Percutaneous nephrolithotomy vs. retrograde intrarenal surgery for renal stones larger than 2cm in patients with a solitary kidney: A systematic review and a meta-analysis

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Abstract

Background: The safety and feasibility of percutaneous nephrolithotomy (PCNL) compared with retrograde intrarenal surgery (RIRS) are debated. This systematic evaluation was performed to obtain comprehensive evidence with regard to the treatment outcomes of PCNL compared with RIRS for management of renal stones in patients with solitary kidney. Methods: A systematic search of Medline, Embase, Pubmed, and the Cochrane Library was performed to identify studies that compared PCNL with RIRS. Outcomes of interest included perioperative variables, complications, and stone-free rate (SFR). Results: 4 studies assessing PCNL vs. RIRS were included for meta-analysis. Although patients underwent PCNL have higher initial SFR than RIRS (OR: 3.72, 95% CI:2.38 to 5.83; P□0.001), patients underwent RIRS have less intraoperative blood loss (dropped Hb: WMD= 3.49 g/L, 95% CI:2.83 to 4.15; P□ 0.001), lower blood transfusion rates (OR= 5.31, 95% CI:1.36 to 20.68; P=0.02), and higher incidence rate of steinstrasse (OR:0.20, 95% CI:0.04 to 0.91; P=0.04). All the other calculated results including operation time (WMD: -9.87 minute, 95% CI:-30.11 to 10.37; P=0.34), final SFR (OR:1.65, 95% CI:0.80 to 3.42;P=0.18) and overall complications (OR:1.22, 95% CI:0.78 to 1.93; P=0.38) are similar between the two groups. Conclusions: Our results indicate that PCNL has higher initial SFR than RIRS in the treatment of renal stones in patients with a solitary kidney; the overall complications were comparable in both groups. However, RIRS, with less blood loss and transfusion rate, may be an alternative in selected patients.

Introduction

Currently, the main approaches for managing kidney stones are percutaneous nephrolithotomy (PCNL) along with retrograde intrarenal surgery (RIRS) [1]. However, managing large kidney stones in solitary kidney patients differs from that of other kidney stones and remains as one of the clinical challenges for many urologists[2, 3]. The main clinical targets for managing a solitary kidney with renal stones span from ensuring a high stone-free rate (SFR), curtailing complications to maximizing the preservation of the existing renal function. The ultimate treatment of choice for large kidney stones (□2 cm) in solitary kidney patients is a protracted dilemma which has received heightened attention among urologists.

Commensurate with the European Association of Urology (EAU) guidelines, PCNL is endorsed as the first-line therapy for larger kidney stones since it correlates highly with the highest SFR although considered to be a very invasive technique[4] with potentially severe complications such as bleeding, urosepsis besides visceral injuries. A large number of studies reported a higher SFR coupled with higher complication rates during PCNL for treating kidney stones in solitary kidney patients than those with two normal functioning kidneys, while their kidney function seemed relatively unchanged[2, 5-7]. However, with advancing minimally invasive technology, RIRS is progressively being utilized as the best alternative therapy to PCNL for managing kidney stones owing to negligible complications. For solitary kidney patients, RIRS plays an essential role in preserving renal parenchyma[3, 8, 9]; nevertheless, lower SFR has been reported for large kidney stones[3, 8-11].

Numerous studies comparing PCNL and RIRS for large kidney stones in solitary kidney patients have been reported recently[12-15]. However, no evaluation outcomes comparing PCNL with RIRS have been published yet. Moreover, no conclusive illation has been suggested regarding the clinical application of either PCNL or RIRS in solitary kidney patients with large stones. Hence, we aimed to conduct a meta-analysis of published studies to analyze the efficacy as well as safety of PCNL and RIRS in managing kidney stones large than 2cm in solitary kidney patients.

Materials And Methods

Search strategy

Commensurate with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines together with the *Cochrane Handbook for Systematic Reviews of Interventions[16]*, this systematic review of published literature was performed[17]. With No ethic issues involved, a systematic search was carried out using Embase, Medline, Pubmed, CNKI databases and all relevant studies were established with the help of the Cochrane Library using keywords such as "percutaneous nephrolithotomy", or "PCNL", or "retrograde intrarenal surgery", or "RIRS ", or "flexible ureteroscopy", or "FURS", or "renal stones", or "kidney stone", or "renal calculus", and "solitary kidney ".

Data Extraction and outcomes of interest

Two independent authors (SF and JKH) educed data from the studies selected such as author details, country, year of publication, study design, age, as well as the number of patients. Any disagreements regarding the eligibility of any studies were resolved by consentience upon discussion. Perioperative outcomes such as SFR, drop in Hb levels, transfusion rate, as well as complication rates, were compared between the two procedures from all the selected studies.

