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REVIEW ARTICLE

Safety and Effectiveness of Percutaneous Nephrolithotomy for Patients with Stones in a Solitary Kidney: A Meta-Analysis

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Abstract
Percutaneous nephrolithotomy (PCNL) has been widely applied in the treatment of isolated renal stones in recent years. However, its safety and effectiveness for patients with isolated renal stones remains controversial. In this work, "nephrolithiasis", "stones", "renal", "nephrolithotomy", "percutaneous", "PCNL", "solitary", "single", and "kidney" were taken as key words to search the relevant studies of PCNL in patients with solitary kidney stones in PubMed, Web of Science, and Embase. The type of literature included was case series study, and the search period was from January 1, 1990 to October 31, 2021. Basic data, stone size, stone removal rate (SFR), complications, mean operation time, and mean length of stays were extracted. The quality of the included literature was assessed using the National Institute for Health and Care Excellence (NICE) case series system, data were analysed using metan and metareg commands in Stata14.1, and sensitivity of the included literature was analysed using metaninf. Finally, 14 studies with a total of 1256 patients were included. The mean adjuvant rate of percutaneous nephrolithotomy for solitary kidney stones was 20.3% (95% CI: 11.8%, 28.9%), initial SFR was 71.8% (95% CI: 64.9%, 78.8%), and final SFR was 89.7% (95% CI: 86.0%, 93.4%). The overall complication rate was 25.5% (95% CI: 18.8%, 32.3%), the incidence of major complications was 6.3% (95% CI: 3.8%, 9.3%), the blood transfusion rate was 7.4% (95% CI: 5.3%, 9.9%), and the incidence of fever was 9.1% (95% CI: 5.3%, 13.7%). It is suggested that percutaneous nephrolithotomy has a low complication rate in the treatment of solitary kidney stones.

Keywords Percutaneous Nephrolithotomy · Solitary kidney · Meta-analysis

Abbreviations

PCNL	Percutaneous nephrolithotomy
RCT	Randomized controlled trial
BMI	Body mass index
SFR	Stone-free rate
eGFR	Estimated glomerular filtration rate
CT	Computed tomography
UTI	Urinary tract infection
SIRS	Systemic inflammatory response syndrome
DVT	Deep vein thrombosis
SWL	Shockwave lithotripsy
RIRS	Retrograde intrarenal surgery
ESWL	Extracorporal shock wave lithotripsy
URS	Ureteroscopy
SK	Solitary kidney
BKs	Bilateral kidneys

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Introduction

Solitary kidney results from various causes, mainly including congenital factors and iatrogenic factors. The prevalence of kidney stones is 8.8% [1], and patients with a solitary functioning kidney are also at a high risk of developing kidney stones; an untreated staghorn stone is likely to destroy the kidney and cause life-threatening sepsis [2]. A solitary kidney would compensate for hypertrophy, and its cortex would incrassate, which makes it vulnerable. From this aspect, management of stones in a solitary kidney is intractable for urologists. In a solitary kidney case, the luxury of bilateral fully functioning kidneys no longer exists, and a surgeon must choose the proper method to ensure that the stone is removed clearly and that renal function is well preserved at the same time.

As a minimally invasive method of treatment for kidney calculi, percutaneous nephrolithotomy (PCNL) was first introduced in 1976 [3]. Since then, PCNL has become a commonly used method for renal calculi, especially in cases with staghorn stones or cases in which stones are larger than

2 cm. Due to the continuous improvement of percutaneous nephroscopy instruments, PCNL has become one of the preferred choices to treat large and complex renal stones. PCNL in patients with a solitary kidney might have a higher morbidity rate than that in patients with double functioning kidneys [4], and the need for blood transfusion and the risk of severe bleeding were higher after PCNL in a solitary kidney [4, 5]. Nephrectomy may be necessary if bleeding is severe and uncontrollable, which is unacceptable for patients with a solitary functioning kidney. Despite its potential surgical complications, including infection, severe bleeding and urinary fistula, PCNL remains the "gold standard" treatment for complex kidney stones, even for patients with a solitary kidney, providing reasonable SFRs while preserving renal function [6-8].

In recent years, there have been an increasing number of studies on PCNL for stones in a solitary kidney, which hold different opinions. The efficacy and safety of PCNL for stones in a solitary kidney requires evaluation. Here, we conducted this meta-analysis to quantitatively evaluate the safety and effectiveness of PCNL for stones in a solitary kidney.

Methods

Literature search and inclusion criteria

In accordance with the *Preferred Reporting Items for Systematic Reviews and Meta-analysis Statement* [9], an electronic search of published literature was performed using PubMed, Web of Science and Embase. Time was restricted between Jan 1, 1990, and Oct 31, 2021. A literature search was performed by two authors independently according to the following search terms: "nephrolithiasis," "stones," "renal," "nephrolithotomy," "percutaneous," "PCNL", "solitary," "single," and "kidney".

Observational studies and randomized trials were eligible for inclusion if the following requirements were met: (1) published studies on adult patients with a solitary kidney who underwent PCNL intervention in any language; (2) randomized controlled trials (RCTs), nonrandomized controlled trials (non-RCTs) or case series; and (3) studies reporting outcomes on adult patients. However, the following studies were excluded from this study: (1) studies that reported pediatric patients; (2) studies that reported patients with tumors or transplanted kidneys; and (3) studies in which no outcomes of interest (specified later) were reported or impossible to calculate or extrapolate the necessary data for further analysis. We considered various study designs, including observational studies, noncomparative case series and randomized control trials (RCTs), while review articles, conference abstracts and comments were excluded. The flow diagram of the literature selection process is shown in Fig. 1.

Data extraction

The following information was independently extracted from the included studies by two reviewers. The extracted information included first author, country, date of publication, number of patients included, patient characteristics (including mean age, man/women rate, body mass index (BMI), cause of solitary kidney), stone size (or stone burden), stone free rate (SFR) (or data to calculate this rate) including initial

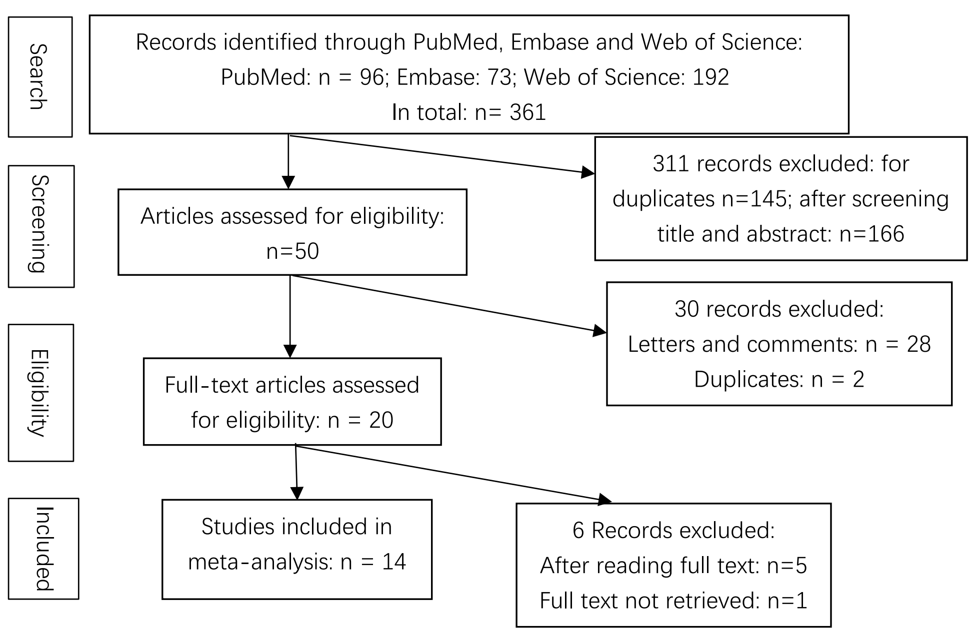


Fig. 1 Flow diagram of the literature selection process in this study

and final SFR, comorbidities (including diabetes mellitus, hypertension, heart diseases and obesity), mean operation time (minutes), and mean hospital stay (days). Finally, the third author checked the extracted data, which were inputted into an Excel file by the first two authors. Disagreements were resolved by consulting with the third author.

Quality assessment

Two reviewers independently assessed the quality of the included studies. The quality of the studies was considered by two aspects: study type and data collected. However, all of the included studies were case series, so only the National Institute of Clinical Excellence Checklist for Appraising Quality of Case Series Studies [10] was used. This checklist includes eight aspects and mainly assesses the characteristics of methodology, outcomes, and interpretation of the study from a possible score of 8. In this meta-analysis, we considered a study as "higher quality'' if the total score was greater than or equal to 4. Otherwise, the study was considered "lower quality" if the score was less than 4 (Table 1).

