkey	2012-2014	Prospective	3b	2-3 cm, single stone	6
Shi X, et al. 2018[24]	China	2010-2016	Retrospective, PSM	3b	>2 cm, single or multiple stones, solitary kidney	7
Sari S, et al. 2017[7]	Turkey	2011-2014	Retrospective	3b	>2 cm, single or multiple stones	6

Zhang Y, et al. 2018[27]	China	2013-2016	Retrospective	3b	2-3 cm, single stone, solitary kidney	6
Zhao Z, et al. 2020[28]	China	2015-2016	Retrospective	3b	2-3 cm, single or multiple stones	7

Table 2: Treatment methods in each included study.

First author, year	RIRS technique	PCNL technique	Case	
			RIRS	PCNL
Ibis MA, et al. 2022[12]	Flexible ureteroscope, holmium laser	Miniperc, 20F, holmium laser	126	440
Atis G, et al. 2017[13]	7.5 F flexible ureteroscope, holmium laser 273µm	Standard 28-30F, pneumatic lithotripsy	146	146
Bai Y, et al. 2017[14]	7.5 F flexible ureteroscope, holmium laser	Standard 26F, holmium laser	56	60
Ucer O, et al. 2022[15]	7.5 F flexible ureteroscope, holmium laser 272µm	Standard 30F, pneumatic or laser lithotripsy	52	50
Erkoc M, et al. 2021[16]	7.5 F flexible ureteroscope, holmium laser 273µm	Miniperc,18F, holmium laser 1000µm	60	65
Lv G, et al. 2022[17]	Flexible ureteroscope, holmium laser 200µm	Miniperc,16F, holmium laser	81	81
Karakoyunlu AN, et al. 2019[18]	7.5F flexible ureteroscope, holmium laser 200µm	Standard 30F, pneumatic lithotripsy	27	67
Saad KS, et al. 2015[19]	7.5F flexible ureteroscope, holmium laser	Miniperc,22F · pneumatic lithotripsy	21	22
Deng YQ. 2021[21]	Flexible ureteroscope, holmium laser 200µm	Miniperc,18F, pneumatic or laser lithotripsy	37	37
Li JW, et al. 2016[20]	7.5F flexible ureteroscope, holmium laser 200µm	Miniperc,18F, holmium laser 500µm	35	35
Akman T, et al. 2012[4]	7.5 or 8.7F flexible ureteroscope, holmium laser 200 or 273µm	Standard 30F, pneumatic or ultrasonic lithotripsy	34	34
Pan J, et al. 2013[23]	8.4F flexible ureteroscope, holmium laser	Miniperc, 18F, holmium laser	56	59
Bryniarski P, et al. 2012[5]	10-12F semirigid ureteroscope, holmium laser 200µm	Standard 30F, ultrasonic lithotripsy	32	32
Zeng G, et al. 2014[25]	7.5F flexible ureteroscope, holmium laser 200µm	Miniperc 18F, pneumatic or holmium laser lithotripsy	53	53
Karakoç O, et al. 2015[6]	7.5F flexible ureteroscope, holmium laser 200µm	Standard 30F, pneumatic lithotripsy	57	86
Karakoyunlu N, et al. 2015[22]	7.5F flexible ureteroscope, holmium laser 200 or 365µm	Standard 30F, holmium laser 200 or 365µm	30	30
Zengin K, et al. 2015[26]	7.5F flexible ureteroscope, holmium laser	Standard 30F, pneumatic lithotripsy	80	74
Shi X, et al. 2018[24]	7.5F flexible ureteroscope, holmium laser 200µm	Standard 30 F, holmium laser 1000µm	43	43
Sari S, et al. 2017[7]	7.5F flexible ureteroscope, holmium laser 200µm	Standard 30 f, pneumatic lithotripsy	185	254
Zhang Y, et al. 2018[27]	7.5F flexible ureteroscope, holmium laser 200µm	Miniperc, 18F, holmium laser	34	42
Zhao Z, et al. 2020[28]	8.4F flexible ureteroscope, holmium laser 200µm	Miniperc 18F, pneumatic lithotripsy	147	129
Total			1392	1839

Meta-Analysis of Related Outcome indicators

Operation Time

Nineteen studies included this outcome indicator, and the heterogeneity test ($P < 0.00001$; $I^2 = 95\%$) indicated that there was a significant difference among the studies; therefore, a random effect model was used for the meta-analysis. The results indicated that the operative time was significantly shorter in the PCNL group than in the RIRS group (WMD = 7.81; 95% CI [0.60, 15.02]; P = 0.03) (Figure 3).