Inclusion criteria and exclusion criteria

Studies included must: (1) be comparing PCNL with RIRS for managing kidney stones in solitary kidney patients, (2) demonstrate the outcomes of two procedures, (3) clearly establish the indications for large kidney stones in solitary kidney patients, (4) document the procedure either as PCNL or RIRS.

Studies were excluded in the event (1) the study did not meet above inclusion criteria or (2) the outcomes of studies were not reported, or the parameters were preposterous to analyze for either PCNL or RIRS from the published literature.

Study Quality assessment and level of evidence

In conformity with the standards of Centre for Evidence-Based Medicine in Oxford, we assessed the level of evidence (LOE) of all the included studies. We used the Jaded Score to evaluate the methodological quality of RCTs[18]. Furthermore, the Newcastle-Ottawa Scale(NOS) was employed to evaluate the methodological quality of the non-RCTs observational studies[19]. Two authors (SF and JKH) assessed

the quality of the selected studies, and any disparities were reanalyzed by the third reviewer (ZJG), and a consonance was reached through discussion.

Statistical analysis

This meta-analysis was done with Review Manager 5.3 (Cochrane Collaboration, Oxford, UK). We analyzed continuous as well as dichotomous variables by odds ratios (ORs) and weighted mean differences (WMDs). All the outcomes of the analysis were documented with the confidence intervals (CIs) of 95%. We evaluated the quantity of heterogeneity using I^2 test and chi-square-based Q test, the evidence of heterogeneity was considered substantial when I^2 50% and then the random effects (RE) model utilized, or else, the fixed effects (FE) model was employed. The Egger's test, as well as funnel plot, were employed to evaluate any presence of publication biases. Furthermore, we used sensitivity analysis to approximate the impact of studies with a greater risk of bias on the overall effect.

Results

Characteristics of eligible studies

A total of 4 studies[12-15] assessing PCNL vs. RIRS for treating renal stones large than 2cm in solitary kidney patients fulfilled all the desired inclusion criteria; thus they were used for this meta-analysis (Fig 1). The baseline data of the included 4 studies were outlined in Table 1.

Quality of the studies and level of evidence (Table 1)

The quality of included studies was assessed by the NOS quality assessment method[19] along with the US Preventive Services Task Force grading system[18]. Three studies were identified as high-quality studies. Besides, the clinical variables of PCNL, as well as RIRS, were independently extracted from all the included studies (Table 1).

Description of included studies and patients Demographics (Table 2)

The PCNL group had more patients with moderate hydronephrosis than the RIRS group (OR= 2.23; 95% CI: 1.32 to 3.77; *P*=0.003) (Table 2) while the RIRS group had more patients with mild hydronephrosis than the PCNL group (OR= 0.45; 95% CI: 0.27 to 0.76; *P*=0.003) (Table 2). All the other preoperative variables were similar between the two groups (Table 2).

Outcomes of perioperative variables (Table 3, 4)

Regarding perioperative variables, patients who underwent PCNL had higher initial SFR than RIRS (OR: 3.72, 95% CI:2.38 to 5.83; *P* 0.001) whereas those who underwent RIRS had minimal intraoperative blood loss (dropped Hb: WMD= 3.49 g/L, 95% CI:2.83 to 4.15; *P* 0.001) which translated into lower blood transfusion rates (OR= 5.31, 95% CI:1.36 to 20.68; *P*=0.02) as well as soaring incidence rate of steinstrasse (OR:0.20, 95% CI:0.04 to 0.91; *P*=0.04). moreover, all the other calculated results including

operation time (WMD: -9.87 minute, 95% CI:-30.11 to 10.37; *P*=0.34), final SFR (OR:1.65, 95% CI:0.80 to 3.42;*P*=0.18), overall complications (OR:1.22, 95% CI:0.78 to 1.93; *P*=0.38), and stone composition were similar between the two groups (Table 3,4).

Sensitivity Analysis

Sensitivity analysis was performed for studies matched for general variables by the method for higher quality studies (Table 5). Compared with the original analysis, there was no significant change in any of the other outcomes apart from operation time (*P*=0.34 vs. *P*=0.001) (Table 5) and steinstrasse (*P*=0.04 vs. *P*=0.05) (Table 5) which were significantly at variance in the sensitivity analysis. The method of sensitivity analysis can reduce the heterogeneity of studies to a certain extent.