Heterogeneity

Because all of the studies included in this meta-analysis were case series analysis studies, the heterogeneity between studies was substantial. We further investigated potential sources of heterogeneity by meta-regression analysis, which attempts to relate differences in effect sizes to study characteristics [11]. We also examined the following factors: year of publication, geographical region (by comparing Asia-based studies with those based elsewhere) and study size (by comparing investigations of more than 90 individuals with smaller studies and additionally through use of sample size as a continuous variable) by both individually and in multiple-variable models, correspondingly. Because all the included studies were case series analysis studies and were mixed-sex samples, study type and sex were not included in the examined factors for sources of heterogeneity. The results showed that geographical region and study size were possible sources of heterogeneity.

Statistical synthesis

We carried out this meta-analysis in Stata (version 14.1) with the commands metan and metareg. We estimated heterogeneity between studies with Cochran's Q (reported as χ^2 and p values) and I^2-test, which describes the percentage of variation between studies that is due to heterogeneity rather than chance. If a p value for heterogeneity was >0.05 in an X^2-test, which indicates no heterogeneity among the included studies, fixed-effects models were applied. Otherwise, random-effects models were used. The I^2-value in the I^2-test described the proportion of total variation due to heterogeneity instead of errors of sampling. In the present study, we used random-effects models for summary statistics if the heterogeneity was high ($I^2>75\%$) [12]. These models produce study weights that mainly show between-study variation and thus provide close to equal weighting. For all studies analysed, a p value of <0.05 was considered statistically significant. When calculating the rates of blood transfusion, fever and major complications, the variance-stabilizing double arcsine transformation [13] was used, and studies with rates of zero can thus be included in the analysis. Complications were classified by using the Clavien grading system [14]. Clavien grades I and II were considered minor complications, while Clavien grades III, IV and V were classified as major complications.

Table 1 Center for reviews and dissemination partial checklist and the national institute of clinical excellence checklist for appraising quality of case series studies

Center for Reviews and Dissemination checklist: core domains	NICE checklist
(1) Were selection/eligibility criteria adequately reported?	(1) Case series collected in more than one center?
(2) Were patients recruited consecutively?	(2) Is the objective of the study clearly described?
(3) Were patients recruited prospectively?	(3) Were data collected prospectively?
(4) Was loss to follow-up reported or explained?	(4) Is there a clear definition of the outcome reported?
(5) Were at least 90% of those included at baseline followed up?	(5) Are the inclusion and exclusion criteria clearly reported?
	(6) Is there an explicit statement that the patients were recruited consecutively?
	(7) Are the main findings of the study clearly described?
	(8) Are outcomes stratified?
	Total NICE score (out of 8)

Traits of different quial varities with different superscripts are significantly different ($P<0.05$)

Results

Study characteristics and quality assessment

A total of three hundred and sixty-one citations were identified from the literature search. Finally, 14 studies [4, 8, 15-26] (reporting 1256 patients) that satisfied our predetermined inclusion criteria were included in this meta-analysis. The whole process of the literature selection is demonstrated in Fig. 1.

The baseline characteristics of the included studies in this meta-analysis are shown in Table 2. All studies were published after 2011. The number of patients enrolled in each study ranged from 16 to 412. All fourteen studies included in this meta-analysis were case series analysis studies from archived databases. There was a clear description of the outcomes to be measured and the main findings by all studies. Therefore, we assessed the quality of the included studies by using the National Institute for Health and Care Excellence (NICE) Quality Assessment for Case Series system[10]. These studies scored from 5 to 7 out of a full credit of 8, indicating that all the included studies were considered to be of high quality.

Stone burden and types of solitary kidney and comorbidities

Among the studies, twelve (n = 1012) [4, 8, 15, 17-21, 23-26] reported stone burden, three of them considered the stone burden by maximum stone diameter [8, 18, 25], while the other nine [4, 15, 17, 19-21, 23, 24, 26] calculated it by stone surface area (Table 3). Nine studies (n = 824) [15, 16, 18, 19, 21, 24-26] showed the types of solitary kidney. The reasons leading to solitary kidney included congenital,

Table 2 Summary of baseline characteristics

Author, Year	Country	Data collection dates	Journal	Patient number	Mean (SD) age(year)	Mean (SD) BMI(kg/m2)
Hosseini,2015	Iran	Sep. 2000 to Mar. 2014	Urolithiasis	412	46.4 (19–71)	NR
Liu, 2016	China	Jul. 2012 to Jun. 2014	Urolithiasis	105	52.08 ± 13.34	22.91 ± 3.02
Haberal, 2017	Turkey	Jan. 1998 to Aug. 2014	Urology	91	48 (18–78)	NR
Akman, 2011	Turkey	Oct. 2002 to Dec. 2009	Urology	47	44.1 ± 14.1	25.5 (3.7)
Huang, 2012	China	Mar. 2009 to Feb. 2011	Plos One	41	51.46 ± 14.7	NR
Torricelli,2015	Brazil	Jan. 2005 to Oct. 2013	IBJCU	27	45.6 ± 14.6	28.8 (4.7)
Resorlu, 2011	Turkey	Nov. 2006 to Mar.2009	Urol Res	16	49.6 (31–55)	NR
Wong, 2013	UK	Jan. 2003 to Sep. 2011	Urology	17	51.5(24–87)	NR
Wang, 2012	China	Mar. 2004 to Oct. 2011	IBJCU	18	44.1(29–54)	24.3† (NR)
El-Tabey, 2014	Egypt	Jan. 2002 to Dec.2009	Urology	200	52.3 ± 11.7	NR
Basiri, 2012	Iran	NR	J ENDOUROLOGY	30	38.5(15.6)	NR
Süelözgen,2014	Turkey	Jan. 2008 to Jan. 2014	AIUA	19	42.52 ± 16.72	NR
Bucuras, 2011	Europe, USA India, China	NR	J ENDOUROLOGY	189	51.6(15)	27.0† (NR)
Su, 2018	China	Oct. 2014 to Dec. 2016	World Journal of Urology	44	51.4 ± 12.0	NR
Author, Year	Man/women	Right/ left side	Study design	NICE score		
Hosseini,2015	279/133	258/154	Case series analysis	7		
Liu, 2016	70/31	58/47	Case series analysis	7		
Haberal, 2017	60/31	57/34	Case series analysis	6		
Akman, 2011	NR	NR	Case series analysis	6		
Huang, 2012	27/14	22/19	Case series analysis	6		
Torricelli,2015	8/19	13/14	Case series analysis	6		
Resorlu, 2011	14/2	9/7	Case series analysis	6		
Wong, 2013	15/7	NR	Case series analysis	5		
Wang, 2012	12/6	10/8	Case series analysis	6		
El-Tabey, 2014	67/133	NR	Case series analysis	6		
Basiri, 2012	NR	NR	Case series analysis	6		
Süelözgen,2014	15/4	NR	Case series analysis	6		
Bucuras, 2011	111/88	NR	Case series analysis	7		
Su, 2018	33/15	NR	Case series analysis	6		

NR not reported. Median value, BMI body mass index, IBJCU International Brazilian Journal of Urology, AIUA Archives of Italian Urology and Andrology

Traits of different quial varities with different superscripts are significantly different ($P < 0.05$)

Table 3 Summary of stone burden, definition of "stone free", imaging modalities, time between surgery, initial and final stone free rate

Author, Year	Mean Stone Size/Burden + / − SD	Definition of "Stone Free"	Postop Imaging Modality	Time Between Surgery and Imaging	Mean (SD) Initial Stone Free Rate (%)	Mean (SD) Final Stone Free Rate (%)
Hosseini,2015	(21–55)26.5 mm	NR	XR, KUB	NC	81(NR)	91.3(NR)
Liu, 2016	2009 mm^2	NR	NR	NR	50.0	81.9
Haberal,2017	400(2500–25) mm^2	NR	NR	NR	NR	73
Huang,2012	912 ± 517 mm^2	< = 4 mm	NR	NR	85.4	97.6
Torricelli,2015	503 ± 222 mm^2	NR	NCCT	Day1	NR	67(NR)
Resorlu,2011	10.2 cm^2(6–16)	< 5 mm	NR	NR	81.3	93.7
Süelözgen,2014	405 ± 252.9 mm^2	< 4 mm	NCCT	1 m	84	NR
Wang,2102	3.4(2.2–5.0) cm	< 4 mm	NR	NR	NR	88.9
El-Tabey,2014	NR	NR	NR	NC	81.5	89.5
Bucuras,2011	347* (NR) mm^2	NC	NC	30 Days	65.4	NR
Basiri,2012	2.84 cm (55)	< 5 mm	XR, KUB, USS	6 m	NR	95.3(NR)
Su,2018	NR	< 4 mm	NR	1y	56.8	81.8
Akman,2011	816 ± 487 mm^2 (200–2000)	< 4 mm	XR, KUB NCCT	Day1 and 3–6 m	74.5	90.9
Wong,2013	825 mm^2 (164–2229)	4 mm	XR-KUB USS, CT	6–12 week	59	77

KUB, kidney, ureter, and bladder; NC, not clear; NCCT, noncontrast computed tomography; URS, ureteroscopy; XR, X-ray; USS, ultrasound; *Median

Traits of different quial varities with different superscripts are significantly different ($P < 0.05$)

nephrectomy for various reasons and nonperfusion (functional) solitary kidney. Only two studies [15, 18] described comorbidities, including diabetes mellitus, hypertension, heart diseases, renal insufficiency and obesity. The types of solitary kidneys and comorbidities are shown in Table 4.