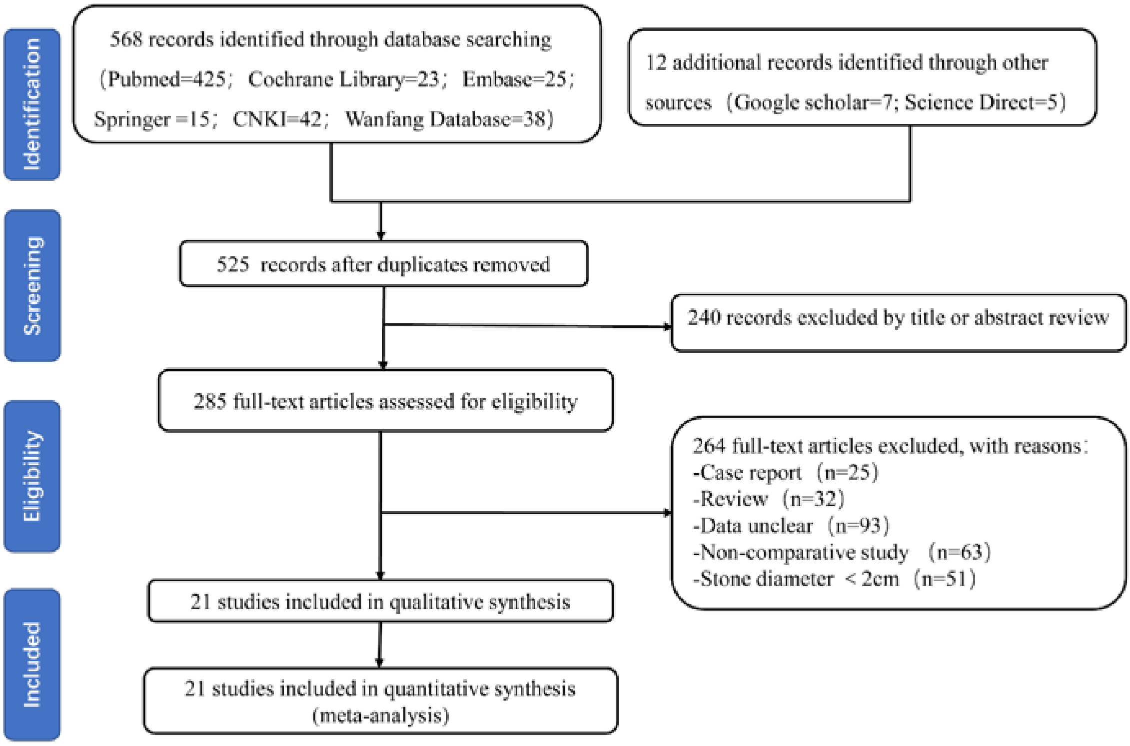

Figure 1: Prism flowchart of the study selection process.