Discussion

The management of renal stones large than 2cm in solitary kidney patients is challenging, and PCNL is the recommended first choice of treatment for these kinds of patients[5, 6]. Compared to bilateral functional kidneys, there were still no technological differences in performing PCNL for renal stones in solitary kidney patients. Several studies have tackled the issue of PCNL in managing renal calculus in a solitary kidney. Haberal HB et al. reported that PCNL was an appropriate and efficient treatment option for managing kidney stones in solitary kidney patients, but highlighted higher complication rates in the solitary kidney group[2]. Zhong et al. reported that PCNL combined with RIRS had a high SFR for staghorn calculi and that RIRS used simultaneously could lessen the need for multiple tracts and hence reduce blood loss and shorten the operation time[20]. Hosseini et al. also reported that PCNL seems a sound and effective alternative in cases of a single kidney, nonetheless more attention is still needed in order to avert even minute complications that could culminate in an anephric state[7]. Basiri A et al. reported about the safety along with the effectiveness of PCNL for managing large renal stones comparing single functioning kidney and double-kidney patients, and the results showed that mean hemoglobin drop in both groups was significant; besides, the procedure hardly had any adverse effects on renal function in both groups, and no significant difference in terms of complication rate and SFR between two groups[21]. The study by El-Tabey NA et al. demonstrated that PCNL for kidney stones in solitary kidney patients provides substantial improvement in renal function at long-term follow-up and that manifold punctures, as well as severe hemorrhage, were independent risk factors for exacerbation of the renal function[22].

Although the incidences of major complications are rare, they can result in severe consequence in solitary kidney patients. These include severe hemorrhage which may require embolization or nephrectomy; in addition, dialysis is a requirement for such patients. Moreover, the transfusion rate in solitary kidney patients who take PCNL is reported to be roughly 10% and may be attributed to the upsurge in the thickness of the renal parenchyma as a result of compensatory hypertrophy[12]. Furthermore, El-Nahas et al.[23] reported that a 25% incidence rate of acute kidney injury (AKI) after PCNL in solitary kidney patients. There was a 92% probability of renal function recuperation although multiple PCNL tracts along

with postoperative ureteric obstruction were the risk factors that result in AKI. Therefore, RIRS has been adopted as the preferred choice of management of kidney stones because of its low complication rate, especially for solitary kidney patients. Moreover, multiple studies demonstrated RIRS as an efficient and safe procedure which could be utilized to manage kidney stones in with solitary kidney patients[3, 8, 9, 11]. From the study of 29 RIRS patients who were treated with renal stones by Giusti G et al.[24] reported outcomes, it was found that 72.4% and 93.1% were as the result of primary SFR and the secondary SFR respectively, with hardly any major complications noted and thus these results indicated that RIRS was safe and productive in the treating renal calculi in solitary kidney patients without deterioration of the renal function. Furthermore, Kuroda S et al.[3] also showed that RIRS for managing renal stones in solitary kidney patients was as efficient and safe as in bilateral kidney patients.

When Zeng et al.[12] compared the treatment outcomes between PCNL and RIRS for treating stones in solitary kidney patients, the results showed that the PCNL group had a shorter operation time and higher SFR than RIRS group, but the overall operative rate of complications between the two groups was comparable. However, Shi et al[15] reported that PCNL group had longer operative time than RIRS group. In our meta-analysis, the results indicated that patients underwent PCNL had higher initial SFR than RIRS (OR: 3.72, P<0.001) while those that underwent RIRS had less intraoperative blood loss (dropped Hb: WMD= 3.49 g/L, P<0.001), lower blood transfusion rates (OR= 5.31, P=0.02), and higher rate of incidence of steinstrasse (OR:0.20, P=0.04). However, all the other calculated results including operation time (WMD: -9.87 minutes, P=0.34), final SFR (OR:1.65, P=0.18), overall complications (OR:1.22, P=0.38) and stone composition were similar between the two groups. Bai et al[14] also compared PCNL with RIRS for the treatment of kidney stones larger than 2cm in solitary kidney patients, 116 patients were included in the study, and the results demonstrated that PCNL group had higher initial SFR and shorter operative time than RIRS group, but the mean postoperatively hospital stay was shorter and bleeding was lower in RIRS group than PCNL group. Zhang et al[13] showed that similar results with Zeng et al. and Bai et al. These studies strengthen our results.

Nonetheless, this meta-analysis had a number of limitations during analysis and interpretation of results. The main limitation was the absence of well-conceived prospective and randomized control studies in this meta-analysis. Furthermore, the presence of heterogeneities of studies, particularly during the comparison of the continuous data, for instance, operative time, length of hospital stay; these parameters were induced by the heterogeneities of the conditions patients, surgical skills of the surgeons as well as the sample size of studies. Lastly, the sample size of all the included studies was comparatively minuscule, which resulted in a limited impact on the outcomes. Therefore, well- formulated, prospective, multicentre randomized control studies and large sample are necessary for the future to assist us better illustrate the advantages and flaws of this novel approach.