Operative time and renal function

A total of 12 studies (n = 965) [4, 15, 16, 18-26], except for two[16, 17], reported the mean operative time. The operative time ranged from 40 to 300 min, and the overall mean operative time was 85.1 min.

Nine studies (n = 825) [4, 8, 16, 17, 19, 21, 24-26] specified the changes in serum creatinine before, after, and during follow-up. Bucuras et al. [4] observed the change in renal function just one day after the operation, while the longest change lasted to 3 ± 1.4 years after the operation [16]. Seven [4, 16, 19, 21, 24-26] out of nine studies found that serum creatinine was reduced after the operation, four [4, 16, 19, 21] of which provided the p value, and all of the results were statistically significant; the remaining two studies [8, 17] reported the opposite results, and Haberal et al. [17] did not provide the p value, while another study [8] reported the p value as 0.111. Eight studies [15-17, 19, 21, 22, 24, 26] reported the mean estimated glomerular filtration rate (eGFR) before and after PCNL; six [15, 16, 19, 21, 22, 26] found that the mean eGFR was elevated after the operation, four reported p values, and all of the results were statistically significant; one study [17] found the opposite result, and the p value was 0.019; and the remaining study [24] reported that the mean eGFR remained almost stable and did not provide the p value. A total of five studies [15, 16, 19, 22, 26] involving 346 patients summarized the change in mean eGFR after PCNL. The results showed that in 113 patients, the mean eGFR was improved, in 194 patients, it was stationary, and only in the remaining 39 patients did the mean eGFR deteriorate after the operation (Table 5).

Length of hospital stay and auxiliary procedures rate

A total of twelve studies (n = 867) [8, 15, 17-26] reported the length of hospital stay, and the overall mean hospital stay was 4.8 days. Hosseini et al. [18] reported the shortest mean hospital stay as 2 days, while Wang [25] and his colleagues reported the longest mean hospital stay as 9.1 days.

The enrolled studies included 6 studies (n = 836) [16, 18-22, 25] that reported the auxiliary procedure rate. Meta-analysis showed that there was evidence for heterogeneity between the studies that reported auxiliary procedure rates ($X^2 = 49.48$, p = < 0.001, $I^2 = 87.9\%$). The random-effects model showed that the mean auxiliary procedure rate was 20.3% (95% CI: 11.8%, 28.9%; Fig. 2). The results of the auxiliary procedure rate sensitivity analysis are shown in Fig. 3. Seven studies were included, and after excluding any one study, the combined results of the remaining 6

Table 4 Summary of the reasons leading to solitary kidney and comorbidities

Author, Year	No. of patients	Reasons for solitary kidney			
		Functional		Congenital	Nephrectomy
Hosseini, 2015	412	161		36	215
El-Tabey, 2014	200	148		52 (anatomic)	
Akman, 2011	47	15		10	22
Huang, 2012	41	7		4	30
Torricelli, 2015	27	0		3	24
Süelözgen, 2014	19	9 (physiological)			10
Wang, 2012	18	6		4	8
Wong, 2013	17	11		2	9
Resorlu, 2011	16	2		3	11
Comorbidities					
Author, Year	Diabetes mellitus	Hypertension	Heart diseases	Renal insufficiency	Obesity
Hosseini, 2015	66	104	47	56	65
El-Tabey, 2014	NR				
Akman, 2011	7	11	NK	NK	NK
Huang, 2012	NK				
Torricelli, 2015	NR				
Süelözgen, 2014	NR				
Wang, 2012	NR				
Wong, 2013	NR				
Resorlu, 2011	NR				

Traits of different quial varities with different superscripts are significantly different ($P < 0.05$)

NK, not known, NR, not reported

studies were statistically significant. The auxiliary procedure rate was 14.0% (95% CI: 12.0%, 17.0%), which was consistent with the original results, indicating that the results were stable. Individual variable metaregression analysis showed that sample size (continuous) was related to high heterogeneity between these studies (p = 0.008; Table 6), but the relation did not remain significant after multivariate metaregression.

Stone-free rate

Eight enrolled studies (n = 232) [8, 15, 19, 21-23, 25, 26] described the criteria for "free stone". Basiri et al.[8] and Resorlu et al. [21] employed 5 mm, and the remaining six studies [15, 19, 22, 23, 25, 26] used 4 mm. However, the other six studies did not specifically mention the stone clearance standard. Six studies [8, 15, 18, 23, 24, 26] mentioned the postoperative imaging modalities they used to check the stone clearance rate. The imaging modalities varied among postoperative plain kidney-ureter-bladder (KUB), ultrasound and noncontrast computed tomography (CT) scans. The time between surgery and imaging ranged from one day [24] to 6 months [8] after the operation (Table 3).

A total of eleven studies (n = 1181) [4, 15-23, 26] out of the fourteen included studies described the initial SFR after PCNL, and the initial SFR ranged from 50.5% to 85.4%. There was evidence for heterogeneity between the studies that reported the initial SFR ($X^2 = 49.48$, $p < 0.0001$, $I^2 = 83.9\%$). The random-effects model showed that the mean initial SFR was 71.8% (95% CI: 64.9%, 78.8%; Fig. 4). The initial SFR sensitivity analysis results are illustrated in Fig. 5. Eleven studies were included, and the combined results of the remaining 10 studies were statistically significant if any one study was excluded. The initial SFR was 72.0% (95% CI: 65.0%, 79.0%), which was consistent with the original merger results, indicating that the results were stable. None of the factors we explored further was significantly associated with heterogeneity in metaregression (Table 6).

Eleven studies (n = 957) [4, 8, 15, 16, 18-22, 25, 26] among the included studies reported the final SFR after applying the ancillary procedure. Torricelli and his colleagues [24] reported the lowest final SFR. In their study, only 66.7% of patients were stone free when discharged, while Huang [19] and his colleagues achieved the highest final SFR, and 97.6% of the treated patients were stone free after using ancillary procedures. There was moderate heterogeneity between the thirteen studies that reported final SFR ($X^2 = 28.74$, $p = 0.001$, $I^2 = 65.2\%$). The random-effects model of meta-analysis revealed that the mean final SFR of the eleven studies was 89.7% (95% CI: 86.0%, 93.4%; Fig. 6). Individual variable metaregression analysis showed

Table 5 Summary of renal function

Author, Year	Follow-up time	Creatinine at last of follow up (mg/dL)	Preoperative creatinine (mg/dL)	*P* value	Mean eGFR at last follow-up (mL/min)	Preoperative eGFR(mL/min)
El-Tabey, 2014	3 ± 1.4 y	1.83 ± 0.7	2 ± 0.8	< 0.01	64 ± 29.5	57 ± 30
Bucuras, 2011	One day	1.4 (0.74)	1.5 (0.8)	< 0.001	NR	NR
Haberal, 2017	1 m	1.35	1.20	NK	50.1	63.1
Akman, 2011	6 m	NR	NR	NR	83.5 ± 29.4	76.4 ± 27.1
Huang, 2012	18.7 m	1.23 ± 0.34	1.49 ± 0.47	< 0.05	83.9 ± 27.4NR	74.9 ± 24.2
Basiri, 2012	1 m	1.71 (0.23)	1.16 (0.41)	0.111	NR	NR
Torricelli, 2015	NK	1.4	1.5 ± 0.8	NK	60	60.5 ± 32.0
Wang, 2012	3 m	0.99 ± 0.15	1.21 ± 0.31	NK	NR	NR
Wong, 2013	3 m	1.43	1.63	NK	59	51
Resorlu, 2012	1 y	1.28 (0.22)	1.49 (0.46)	0.05	82.5 (15.65)	75.56(22.3)
Su, 2018	12 y	NR	NR	NR	61.3 ± 25.4	53.9 ± 24.0
Author, Year	*P* value	No. of patients eGFR was improved	No. of patients eGFR showed deterioration	No. of patients eGFR showed stationary		
El-Tabey, 2014	< 0.01	62(31%)	31 (15.5%)	107 (53.5%)		
Bucuras, 2011	NR	NR	NR	NR		
Haberal, 2017	0.019	NR	NR	NR		
Akman, 2011	< 0.01	13(29.5%)	3(6.8%)	28(63.6%)		
Huang, 2012	< 0.05	11 (26.8%)	1(2.5%)	29 (70.7%)		
Basiri, 2012	NR	NR	NR	NR		
Torricelli, 2015	NR	NR	NR	NR		
Wang, 2012	NR	NR	NR	NR		
Wong, 2013	NK	15(88.2%)	1(8.9%)	1(8.9%)		
Resorlu, 2012	0.033	NR	NR	NR		
Su, 2018	< 0.01	12(27.3%)	3(6.8%)	29(65.9%)		

