ORIGINAL RESEARCH

Mini-Percutaneous Nephrolithotomy versus Standard Percutaneous Nephrolithotomy for Stones 2 cm and Above: A Meta-analysis

Nytte Celle Janne Magallanes-Mascarinas, MD; Marc Vincent Trinidad, MD; Oyayi Arellano, MD and Joseph Michael Ursua, MD, FPUA

Department of Urology, East Avenue Medical Center

The current standard in the management of large burden renal stones is conventional percutaneous nephrolithotomy. Mini-percutaneous nephrolithotomy (mini-PCNL) is a procedure developed to decrease complications of standard PCNL by decreasing the size of access. Recent studies have shown high stone free rates with minimal complications in utilizing mini-PCNL in larger stones.

Objective: This study aims to assess the safety and efficacy of mini-PCNL for stones with sizes 2 cm and above versus standard PCNL.

Methods: This is a meta-analysis comparing mini-PCNL and standard PCNL in the management of renal stones 2 cm and above. A PUBMED search was done to acquire randomized controlled trials (RCTs), prospective and retrospective studies of mini-PCNL and standard PCNL assessing large burden renal stones, defined as 2 cm and above. Two authors independently assessed the studies for selection. Comparison of mini-PCNL and standard PCNL was done according to following parameters: stone-free rate, operative time, postoperative decrease in hemoglobin levels, length of hospital stay, rate of transfusion, occurrence of fever, postoperative pain scores, and occurrence of urine leakage.

Results: Results of this meta-analysis showed that standard percutaneous nephrolithotomy has an advantage over mini percutaneous nephrolithotomy only in terms of having a shorter operative time for larger stones (MD: 8.44 min, 95% CI 6.36 – 10.52 min, $p \leq 0.00001$). No difference was found in the outcomes of postoperative pain scores (MD 0.19 VAS score, %CI 0.16 – 0.54, p = 0.29), occurrence of postoperative fever (OR 0.33, 95% CI 0.18 – 0.61, p = 0.06) and the stone-free rate (OR 0.97, 95% CI 0.67 – 1.41, p = 0.88). Mini-percutaneous nephrolithotomy has advantage over standard percutaneous nephrolithotomy for large-burden stones in terms of shorter length of postoperative hospital stay (MD 1.44 day, 95% CI 1.22-1.66, P <0.00001), lower hemoglobin drop (MD 0.48 mg/dl, 95% CI 0.39–0.66, p < 0.00001), lower rate of transfusion (OR 0.40, 95% CI 0.20 – 0.99, p = 0.01), urine leakage (OR 0.11, 95% CI 0.03 – 0.39, p = 0.0008) and an overall lower occurrence of complications (OR 0.42, 95% CI 0.28 – 0.62, p < 0.0001).

Conclusion: Mini-percutaneous nephrolithotomy is a safe and effective intervention in large-burden stones 2 cm in size and above.

Keywords: mini-percutaneous nephrolithotomy, meta-analysis

Introduction

Renal stone disease has been found to affect 14% of the population with a recurrence rate of 50% or more within 10 years.[1] Currently, conventional percutaneous nephrolithotomy (tract dilated to 24 - 30 Fr) is considered the standard treatment for staghorn and large-volume kidney stones. It is also performed in other upper tract calculi not successfully treated by other modalities, difficult lower pole stones, cystine nephrolithiases and stones in anatomically abnormal kidneys.[2] Although this is a relatively safe and well-tolerated procedure, it is not free of complications. A multi-center study of patients undergoing PCNL showed an overall complication rate of 21.5%. Most of the complications were noted to be minor complications (5.3% - 11.1% of the study population). There was a 0.03% – 3.6% of the study population that had major complications. Minor complications included nephrostomy tube leakage and transient fever. Major complications include injury to adjacent organs, violation of the pleural space, bleeding or infection.[2]