Conclusions

Our results indicate that PCNL has higher initial SFR than RIRS in the treatment of renal stones in patients with a solitary kidney; the overall complications were comparable in both groups. However, RIRS, with less

blood loss and transfusion rate, may be an alternative in selected patients.

Abbreviations

PCNL: percutaneous nephrolithotomy; RIRS: retrograde intrarenal surgery; SFR: stone-free rate; LOE: level of evidence; WMDs: weighted mean differences; ORs: odds ratios; CIs: confidence intervals; RE: random effects; FE: fixed effects.

Declarations

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Not applicable.

Authors' contributions

Manuscript writing and editing: JKH, SF. Project development: SF. Data collection: LGH, HJX, data management/analysis: LGH, ZJG. All authors reviewed the manuscript. All authors read and approved the final manuscript.

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Availability of data and materials

All data generated or analyzed during this study are included in this published article.

Ethics approval and consent to participate

Not applicable.

Consent for publication

Not applicable.

Competing interests

The authors declare that they have no competing interests

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Tables

Table 1 Characteristics of included studies

hor	Country	Study interval	Design	LOE	No.of patients PCNL/RIRS	Matching/ comparable*	Quality score△
in,2017	China	2010-2015	Retrospective	3b	60/60	1, 2,3, 4,5,6,7,8,9	▯▯▯▯▯
lei,	China	2010-2016	Retrospective	3b	111/70	1, 2,3, 4,5,7,9	▯▯▯▯
2014	China	2012-2014	Prospective	3b	82/135	1, 2,3, 4,5,6,7,8,9	▯▯▯▯▯▯▯
u,2018	China	2013-2016	Retrospective	3b	1413/491	1, 2,3, 4,5,6,8,9	▯▯▯▯▯

PCNL= percutaneous nephrolithotomy; RIRS= retrograde intrarenal surgery; NA= data not available; LOE= level of evidence.

*:Matching/comparable variable: 1= age, 2= BMI, 3= gender, 4= stone size or stone burden, 5= stone laterality, 6= site of stone, 7= comorbidities, 8= hydronephrosis, 9= follow up

△:based on Newcastle-Ottawa Scale.

Table 2 Overall analysis of demographic and clinical characteristics compared PCNL with RIRS

s of interest	No. of studies	No. of patients PCNL/RIRS	OR/WMD(95% CI)	*P*-value	Study heterogeneity			
					Chi2	df	I^2	*P*-value
	4	198/186	1.20[-1.52,3.92]	0.39	7.29	3	59%	0.06
^{2})	3	138/130	-0.23[-1.11,0.66]	0.62	1.13	2	0%	0.57
ale	4	198/186	1.03[0.68,1.58]	0.87	1.11	3	0%	0.77
left	4	198/186	0.98[0.65,1.47]	0.92	0.96	3	0%	0.81
ale	4	198/186	1.03[0.68,1.58]	0.87	1.11	3	0%	0.77
left	4	198/186	0.98[0.65,1.47]	0.92	0.96	3	0%	0.81
den,mm^2	2	96/96	5.03[-56.03,66.10]	0.87	0.19	1	0%	0.66
hrosis								
mild	3	155/143	0.45[0.27,0.76]	**0.003**	0.71	2	0%	0.70
te	3	155/143	2.23[1.32,3.77]	**0.003**	0.71	2	0%	0.70
lities								
ension	3	156/152	0.86[0.49,1.50]	0.59	2.43	2	18%	0.30
s mellitus	3	156/152	0.63[0.28,1.42]	0.26	3.62	2	45%	0.16

ercutaneous nephrolithotomy; RIRS= retrograde intrarenal surgery; OR = odds ratio; WMD = weighted mean difference; CI = e interval; BMI = body mass index.

Table 3 Overall analysis of perioperative outcomes comparing PCNL with RIRS

come of interest	No. of studies	No.of patients PCNL/RIRS	OR/WMD(95%CI) †	*P*-value	Study heterogeneity Chi^2 value	df	I^2	*P*-value
eration time, min	4	198/186	-9.87[-30.11,10.37] †	0.34	44.09	3	93%	**0.001**
ial SFR	4	198/186	3.72[2.38,5.83]	**0.001**	1.09	3	0%	0.78
al SFR	3	145/133	1.65[0.80,3.42]	0.18	0.28	2	0%	0.87
toperative serum	2	103/99	-4.20[-22.54,14.13]	0.65	0.02	1	0%	0.89
dropped, g/L	3	155/143	3.49[2.83,4.15] †	**0.001**	1.49	2	0%	0.47
rall complications	4	198/186	1.22[0.78,1.93]	0.38	2.67	3	0%	0.45
ood transfusion	4	198/186	5.31[1.36,20.68]	**0.02**	1.28	3	0%	0.73
ver	3	155/143	0.74[0.38,1.46]	0.39	0.28	2	0%	0.87
osepsis only uire	3	156/152	2.30[0.95,5.57]	0.06	1.56	2	0%	0.46
tibiotics								
psis	2	113/109	0.57[0.07,4.43]	0.59	0.23	1	0%	0.63
nbolism	2	95/87	2.76[0.28,27.07]	0.38	0.01	1	0%	0.93
einstrasse	4	198/186	0.20[0.04,0.91]	**0.04**	0.36	3	0%	0.95