NK, not known; NR, not reported, e-GFR, estimated glomerular filtration rate, m moth, y year

Traits of different quial varities with different superscripts are significantly different ($P < 0.05$)

Fig. 2 Forest plot and meta-analysis of auxiliary procedure rates. Weights are from random-effects analysis. SD Standard Definition

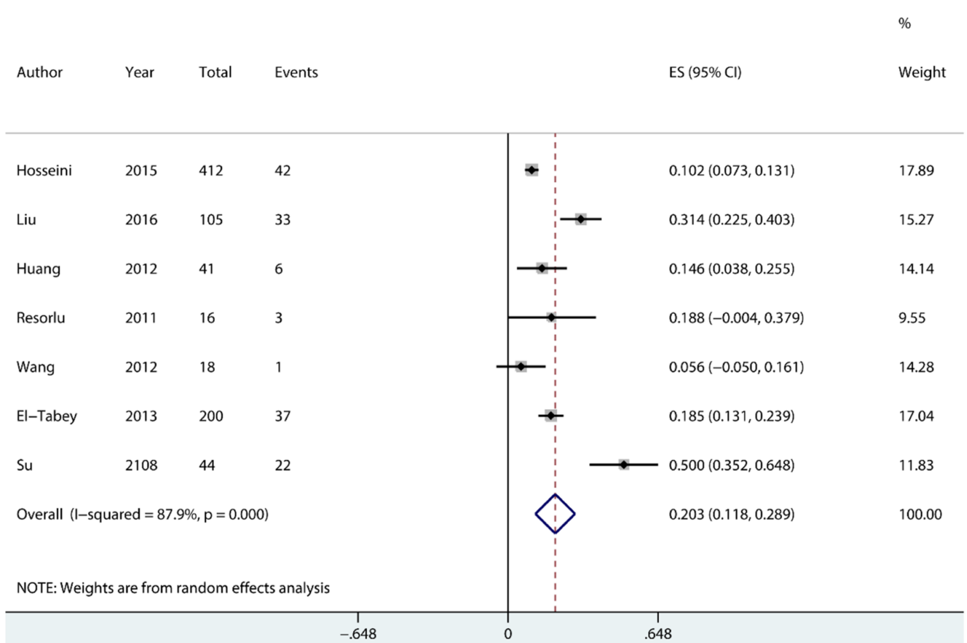
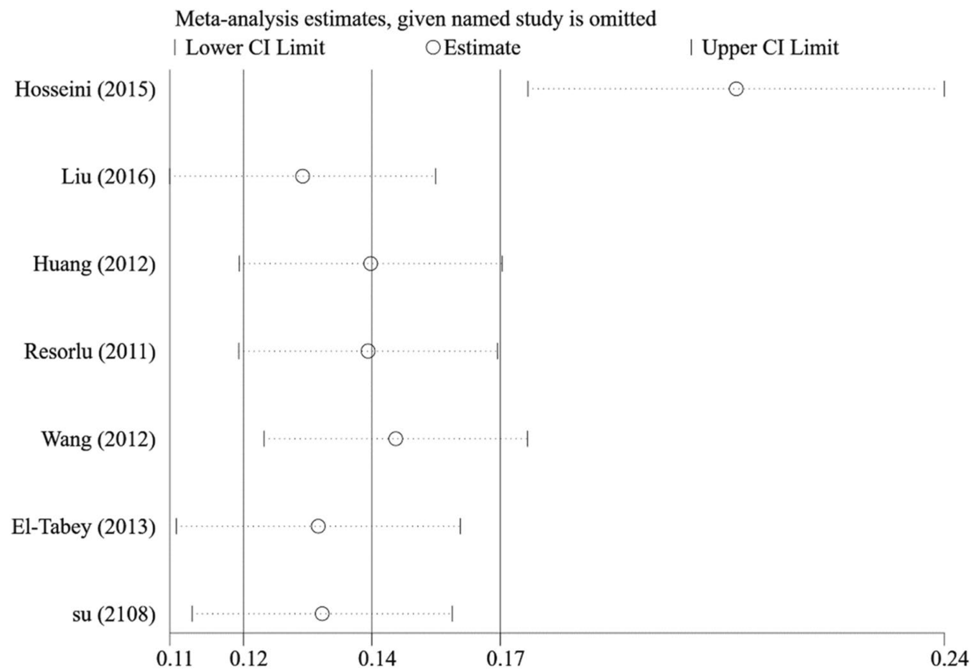


Fig. 3 Forest map for sensitivity analysis of auxiliary procedure rate



that sample size (> 90 vs < 90) was possibly related to high heterogeneity between these studies ($p = 0.045$; Table 6), but the relation did not remain significant after multivariate metaregression.

Among all studies, 5 ($n = 222$) [8, 19, 20, 23, 24] mentioned the hemoglobin drop in patients after surgery. The mean hemoglobin drop ranged from 1.34 g/dL to 2.7 g/dL, and the transfusion rate varied from 0% to 10.0% among the five studies that reported a hemoglobin drop after the operation. See Table 7 for a summary of the hemoglobin drop.

Complications

All of the included studies ($n = 1256$) [4, 8, 15-26] reported total complication rates. There was high heterogeneity between the studies ($X^2 = 86.01$, $p < 0.0001$, $I^2 = 84.9\%$). The random-effects model showed that the overall complication rate was 25.5% (95% CI: 18.8%, 32.3%, Fig. 7). The sensitivity analysis results of the overall postoperative complication rate are shown in Fig. 8. Fourteen studies were included, and the combined results of the remaining 13 studies were statistically significant after one study was excluded. The overall postoperative complication rate was 26.0% (95% CI: 19.0%, 32.0%), which was consistent with the original combined results, indicating the stability of the results. None of the factors we explored further was significantly associated with heterogeneity in metaregression (Table 6).

Twelve of the enrolled studies ($n = 825$) [4, 8, 15-17, 19-22, 24-26] mentioned the incidence of major complications (Clavein classification: GIII—GV). In three studies [19, 22, 25], there were no major complications, so the variance-stabilizing double arcsine transformation was used. There was moderate heterogeneity between the studies ($X^2 = 29.52$, $p = 0.002$, $I^2 = 52.4\%$), and random-effects models were used. Finally, the major complication rate was 6.3% (95% CI: 3.8%, 9.3%; Fig. 9). Individual variable metaregression analysis showed that region (Asia vs others) was related to the heterogeneity between these studies ($p = 0.007$; Table 6), but the relation did not remain significant after multivariate metaregression.

All fourteen included studies ($n = 1256$) reported the blood transfusion (Clavein classification: GII) rate. In two studies [23, 25], no patient needed blood transfusion, and the variance-stabilizing double arcsine transformation was used. There was moderate heterogeneity between the studies ($X^2 = 23.97$, $p = 0.031$, $I^2 = 45.8\%$), and the random-effects model was used. Finally, the blood transfusion rate was 7.4% (95% CI: 5.3%, 9.9%; Fig. 10). Individual variable metaregression analysis showed that sample size (continuous) was related to high heterogeneity between these studies ($p = 0.006$; Table 6), but the relation did not remain significant after multivariate metaregression.

A total of thirteen studies ($n = 1165$) [4, 8, 15, 16, 18-26] reported the incidence of fever (Clavein classification: GI). In two studies [15, 24], no patient developed fever. Therefore, the variance-stabilizing double arcsine transformation was used. There was evidence for heterogeneity between the studies ($X^2 = 59.65$, $p < 0.0001$, $I^2 = 79.9\%$), and a random-effects model was used. Finally, the incidence of fever was 9.1% (95% CI: 5.3%, 13.7%; Fig. 11). However, heterogeneity analysis showed that none of the factors we explored further was significantly associated with heterogeneity in metaregression (Table 6).