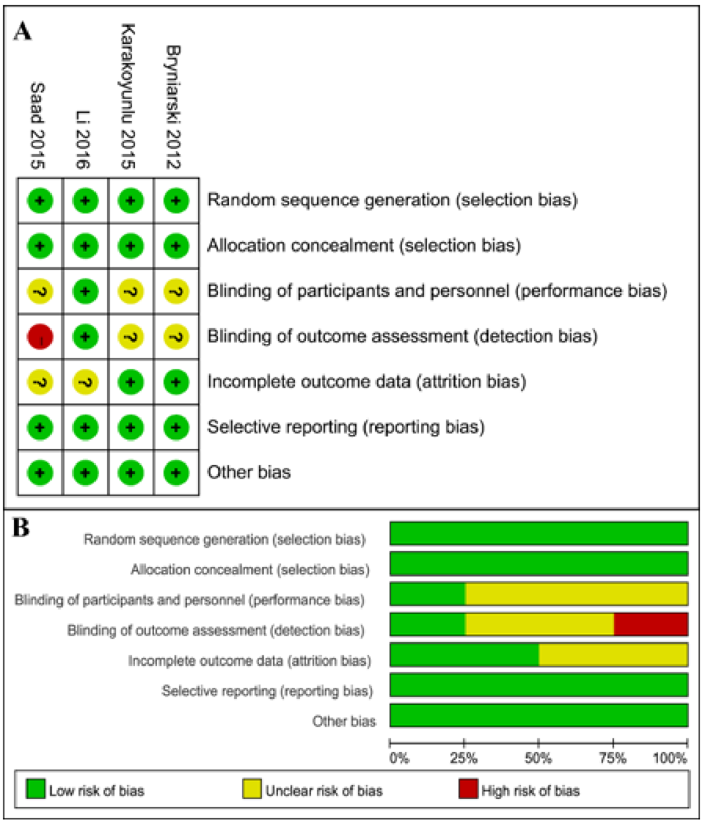

Figure 2: Risk of bias assessment for RCTs.

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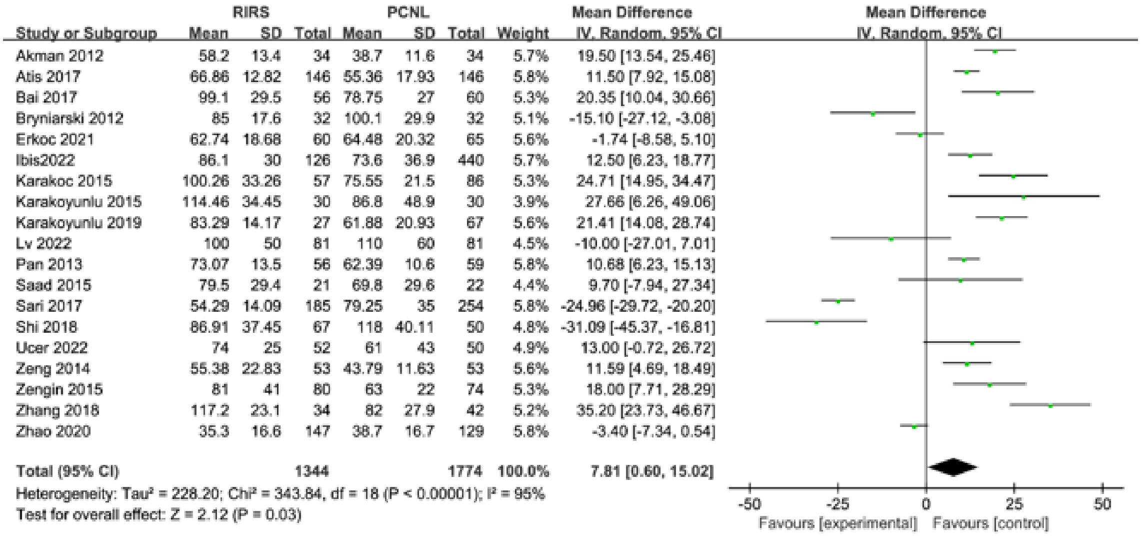

Figure 3: Forest plot of operation time in the PCNL group and RIRS group.