IL = percutaneous nephrolithotomy; RIRS= retrograde intrarenal surgery; Cr = creatinine; SFR= stone-free rate; OR = odds ratio; WMD eighted mean difference; CI = confidence interval; † WMD.

Table 4 Overall analysis of stone composition comparing PCNL and RIRS

come of interest	No. of studies	No.of patients PCNL/RIRS	OR (95%CI)	*P*-value	Study heterogeneity Chi^2	df	I^2	*P*-value
cium based	3	155/143	1.63 [0.76, 3.43]	0.21	4.42	2	55%	0.11
c acid	3	155/143	0.71[0.37, 1.36]	0.30	1.13	2	0%	0.57
ction stone	3	113/109	0.96[0.46, 2.04]	0.92	1.08	1	8%	0.30

IL = percutaneous nephrolithotomy; RIRS= retrograde intrarenal surgery; OR = odds ratio; CI = confidence interval.

Table 5 Sensitivity analysis of high quality studies comparing PCNL with RIRS

come of interest	No. of studies	No.of patients PCNL/RIRS	OR/WMD(95%CI) †	*P*-value	Study heterogeneity Chi^2 value	df	I^2	*P*-
ɜration time, min	3	155/143	-21.78[-35.22,-8.35] †	**0.001**	12.13	2	84%	**0.002**
ɜrall complications	3	155/143	1.02 [0.59,1.75]	0.95	1.14	2	0%	0.57
ɔod Transfusion ɜ	3	155/143	5.87[1.30,26.50]	**0.02**	1.22	2	0%	0.54
ɜosepsis only uire	2	113/109	1.21[0.32,4.65]	0.78	0.06	1	0%	0.80
tibiotics								
ɜinstrasse	3	155/143	0.17[0.03,1.00]	0.05	0.25	2	0%	0.88
ial SFR	3	155/143	3.32[1.99,5.55]	**0.001**	0.26	2	0%	0.88
ɜl SFR	2	102/90	1.81[0.77,4.29]	0.17	0.11	1	0%	0.74

IL = percutaneous nephrolithotomy; RIRS= retrograde intrarenal surgery; SFR= stone-free rate; OR = odds ratio; WMD = weighted n difference; CI = confidence interval; † WMD.