Table 6 Univariate meta-regression for prevalence of initial stone-free rate, final stone-free rate, fever, major complication rate, blood transfusion rate, total complication rate and ancillary procedure rate

	Metaregression Coefficient (%)	95% CI	*P* value
Initial stone free rate			
Year of publication	-0.30	-0.79 to 0.20	0.207
Region (Asia vs others)	-0.07	-0.33 to 0.18	0.540
Sample size(> 90 vs < 90)	-0.45	-0.29 to 0.20	0.689
Sample size, continuous	0.003	-0.0007 to 0.01	0.561
Final stone free rate			
Year of publication	-0.02	-0.04 to 0.0006	0.485
Region (Asia vs others)	0.29	-0.89 to 0.15	0.594
Sample size(> 90 vs < 90)	-0.04	-0.15 to 0.07	0.045
Sample size, continuous	-0.0002	-0.0004 to 0.0005	0.941
Fever			
Year of publication	-0.008	-0.10 to 0.08	0.851
Region (Asia vs others)	0.25	-0.96 to 0.59	0.141
Sample size (> 90 vs < 90)	-0.98	-0.49 to 0.29	0.588
Sample size, continuous	-0.0004	-0.002 to -0.001	0.547
Major complication rate			
Year of publication	-0.007	-0.07 to 0.06	0.816
Region (Asia vs others)	-0.31	-0.52 to -0.11	0.007
Sample size (> 90 vs < 90)	0.10	-0.20 to 0.40	0.473
Sample size, continuous	0.0006	-0.002 to 0.003	0.561
Blood transfusion rate			
Year of publication	0.03	-0.13 to 0.09	0.131
Region (Asia vs others)	-0.13	-0.51 to 0.24	0.453
Sample size (> 90 vs < 90)	-0.17	-0.56 to -0.21	0.342
Sample size, continuous	-0.001	-0.002 to 0.0005	0.006
Total complication rate			
Year of publication	-0.02	-0.15 to 0.11	0.732
Region (Asia vs others)	-0.07	-0.71 to -0.56	0.802
Sample size (> 90 vs < 90)	0.04	-0.0.59 to 0.66	0.904
Sample size, continuous	0.0005	-0.002 to 0.003	0.646
Ancillary procedure rate			
Year of publication	0.01	-0.004 to 0.03	0.118
Region (Asia vs others)	0.20	-1.90 to 2.31	0.831
Sample size (> 90 vs < 90)	-0.53	-2.10 to 1.03	0.425
Sample size, continuous	-0.004	-0.006 to -0.001	0.008

Traits of different quial varities with different superscripts are significantly different ($P < 0.05$)

Complications and their frequencies are listed in Table 8. A total of 368 complications were recorded, of which the largest proportion were Clavien grade I (167 of 368, 45.4%). Complications that were identified as Clavien Grade II (107 of 368, 29.1) included pneumonia, urinary tract infection (UTI), deep vein thrombosis (DVT) and systemic inflammatory response syndrome (SIRS) requiring antibiotics. A total of 59 (16.0% of all complications) patients suffered complications that were identified as Clavien Grade III, and 7 of them suffered severe bleeding that required angioembolization. Thirty-two patients (consisting of 8.7% of all complications) suffered complications identified as Clavien grade IV, including sepsis, heart failure, myocardial infarction and renal insufficiency. Hosseini [18] and his colleagues reported two cases of death in their study that included 412 patients, but they did not mention the reason for the death, which was classified as Clavein classification grade V and accounted for 0.5% of overall complications.

Discussion

This meta-analysis quantitatively summarized the efficacy and safety of PCNL for the treatment of stones in a solitary kidney. As patients with a solitary kidney are at high risk of developing kidney stones[2] and management of stones in a solitary kidney still represents a dilemma for urologists all over the world, this meta-analysis seems important. Fourteen studies involving 1225 patients were included in this meta-analysis. Our main findings were that PCNL was an effective method with a mean initial SFR of 71.3%, which could reach 89.7% after using auxiliary procedures (some 20.3% patients needed auxiliary procedures); it was also a relatively safe method with an acceptable postoperative complication rate, and it could, at the same time, preserve kidney function in a solitary kidney. However, PCNL can lead to some unpleasant complications, such as severe bleeding and even death of the patient. Our investigation of potential sources of heterogeneity showed that sample size and region might be potential sources of heterogeneity. In recent years, the number of studies on the safety of PCNL for stones in a solitary kidney has increased rapidly, and some of them are multicenter studies [4, 18], although most of them are also retrospective.

SFR represents one of the key parameters when evaluating the efficacy of a stone surgical procedure [34]. In a study involving 156 cases of Shockwave lithotripsy (SWL) monotherapy, the overall SFR was 80.8% at 3 months after SWL, and only 62.8% stone clearance was achieved after one session[35]. According to our results, the mean initial and final SFRs of PCNL can reach 71.3% and 89.7%, respectively, and it needs to be emphasized that most of the kidney stones reported in our meta-analysis are staghorn stones or stones that are larger than 2 cm. A study demonstrated that for stones < 1 cm, PCNL provided a 100% SFR compared with 67% for SWL [36]. PCNL could reach a superior SFR compared with SWL (95% vs 37%) at a 3-month follow-up; furthermore, the SFRs for stones < 1, 1 to 2, and 2 to 3 cm were 100%, 93%, and 86%, respectively, while the SFRs of SWL for stones < 1, 1–2, and 2–3 cm were 63%, 21%, and 14%, respectively. This study revealed that the treatment efficacy for PCNL was significantly better than that for SWL for all stone sizes. However, longer hospital stays and higher complication rates for PCNL compared with SWL

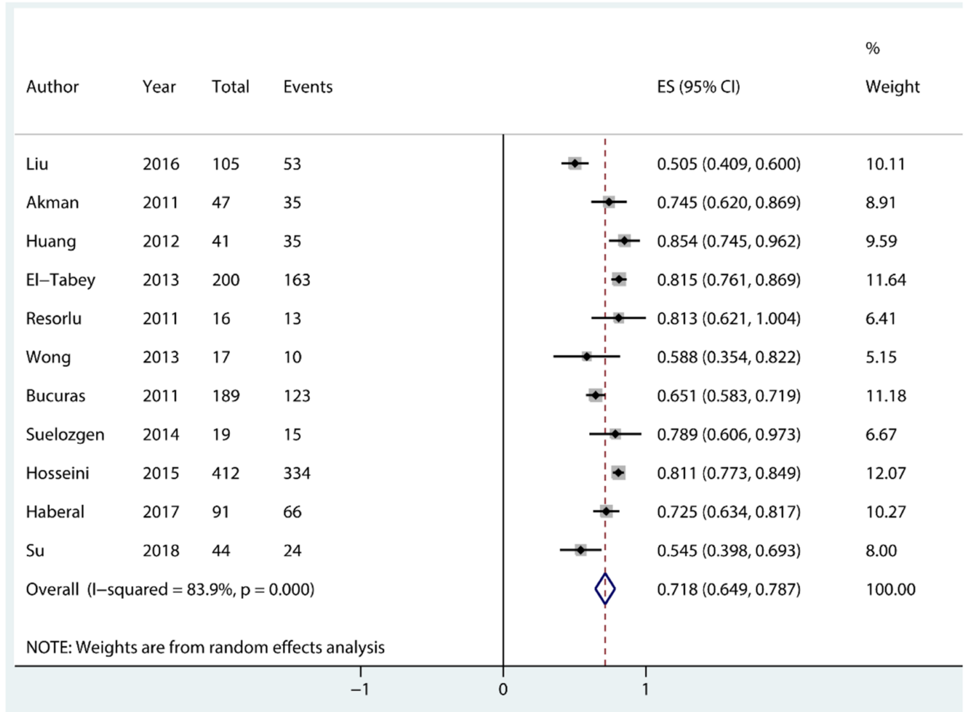


Fig. 4 Forest plot and meta-analysis of initial stone-free rate. Weights are from random-effects analysis. SD Standard Definition

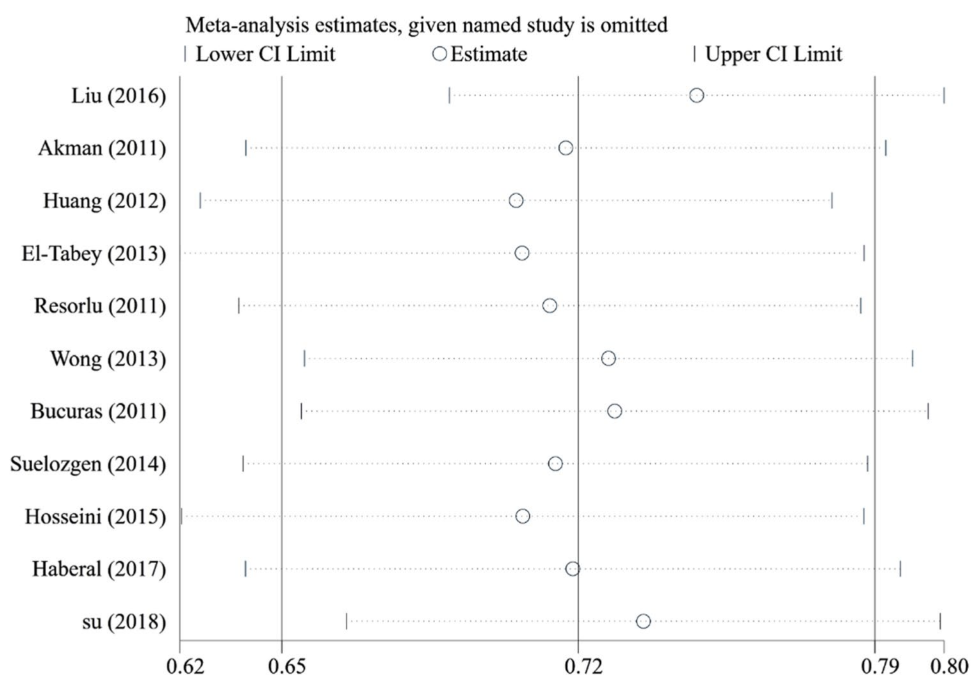


Fig. 5 Forest map for sensitivity analysis of initial stone-free rate

were reported by both randomized trials, which indicates that PCNL may be a more invasive technique [37, 38].