Initial Stone Clearance Rate

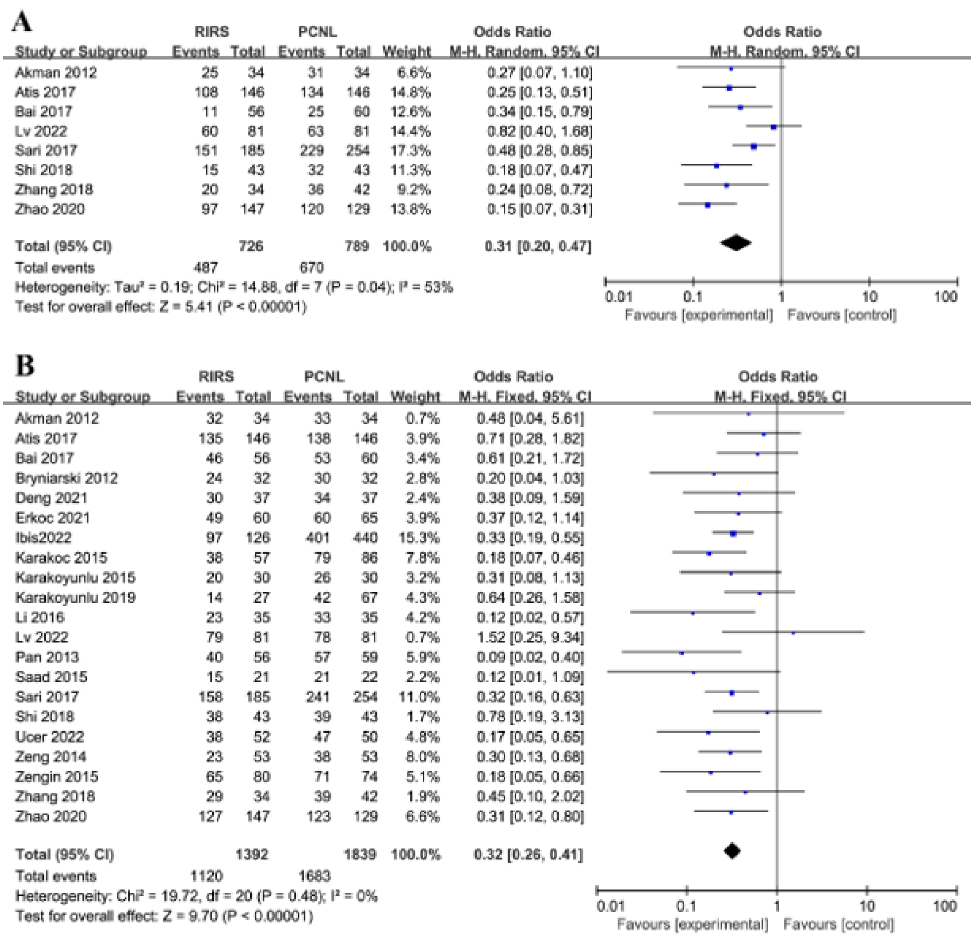

Figure 4: Forest plot of the initial stone clearance rate and the final stone clearance rate in the PCNL group and RIRS group A: the initial stone clearance rate; B: the final stone clearance rate.

Initial stone clearance rate means the stone clearance rate after first procedure (one session). Eight studies included this outcome indicator, and the heterogeneity test ($P = 0.04$; $I^2 = 53\%$) indicated that there was a significant difference among the studies; therefore, a random effect model was used for the meta-analysis. The results indicated that the initial stone clearance rate was higher in the PCNL group than in the RIRS group; the difference was significant (OR = 0.31; 95% CI [0.20, 0.47]; P < 0.00001) (Figure 4A).

Final Stone Clearance Rate

All included studies included this outcome measure. The heterogeneity test ($P = 0.48$; $I^2 = 0\%$) indicated that there was no significant difference among the studies; therefore, a fixed effect model was used for the meta-analysis (Figure 4). The results indicated that the final stone clearance rate was significantly higher in the PCNL group than in the RIRS group (OR = 0.32; 95% CI [0.26, 0.41]; P < 0.00001) (Figure 4B).

Auxiliary Procedure

If stone removal is unsatisfactory after the first procedure, further procedure, such as extracorporeal shock wave lithotripsy, RIRS or PCNL, is required to address the residual stone. Sixteen studies included this outcome measure, and the heterogeneity test ($P = 0.01$; $I^2 = 49\%$) indicated that there was a significant difference among the studies; therefore, a random effect model was used for the meta-analysis. The results showed that the number of patients requiring auxiliary procedures were significantly lower in the PCNL group than in the RIRS group (OR = 6.01; 95% CI [3.95, 9.15]; P < 0.00001) (Figure 5), which means that RIRS needs auxiliary or staged procedure in more patients to improve stone clearance rate.