Figures

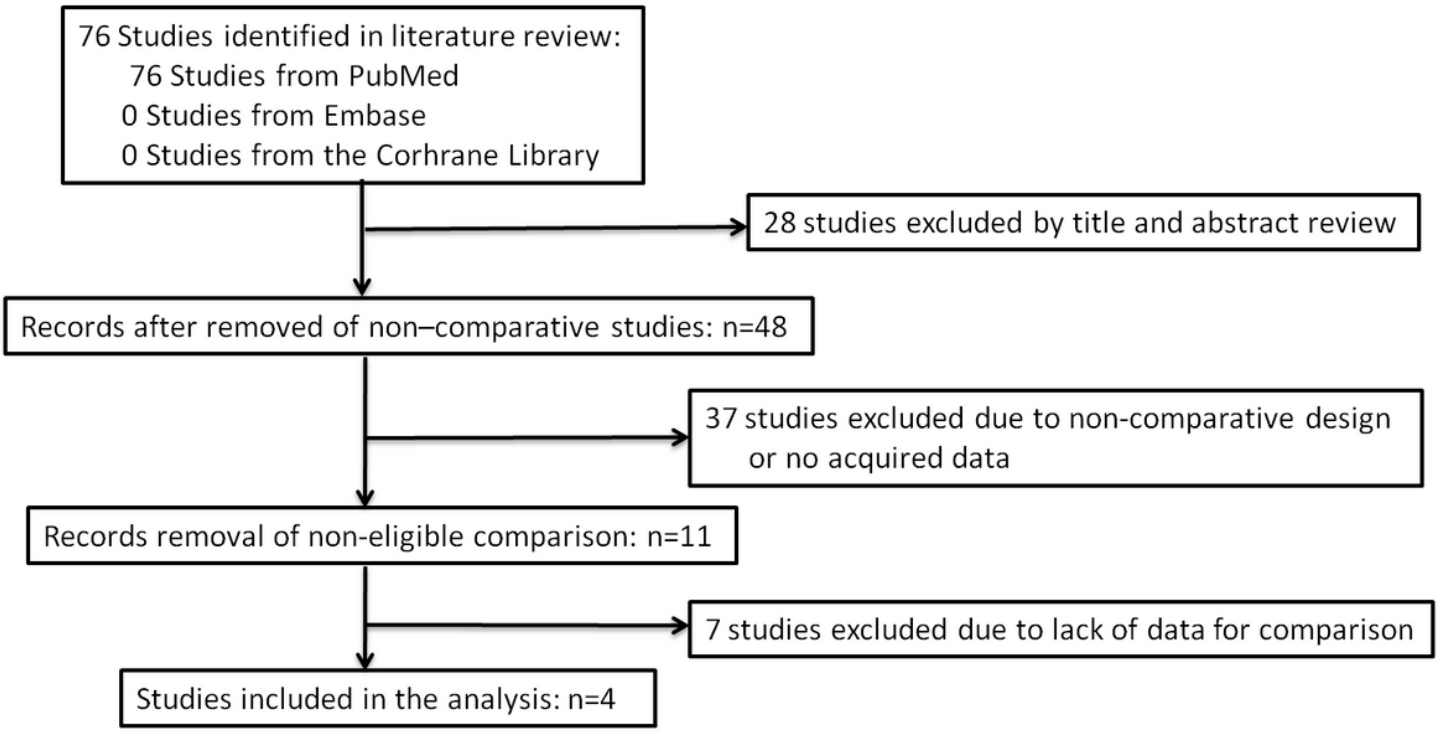

Figure 1

PRISMA diagram. The search strategy and number of studies identified for inclusion in this meta-analysis.