In the attempt to minimize the major complications of standard PCNL, mini-PCNL was developed, wherein the size of the tract was minimized to less than or equal to 18Fr. Initially, this was used in the pediatric population and has gained popularity in use for the adult population.[3] It has a relatively high stone-free rate of 82% and a smaller complication rate, specifically the bleeding complications (1.4%). One disadvantage, however, was longer operative times for larger stones.[3]

Although the recent acceptable high stone-free rates for mini-PCNL were seen in stones 1.5 cm and below[4], more studies have shown acceptable stone-free rates in larger stones as the use of this minimally invasive procedure has become more popular.[5] This study aims to assess the efficacy and safety of performing mini-percutaneous nephrolithotomy versus standard percutaneous nephrolithotomy for renal stones 2 cm and above.

Methods

Literature Search

A systemic literature search was done through Medline, using Pubmed as the search engine, Google Scholar, and the Cochrane library, to confirm relevant studies in accordance with Cochrane standards, and Preferred Reporting Items for Systemic Reviews and Meta-analyses (PRISMA) guidelines. No restrictions in terms of the publication year was made. Only studies done or translated to English were included. The search was performed with a combination of the following terms to identify relevant studies: ("mini-percutaneous nephrolithotomy" or "mini-PCNL") and ("standard percutaneous nephrolithotomy" or "standard PCNL") and ("2 cm"). Three authors screened all citations and abstracts independently. All potentially eligible studies involving comparison of mini-PCNL and standard PCNL for 2 cm stones and above were included.

Selection Criteria

Inclusion criteria were: 1) Randomized controlled trials (RCT's), prospective or retrospective studies; 2) studies published in English; 3) studies comparing mini-PCNL and standard PCNL with analyses for stones 2 cm and above; 4) studies reported at least one of the following clinical outcomes: operative time, hospital stay, postoperative hemoglobin drop, postoperative pain score, stone free rate, post-operative pain scores, fever, urine leakage and total complications.

The exclusion criteria included: 1) pediatric patients under 18 years of age; 2) patients who underwent bilateral simultaneous PCNL; 3) patients with congenital urinary tract anomalies, serious urinary infection, solitary functioning kidneys, or kidneys with prior open surgery.

Three reviewers completed the selection process independently.

Data Extraction

Data extraction and quality evaluation were carried out by three reviewers. The information including study name, authors, publication year, country, study design, interventions, number of patients, age, gender, stone burden, and clinical outcomes of interest (stone-free rate, operative time, hospital stay, postoperative hemoglobin drop, postoperative pain score, blood transfusion, fever and urine leakage) were extracted from each included study.

Assessment of Quality

The criteria provided by the Oxford Center for Evidence-Based Medicine[6] was used to assess the level of evidence for all studies. Study quality for the retrospective case-control studies were assessed using the Newcastle Ottawa Quality Assessment Scale for Case-Control Studies.[7] The Jadad Scale was used to assess study quality for randomized controlled trials.[8] The risk of bias was evaluated for each randomized controlled trial was assessed by the three reviewers independently, according to the Cochrane Collaboration's tool, which includes six aspects: random sequence generation, allocation concealment, blinding of participants and personnel, blinding of outcome assessment, incomplete outcome data, selective reporting and other biases. For retrospective case-control studies, the Cochrane Risk of Bias Tool for Non-Randomized Studies of Interventions was used which includes the following aspects: bias due to confounding, bias in selection of participants into the study, bias in measurement of interventions, bias due to departures from intended interventions, bias due to missing data, bias in the measurement of outcomes and overall bias. The risk of bias was analyzed via the Cochrane Review Manager (REVMAN 5.3).

Statistical Analysis

A meta-analysis was performed to compare the efficacy and safety of mini-PCNL vs. standard PCNL for the treatment of large burden stones (2 cm and above). All statistical analyses were performed using Cochrane Review Manager (REVMAN 5.3) software. Odds ratio (OR) will be used for dichotomous data, and continuous data will be evaluated using weighted mean difference or standard mean difference. All results are reported with 95% confidence intervals. The Z-test was used to determine the pooled effects and p-value <0.05 will be considered to be statistically significant. Forest plots were created to show the results of the meta-analysis.