Another advantage of PCNL over SWL is the lower need for auxiliary procedures and retreatment rate. SWL failed in more than one-third (37.5%) of the patients, and they might need to repeat the session or even shift to PCNL or retrograde intrarenal surgery (RIRS) to remove the significant fragments [39]. PCNL was considered to have a higher complication rate. In the present meta-analysis, we found that the overall complication rate was 25.5%, and the occurrence of major complications (Clavein classification: GIII to GV) was 5.5%. An SWL solitary kidney is a significant risk factor for hemorrhage [41], and we found that approximately 7.4% of patients with a solitary kidney needed blood

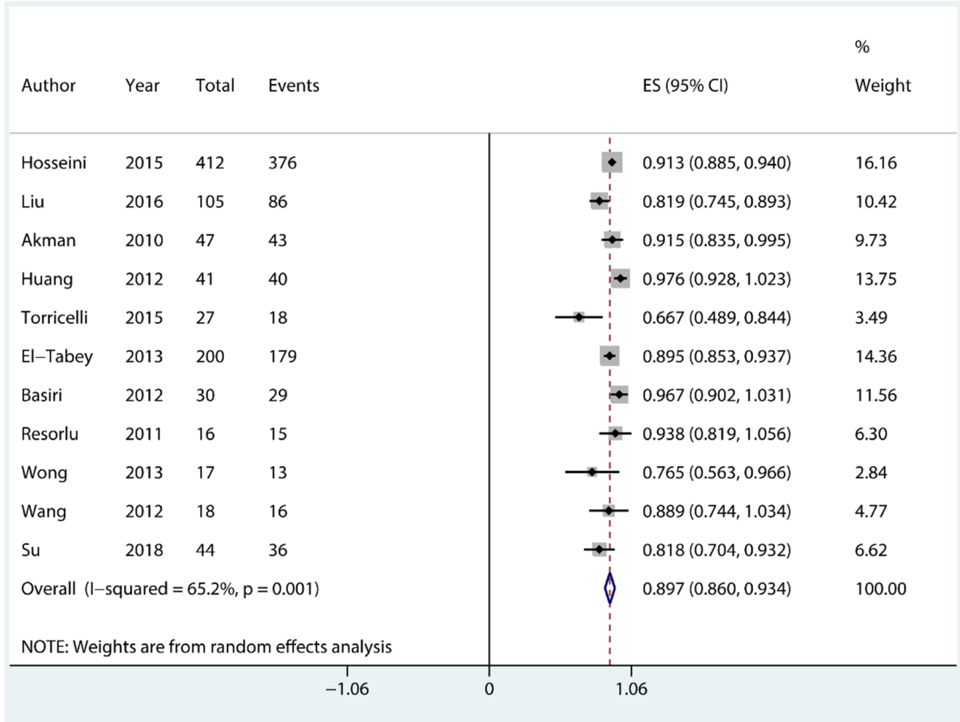


Fig. 6 Forest plot and meta-analysis of final stone-free rate. Weights are from random-effects analysis. SD Standard Definition

Table 7 Summary of hemoglobin drop

Author, Year	Mean (SD) Preop Hemoglobin(g/dL)	Mean (SD) postop Hemoglobin(g/dL)	Mean(SD)Hemoglobin drop (g/dL)	Transfusion Rate (n; %)
Liu, 2106	NR	NR	1.59(SD)	10(9.6)
Torricelli, 2015	13.4 (SD)	10.7 (SD)	2.7(SD)	5(18.5)
Basiri, 2012	12.9 (1.18)	11.56 (1.16)	1.34(SD)	1(3.3)
Süelözgen, 2014	NR	NR	1.75 ± 0.97	0(0)
Huang, 2012	11.48 ± 2.69	NR	NR	1(2.4)

NR, not reported

Traits of different quial varities with different superscripts are significantly different (*P* < 0.05)

transfusion after PCNL. Although SWL has a relatively lower complication rate than PCNL, the total complication rates of SWL and RIRS were almost identical, which meant that SWL was not a so-called noninvasive procedure[42]. However, patients with a solitary kidney are at a greater risk of developing steinstrasse, especially if a large stone burden or a staghorn stone is present [43, 44]. Steinstrasse might occur at a 40% rate if a double-J stent is not placed after SWL for stones > 2 cm [45]. Postprocedure steinstrasse is associated with SWL and occurs in approximately 4–7% of cases according to a study conducted by Jessen and his colleagues [46]. Steinstrasse is not acceptable for a patient with a solitary kidney, which leads to ureteral obstruction and further deterioration of renal function. A study found that extracorporal shock wave lithotripsy (ESWL) combined with PCNL was an effective and safe method to treat complex calculi in a solitary kidney[48].

As minimally invasive procedures, RIRS methods such as flexible ureteroscopy (URS) have pushed the barriers of renal stone management [49]. The mean initial and overall SFRs were 73.4% and 87.2%, respectively, which were similar to the present meta-analysis of 71.3% and 89.7%, respectively[50], but we also noticed that the present PCNL results are based on a greater number of studies and over tenfold as many patients (4 studies vs. 14 studies and 116 patients vs 1256 patients, respectively). Furthermore, they found that URS required 1.23 procedures per patient. In 2015, in a study comparing minimally invasive PCNL and RIRS for stones larger than 2 cm in patients with a solitary kidney, the SFRs after a single procedure were 71.7% in the minimally invasive PCNL group and 43.4% in the RIRS group (p = 0.003) [51], while the complication rates in the two groups were similar. In a randomized trial [38], for patients with stones 1.1 to 2.5 cm, the primary SFR was

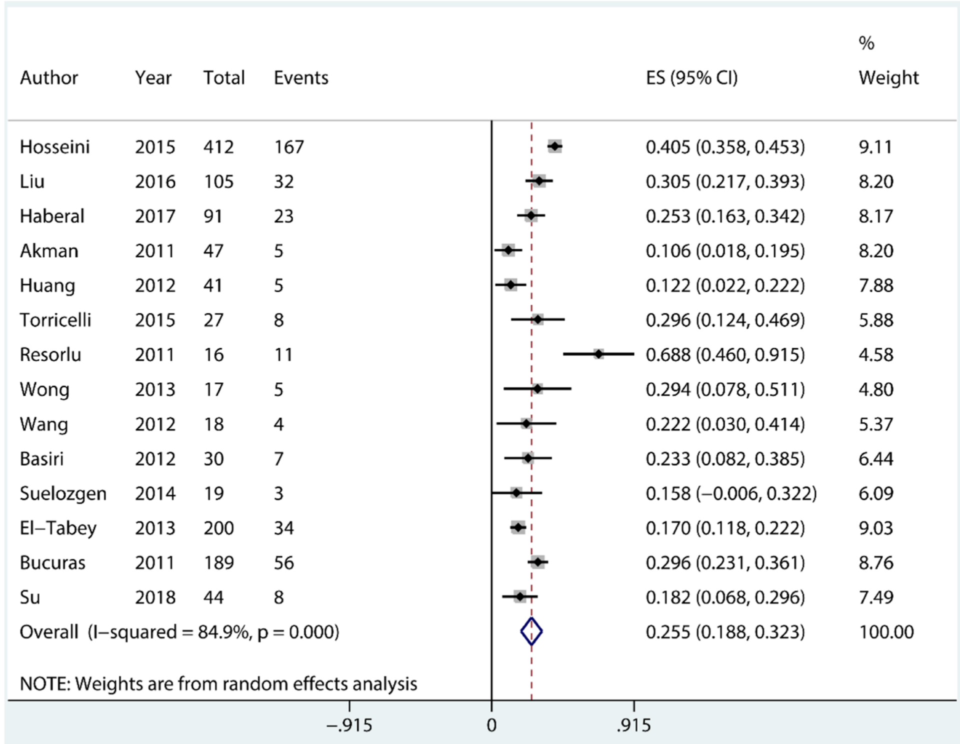


Fig. 7 Forest plot and meta-analysis of overall complication rate. Weights are from random-effects analysis. SD Standard Definition