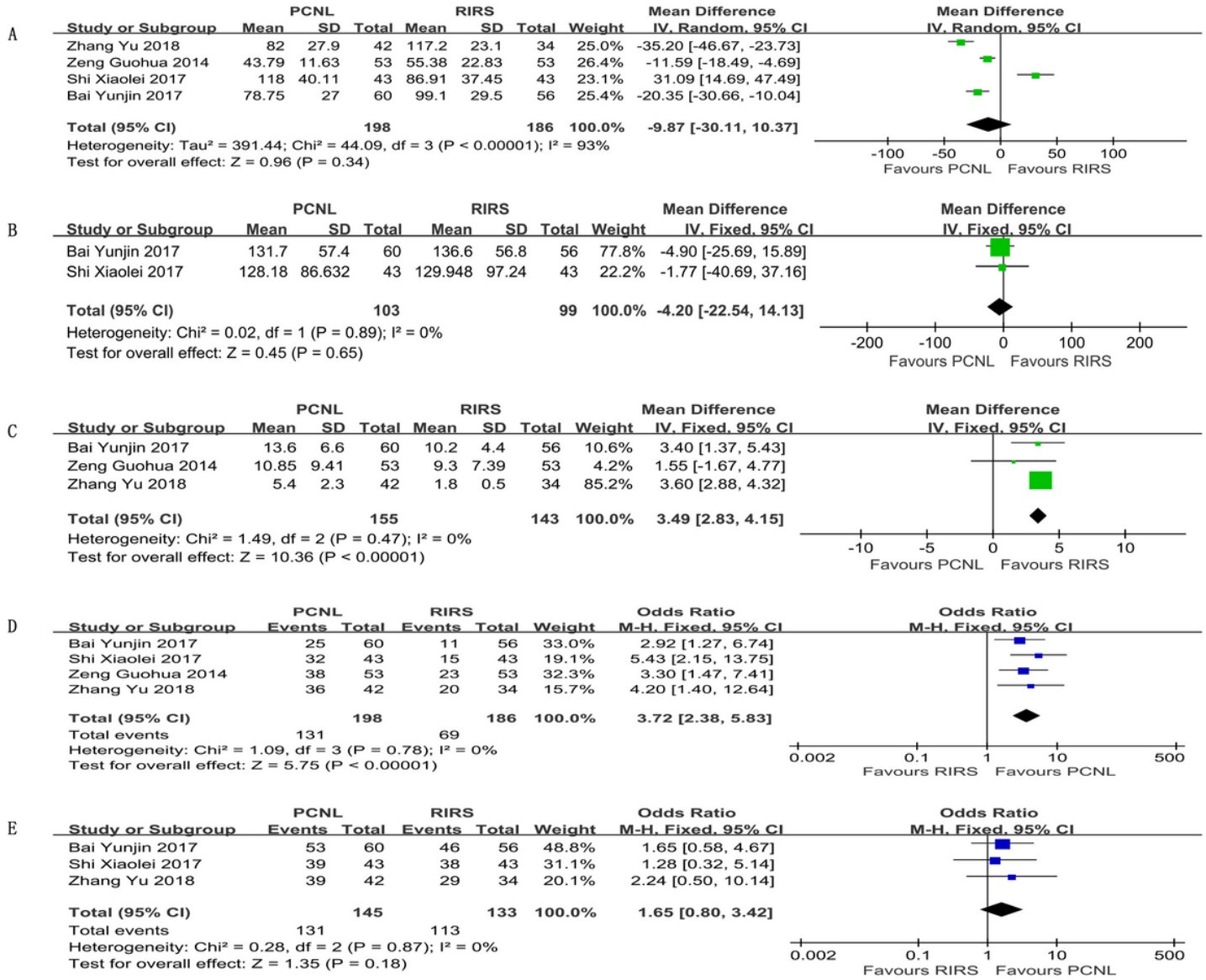

Figure 2

Forest plot and meta-analysis of perioperative outcomes between PCNL and RIRS. PCNL = percutaneous nephrolithotomy; RIRS= retrograde intrarenal surgery. A: Operation time, min; B: Postoperative serum Cr; C: Hb dropped, g/L; D: Initial SFR; E: Final SFR.