Results

Identification

The search results are shown in Figure 1. The literature search showed a total of 369 potentially relevant studies. However, at the end of the search process, only 6 studies were found to be eligible. These include 4 randomized controlled trials and 2 retrospective studies. These included a total sample size of 983, where there were 608 mini-PCNL cases compared with 375 standard PCNL cases.

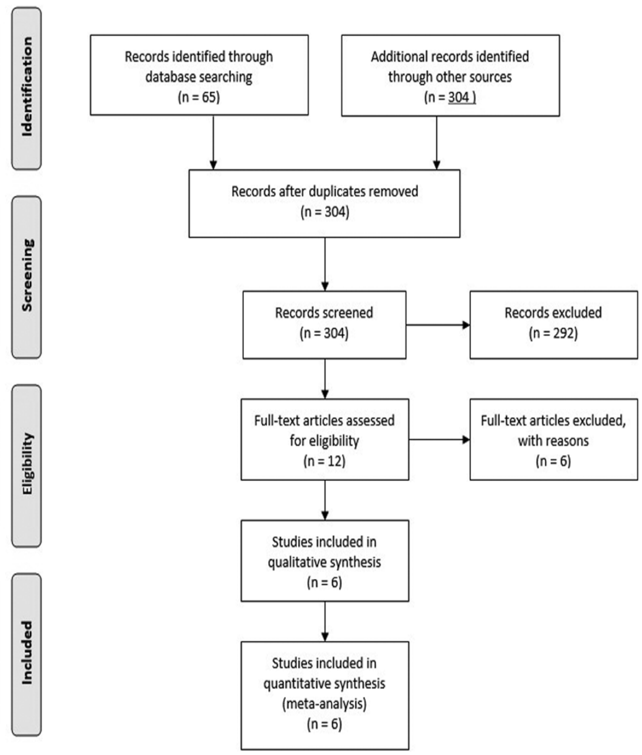

Figure 1. PRISMA flow diagram showing the systematic search strategy and the process of study selection.

Study Characteristics

The basic characteristics of the studies included are presented in Table 1. This includes study, study period, country performed, study design, level of evidence, inclusion criteria, sample sizes for both mini and standard PCNL, and the study quality. Table 2 shows the baseline characteristics of the studies in terms of the characteristics of each of the two comparable interventions per study. The characteristics of both mini and standard PCNL groups for each study are tabulated, including age, stone size, access sheath size, types of dilator used, nephroscope size and the method for lithotripsy.

Table 1. Summary of the basic characteristics of included studies.

Study	Study period	Country	Study Design	LE*	Inclusion Criteria	Cases, n		Study Quality
						Mini-PCNL	Standard PCNL	
Abdelhafez et al[17]	2009-2012	Germany	Retrospective case-control	3b	Pelvic or calyceal stones at least 20 mm in diameter from simple calyceal to complete staghorn stones	71	62	7a
Elsheemy et al[16]	2010-2013	Not specified	Retrospective case-control	3b	Adult patients > 18yo with renal stones, stone size ^{3}20mm or if smaller and lower calyceal, resistant to SWL or to oral chemodissolution therapy	378	151	7a
Kukreja[20]	2015-2017	India	Randomized controlled trial	2b	Medium to large renal stones	61	62	2b
Guler et al[21]	2016-2017	Turkey	Randomized controlled trial	2b	Kidney stone size equal to larger than 2 cm	51	46	2b
Cheng et al[19]	2004-2007	China	Randomized controlled trial	2b	Single tract procedure and single technique (with subgroup analysis on staghorn calculi)	72 (18)$^{+}$	115 (29)$^{+}$	2b
Zhong et al[11]	2008-2009	China	Randomized controlled trial	2b	Patients with staghorn calculi	29	25	2b

**LE – Level of evidence assessed by the Oxford Centre for Evidence-based Medicine*
+ number of cases included in the staghorn calculi subgroup
[a] Newcastle-Ottawa Scale for case-control studies (score 0 – 9)
[b] Jadad Scale for randomized controlled trials (score from 0 – 5)

Table 2. The baseline characteristics of the included studies.