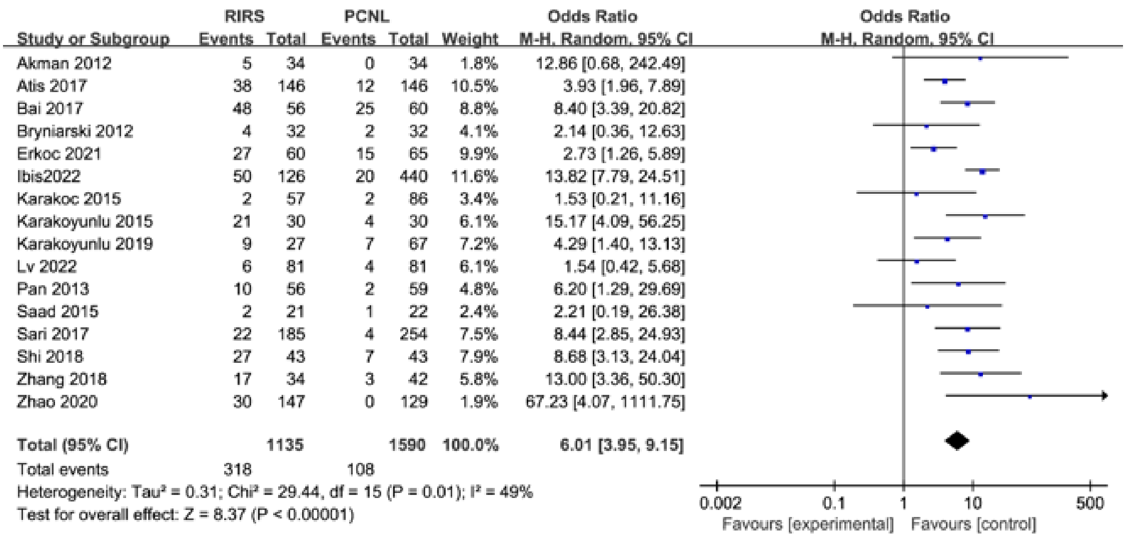

Figure 5: Forest plot of auxiliary procedures in the PCNL group and RIRS group.

Hemoglobin Drop After Surgery

Thirteen studies included this outcome indicator, and the heterogeneity test ($P < 0.00001$; $I^2 = 98\%$) indicated that there was a significant difference among the studies; therefore, a random effect model was used for the meta-analysis (Figure 6). The results indicated that the decrease in hemoglobin was significantly greater in the PCNL group than in the RIRS group (WMD = -0.78; 95% CI [-1.03, -0.53]; P < 0.00001) (Figure 6A).

Complication Rate

All studies included this outcome indicator, and the heterogeneity test ($P < 0.00001$; $I^2 = 70\%$) indicated that there was a significant difference among the studies; therefore, a random effect model was used for the meta-analysis. The results showed that there was no significant difference in the incidence of complications between the PCNL group and the RIRS group (OR = 0.91; 95% CI [0.75, 1.11]; P = 0.35) (Figure 6B).

Length of Hospital Stay

Nineteen studies included this outcome indicator, and the heterogeneity test ($P < 0.00001$; $I^2 = 98\%$) indicated that there was a significant difference among the studies; therefore, a random effect model was used for the meta-analysis. The results showed that length of hospital stay was significantly shorter in the RIRS group than in the PCNL group (WMD=-2.22; 95% CI [-2.77, -1.68]; P < 0.00001) (Figure 7).