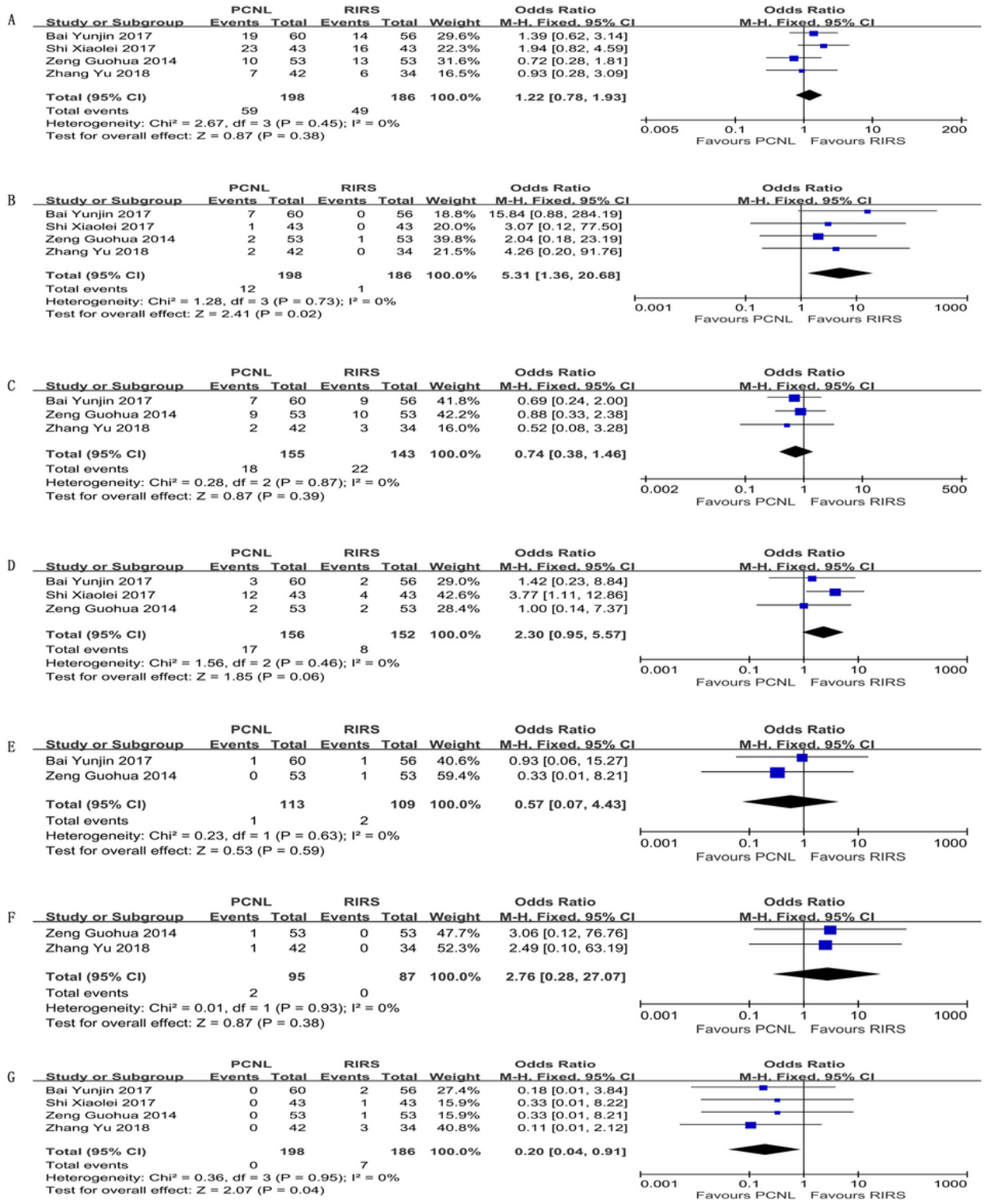

Figure 3

Forest plot and meta-analysis of complications between PCNL and RIRS. PCNL = percutaneous nephrolithotomy; RIRS= retrograde intrarenal surgery. A: Overall complications; B: Blood transfusion; C: Fever; D: Urosepsis only require antibiotics; E: Sepsis; F: Embolism; G: Steinstrasse.

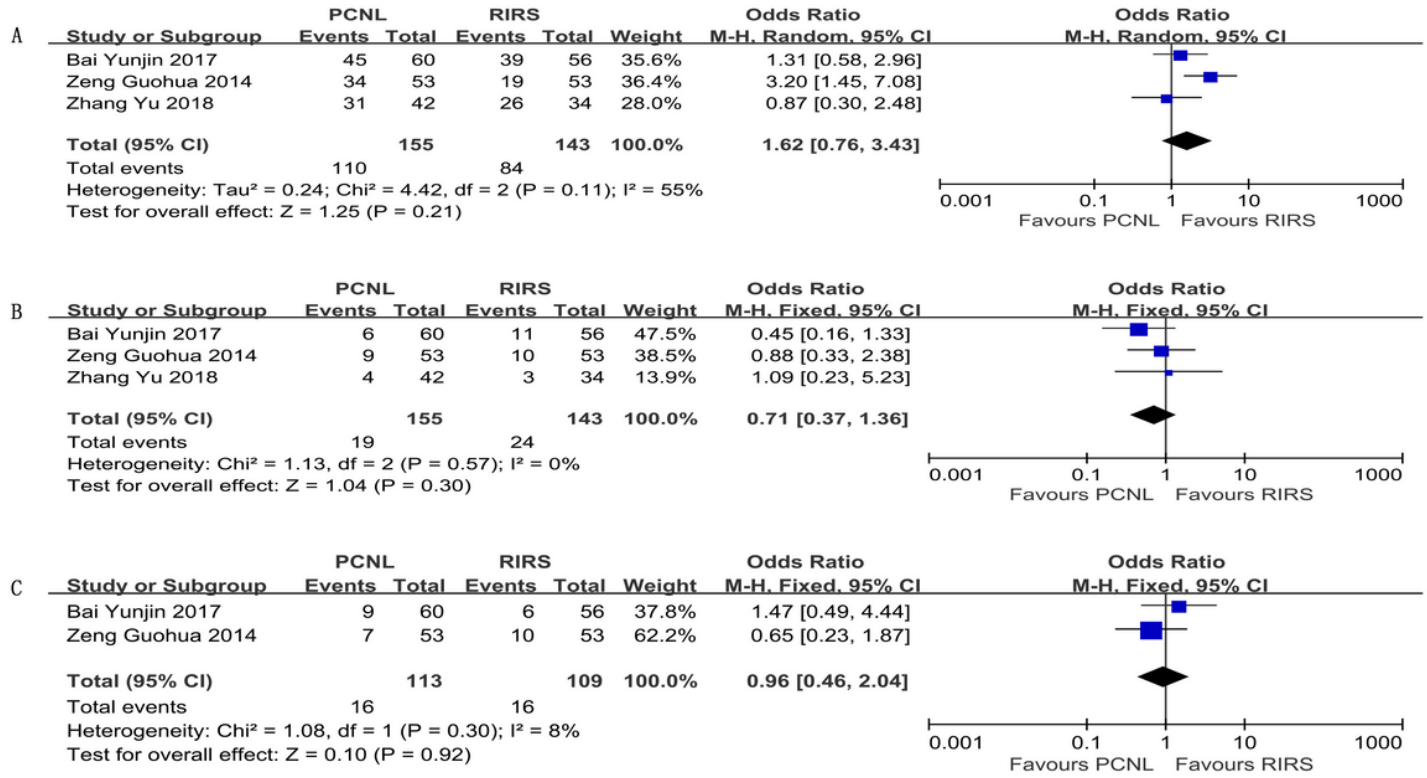

Figure 4

Forest plot and meta-analysis of stone composition between PCNL and RIRS. PCNL = percutaneous nephrolithotomy; RIRS= retrograde intrarenal surgery. A: Calcium based; B: Uric acid; C: Infection stone.

Supplementary Files

This is a list of supplementary files associated with this preprint. Click to download.

- supplement1.pdf