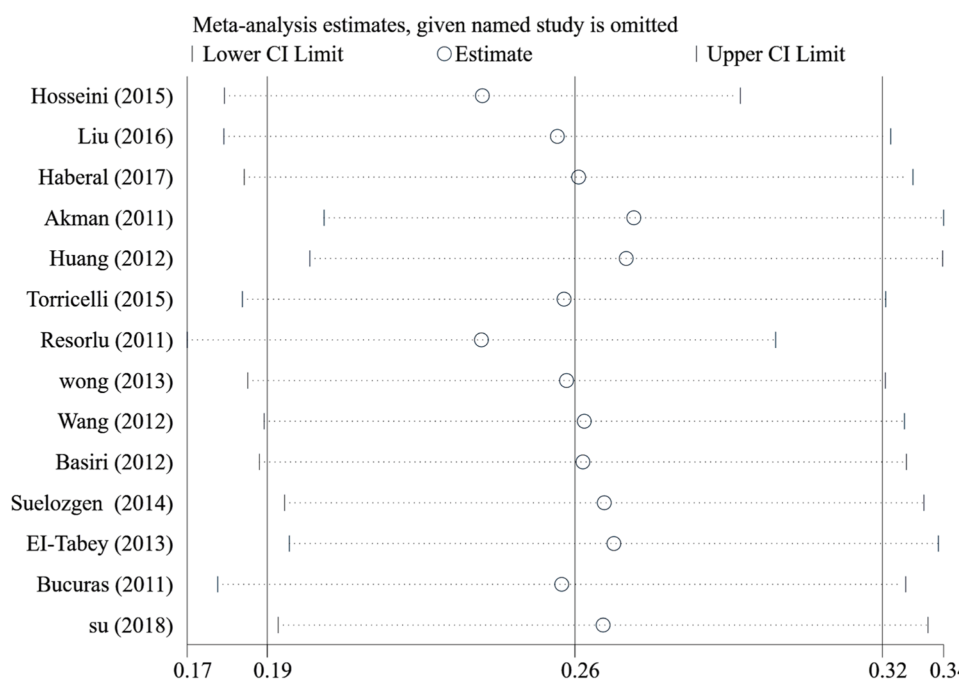


Fig. 8 Forest map for sensitivity analysis of the overall complication rate

more favorable in PCNL than in RIRS (66.7% vs. 45.6%). RIRS has the advantage of not violating the renal parenchyma, which might be an important consideration for patients with a solitary kidney [55]. Some studies comparing PCNL and RIRS for patients with stones in a solitary kidney reported that the transfusion rate in patients who received PCNL was higher than that in patients who received RIRS [51, 56-58]. According to our results, approximately 7.4% of patients with a solitary kidney needed blood transfusion after PCNL.

Our meta-analysis showed that the operative time ranged from 40 to 300 min, and the overall mean operative time was

Fig. 9 Forest plot and meta-analysis of major complications rate. Weights are from random-effects analysis. SD Standard Definition

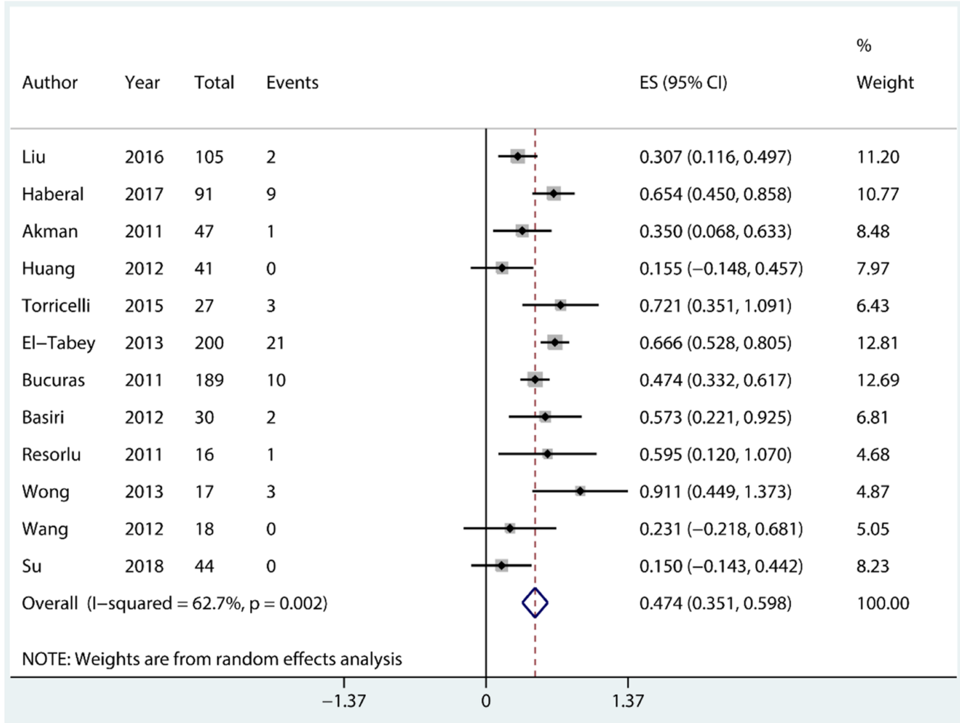
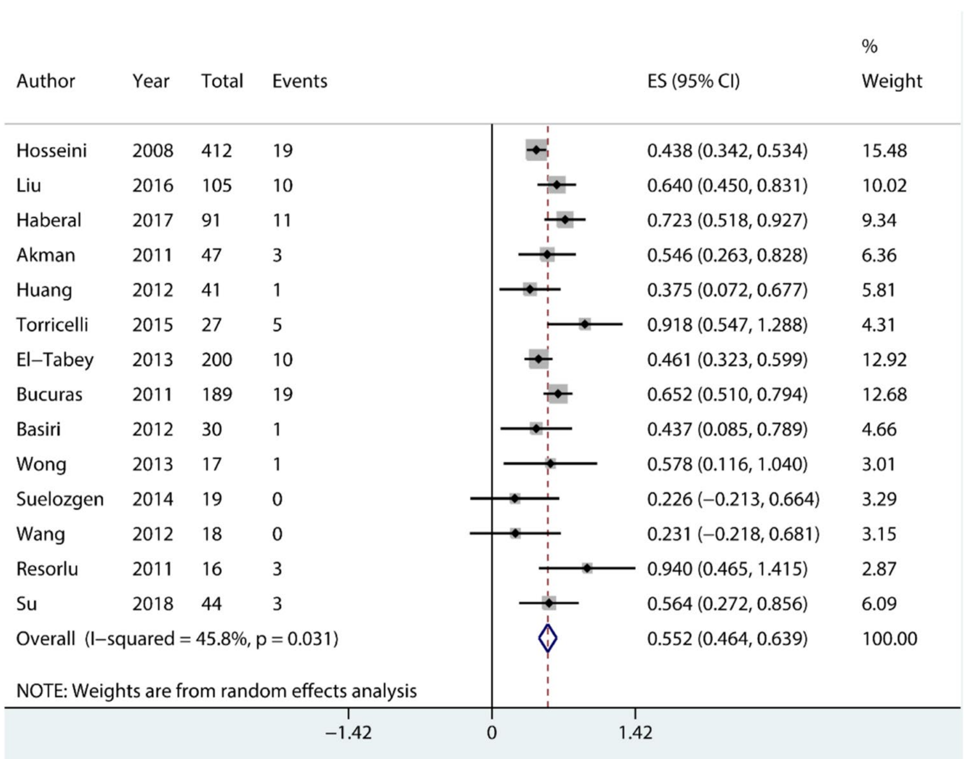


Fig. 10 Forest plot and meta-analysis of blood transfusion rate**.** Weights are from random-effects analysis. SD Standard Definition



85.1 min (range: 40 to 300 min), while a study reported that the mean operating time URS for stones in a solitary kidney was 64.9 min (range: 18 to 190 min) [50]. PCNL had a significantly shorter operative time than RIRS ($p < 0.001$), [42] and a study found a similar result in a matched-pair analysis comparing the effect of PCNL and RIRS for stones larger than 2 cm in patients with a solitary kidney[51]; however, some studies found the opposite result [56, 58]. PCNL leads