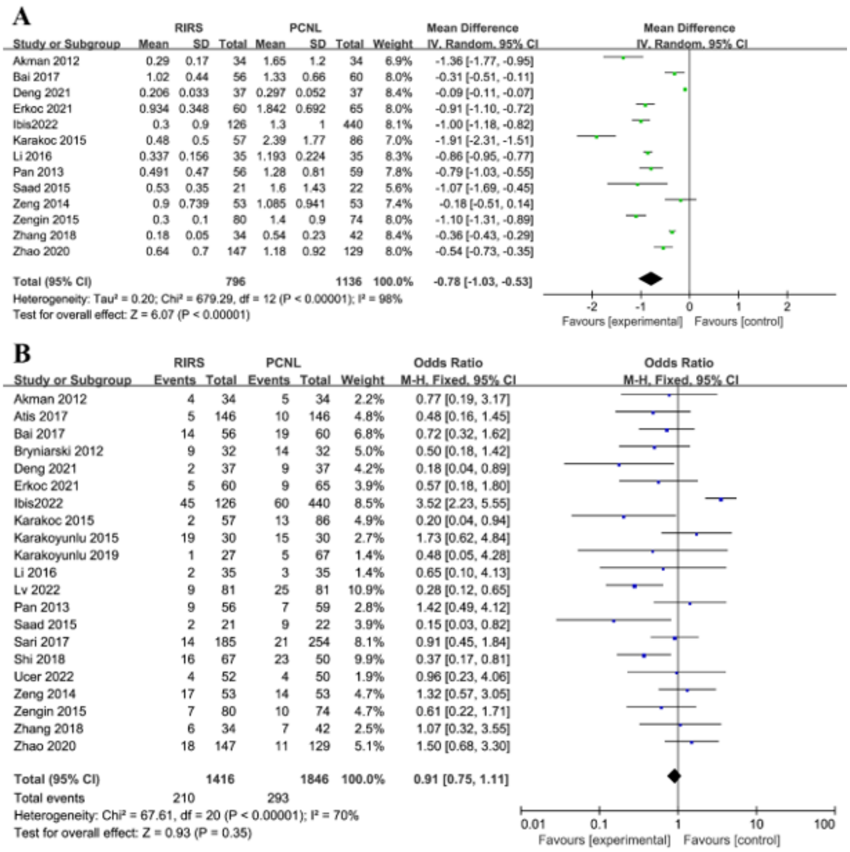

Figure 6: Forest plot of hemoglobin drops after surgery and complication rate in the PCNL group and RIRS group A) hemoglobin drops after surgery; B) complication rate.

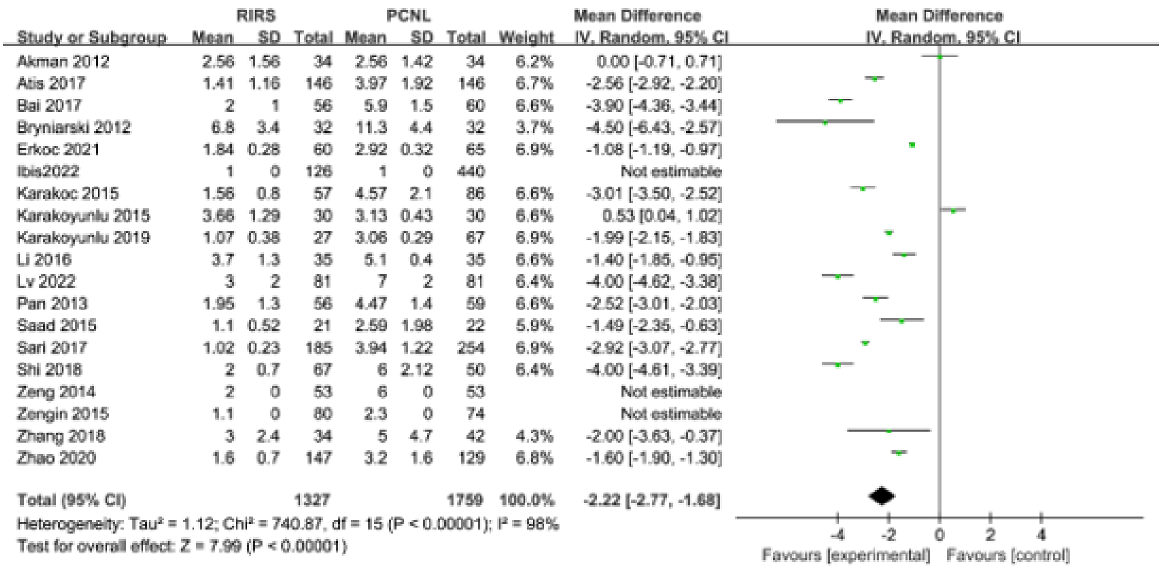

Figure 7: Forest plot of the length of hospital stay in the PCNL group and RIRS group.

Discussion

Currently, the main treatment for renal stones is minimally invasive surgery. Both the EAU and AUA recommend PCNL as the first-line treatment for renal stones larger than 2 cm. Although PCNL has a high stone clearance rate, the complication rate is also high [29,30]. The most common complications are sepsis and bleeding, which may require a blood transfusion or even embolization in severe cases, with an overall mortality rate of 0.3% [31-33]. To reduce these risks, many clinicians have replaced PCNL with RIRS. For larger stone burdens, staged treatment can be used to obtain higher stone clearance rates [34-37]. Some research reports have shown that the overall stone clearance rate with a single RIRS procedure can be as high as 92% [38,39]. Some scholars propose that RIRS can achieve the same stone clearance rate as PCNL for the treatment of renal pelvis stones larger than 2 cm and has the advantages of being minimally invasive and safe, with a quick postoperative recovery [40]. With continuous advancements in surgical techniques and improvements in various medical devices, more feasible solutions have been provided for the treatment of renal stones larger than 2 cm.

The stone clearance rate is the most intuitive evaluation measure of treatment effects. In this study, the meta-analysis indicated that both the initial stone clearance rate and the final stone clearance rate after auxiliary procedures was significantly higher for PCNL than for RIRS, indicating that PCNL has unique advantages in stone removal. Additionally, the analysis indicated that for renal stones larger than 2 cm, more repeated RIRS treatments are required to achieve a higher stone clearance rate. Although some studies suggest that the cost of multiple RIRS treatments is still lower than that of a single PCNL, but the cost is difficult to calculate in terms of time costs and other factors such as anesthesia damage to the body, which may also be another influencing factor for recommending RIRS as a second-line treatment for large renal stones. Postoperative complications are important indicators for evaluating the safety of related surgical methods. Although the meta-analysis showed that there was no significant difference in the incidence of complications between the PCNL group and the RIRS group, the postoperative hemoglobin level was significantly lower in the PCNL group than in the RIRS group.

Moreover, serious complications such as severe bleeding requiring blood transfusions or embolisms, pleural injuries, ileal injuries, and even cardiac arrest, have been reported for PCNL; therefore, RIRS appears to be safer than PCNL. Notably, there is a risk of urosepsis associated with greater stone burden, and the use of access sheath in RIRS effectively reduces intrarenal perfusion pressure, which can prevent the occurrence of urosepsis [41,42]. The complication rate of RIRS decreased further as the body size of ureteroscope decreased, from 6.6% to 1.5% [43]. RIRS is also a safer option for patients with solitary kidneys, spinal deformities, or coagulation disorders [44,45]. In addition, the operative time varies greatly between studies, and this meta-analysis indicated that the operation time for PCNL is shorter, which may be related to RIRS requiring the use of thinner optical fibers, having lower lithotripsy efficiency and a longer in vivo path, and involving inconvenient maneuvers, especially for calyx calculus.

In terms of the length of hospital stay, that for patients who undergo RIRS is significantly shorter than that for patients who undergo PCNL, with an average difference of 2.2 days, which means that patients recover faster after RIRS and can return to normal life and work earlier, which in turn leads to less economic loss. The potential limitations of this study are as follows:

a) The definition of stone clearance rate among the included studies is not completely consistent, and there may be reporting bias.

b) There is a lack of further stratified analysis and comparison of stone size and calyx distribution, and there may be differential results.

c) This study included many retrospective studies, with only 4 RCTs, resulting in a relatively low level of evidence. Therefore, more high-quality RCTs are needed to verify and improve these results.

Conclusion

This meta-analysis indicated that both PCNL and RIRS are safe and effective surgical methods for the treatment of renal stones larger than 2 cm. PCNL has unique advantages in terms of stone clearance rate, while RIRS is less invasive with fewer severe complications and is associated with a faster postoperative recovery, and a satisfactory stone clearance rate can also be achieved through repeated procedures. It is even a better choice than PCNL in certain specific cases such as spinal deformities, coagulation disorders and isolated kidneys.

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Authorship Contribution Statement

Tianmin Li: Methodology (equal); writing – original draft (lead); formal analysis (lead); Data curation (equal); Formal analysis(equal). Chengjie Zhong: Methodology (equal); Software (lead); writing – original draft (supporting); Data curation (equal); Formal analysis (equal). Luofu Wang: Conceptualization (lead); Writing – review and editing (lead).

Author Disclosure Statement

No conflict of interest exists.

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