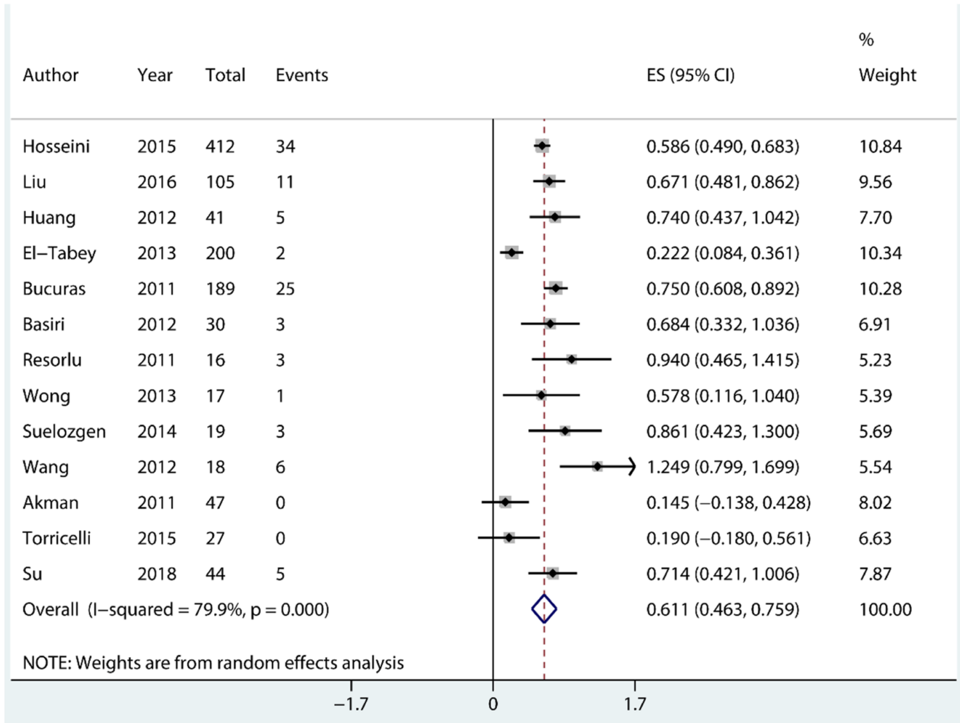


Fig. 11 Forest plot and meta-analysis showing postoperative fever. Weights are from random-effects analysis. SD Standard Definition

to a significantly longer hospital stay than RIRS [42, 51, 56-58]. However, some studies have shown that RIRS also puts patients at risk of developing steinstrasse[43, 59]. The reason why RIRS causes a high frequency of steinstrasse may be that RIRS is often unable to achieve instant stone clearance at the end of surgery and needs postoperative spontaneous expulsion, while in cases with PCNL, stone fragments can be removed through the established tract. Another disadvantage of RIRS is the high requirement for multistage procedures in some patients. Although some studies investigating RIRS for the management of large renal stones also reported promising results, stones larger than 2 cm often required auxiliary or staged procedures [60], and a considerable number of patients required multistage procedures [60-63]. Recently, some studies reported that the combination of PCNL and RIRS was a safe, feasible, and efficient strategy for managing complex stones such as staghorn calculi in a solitary kidney [65-68]. A high success rate and ideal initial and final SFRs are the obvious advantages of PCNL. According to our results, the initial and overall SFRs reached 71.3% and 89.7%, respectively. Furthermore, in the studies included in the present meta-analysis, most of the stones were staghorn stones or (and) stones that were larger than 2 cm.

Renal function is the main concern of operations on solitary kidneys. Some studies found that long-term post-PCNL renal function was generally well preserved. Modest overall renal function improvement was observed during follow-up for as long as 1 year after PCNL[69]. Other studies [70, 71], published some early, also supported the viewpoint that renal function was improved or kept stationary in a long-term flow-up after PCNL. A study reported an acute deterioration in renal function after 48 h, but they noticed that renal function was either preserved or improved after 6 months of follow-up[8]. Yaycioglu [72] and his colleagues obtained similar stone clearance and complication rates with PCNL in patients with impaired and normal renal function, and in a mean follow-up of 15.6 months, mean serum creatinine was decreased from 2.8 to 2.6 mg/dl ($p = 0.273$) in patients in the impaired renal function group. A recent study [73] investigating PCNL on solitary kidney (SK) and bilateral kidneys (BKs) found that PCNL can improve renal function both in SK and BKs, but the renal function gain was delayed in the SK group when compared with BKs group. The results from our meta-analysis also confirmed that renal function was well preserved and even improved after PCNL.

An accepted disadvantage of PCNL on stones in a solitary kidney is the relatively high complication rate, which can reach 25.5% according to our results. Bucuras et al. [4] showed that for patients with a solitary kidney, the frequency of post-PCNL acute renal injury was significantly greater compared to those with two kidneys. Another disadvantage of PCNL when treating stones in a solitary kidney is renal parenchymal injury induced during channel dilatation. Compensatory hypertrophy and dilatation of the remaining renal parenchyma makes a solitary kidney vulnerable, and a solitary kidney is determined to be a significant risk factor for hemorrhage [5]. During the PCNL procedure, a tract is

Table 8 Complications according to Clavien grade

Complication	Clavien Grade	Frequency
Fever	I	99
Bleeding	I	59
Colic	I	9
Azotemia	I	1
Pneumonia	II	7
Transfusion	II	64
Urinary tract infection	II	16
Ileus	II	11
Deep vein thrombosis	II	1
SIRS requiring antibiotics	II	8
PCS perforation	III	12
Clot retention	III	11
Pneumothorax/hydrothorax	III	3
Collection	III	3
Urinary leakage	III	10
Colocutaneous fistula	III	1
Injury of renal pelvis	III	11
Severe bleeding requiring angioembolization	III	8
Clot anuria	IV	4
Sepsis	IV	5
Heart failure	IV	7
Myocardial infarction	IV	4
Renal insufficiency	IV	12
Death	V	2
Total	**G I:167 G II: 107 G III: 59; G IV: 32; G V: 2**	**368**

PCS pelvicaliceal system, SIRS systemic inflammatory response syndrome

made through the renal parenchyma, and in some procedures, multiple tract access is needed, which increases the risk of bleeding and acute renal injury, while RIRS reaches the renal pelvis through the natural body orifice and does not harm the renal parenchyma. Additionally, in the present meta-analysis, we found that PCNL also leads to severe complications, such as severe bleeding requiring angioembolization (n = 8), heart failure (n = 7), renal failure (n = 12) and even death (n = 2), which were not acceptable for stone patients.

A remarkable limitation of our study was the limited number and relatively lower quality of the included studies. All of the included studies were case series analysis studies, and the majority of them were single-center experiences. However, the unfortunate truth is that PCNL for a solitary kidney is a relatively rare procedure, and prospective series are challenging to perform. On the other hand, there were moderate to high degrees of heterogeneity between the included studies. Although we further investigated the potential sources of heterogeneity, we failed to identify factors that were significantly associated with heterogeneity in metaregression, including initial SFR, fever, and total complication rate. The cost of an operation procedure is one of the main concerns of patients and urologists. Unfortunately, none of the fourteen studies mentioned the cost of operation. Therefore, we failed to make a conclusion about it. The lack of concern about the cost effect may lead surgeons to take a lower threshold to admit to intensive care postoperatively or lengthen their hospital stay, which finally increases the patient's financial burden and may lead to a waste of medical resources.

In future studies, surgeons could attempt to conduct more multicenter studies with larger patient numbers, and more random control experiments should be conducted. The "stone free level" should be unified. More attention should be given to recording factors such as calyceal anatomy and BMI, as well as their prognostic importance for stones in a solitary kidney. Additional and detailed information on comorbidities and their effect on complications after PCNL would allow minimization of the complication rate. Above all, a meta-analysis based on results from well-designed RCTs that provides an exact conclusion about the efficacy and safety of PCNL, RIRS and SWL for stones in a solitary kidney is needed.

Conclusion

Management of stones in a solitary kidney is still a complex matter. Percutaneous nephrolithotomy could cause some hard complications, such as severe bleeding requiring angioembolization, heart failure, renal failure and even death of patients, which could occur more frequently in solitary-kidney cases than in double-function kidney cases. We conclude that percutaneous nephrolithotomy should be considered by urologists as an effective choice for cases with a large stone burden or staghorn stones in a solitary kidney. However, the procedure should be performed by a skilled surgeon, and the severe complications of percutaneous nephrolithotomy should be avoided carefully.

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Sidikejiang Niyazi: Manuscript writing; Final approval of manuscript; Collection and assembly of data; Data analysis and interpretation:

Xin Gao: Manuscript writing; Final approval of manuscript.

Ayiding xireyazidan: Manuscript writing; Final approval of manuscript.

Guanglu Song: Manuscript writing; Final approval of manuscript; Administrative support:

Hamulati Tusong: Manuscript writing; Final approval of manuscript; Conception and design; Critical revision of the article and final approval of the article.

All data generated or analysed during this study are included in this article. Further enquiries can be directed to the corresponding author.

Data Availability The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request.

Declarations

Ethics Authors state that this article did not require ethical approval.

Conflict of Interest The authors have no conflicts of interest to declare.

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