References	PCNL (Mini/ Standard)	Age (years)	Stone Size (mm)	Access sheath size	Dilator	Nephro-scope Size	Lithotripsy
Abdelhafez et al	Mini	52 ± 17	38.6 ± 20	18 Fr	SS	NS	Pneumatic
	Standard	58 ± 14	38.2 ± 18	NS	TMD	26 Fr	Ultrasonic/Laser
Elsheemy et al	Mini	37.08 ± 12.62	37.7 ± 22.1	18 Fr	FD	8.5/11.5 Fr	Pneumatic
	Standard	43.42 ± 12.21	37.7 ± 24.3	30 Fr	TMD	24 Fr	Pneumatic
Kukreja	Mini	20.6 ± 3.47	21.5 ± 3.53	16.5/17.5 Fr	SS	12 Fr	Laser/Pneumatic
	Standard			22/24 Fr	SS	20.5 Fr	Laser/Pneumatic
Guler et al	Mini	46.9 ± 13.7	38.7 ± 13.1	16.5/20 Fr	FD	12 Fr	Laser
	Standard	47.4 ± 13.9	42.8 ± 22.5	30 Fr	SS/FD	26 Fr	Pneumatic/Ultrasonic
Cheng et al	Mini	37.2 (24 – 67)	12.8 cm^2	16 Fr	TMD	8/9.8 Fr	Pneumatic
	Standard	39.6 (27 – 72)	13.1 cm^2	24 Fr	TMD	20.8 Fr	Ultrasonic/Pneumatic
Zhong et al	Mini	41 (26 – 76)	11.7 (8.8 – 22.8)	16 Fr	FD	8/9.8 Fr	Pneumatic
	Standard	38 (26 – 64)	10.8 (8.4 – 20.2)	26 Fr	FD	NS	Pneumatic

NS – not specified in the study;
SS – single-step metal dilators, TMD – telescoping metal dilators, FD – fascial dilators

The risk of bias assessment was done for all studies. A summary of the risk of bias in seen in Figures 2 and 3. As noted in the risk of bias summary, studies of Abdelhafez et al and Elsheemy, et al. are both retrospective case control studies and the risks were analyzed according to the Cochrane Risk of Bias Collaboration Tool.[6] Bias due to confounding was low in both studies because the confounding domains, for example, stone characteristics, were matched for both interventional groups. There was low bias in the measurement of interventions because both of the interventions were well-defined from the start of the study and the information on intervention status were recorded at the time of intervention. The intervention also did not change by the knowledge of the outcome or the risk of outcome. There was low risk of bias due to departures from intended interventions because the cases and controls were both treated with either mini or standard PCNL with no shift in the intervention during the course of the study. That is, there were no reports of cases that participants from the mini-PCNL group were converted into standard PCNL. There is also low risk of bias in the measurement of outcomes and selection of the reported results as these were already set at the start of the study. Outcomes were objectively obtained, and the same outcomes were measured for both interventions. However, there was unclear risk for both retrospective studies with regard to bias due to missing data. Although both studies did not report charts with missing data, for chart reviews, there is considerable risk of incomplete data. In the assessment of the risk of bias in the selection of participants into the study, there was low risk for the study of Abdelhafez, et al. However, there was high risk of bias in the study of Elsheemy since the mini-PCNL group had twice the number of participants compared to the standard PCNL group. With unclear risk of bias contributed by retrospective case-control studies amounting to 25% of the study group and high risk of bias at 12.5% of the study group, overall bias from the retrospective case-control studies are assessed to be of low risk (Figure 3).

For the four randomized controlled trials, risk of bias was obtained using Cochrane Collaboration Tool, which included random sequence generation, allocation concealment, blinding of participants and personnel, blinding of outcome assessment, incomplete outcome data, selective reporting and other biases (Figure 2). There was low risk of selection bias because the allotment of intervention for the groups were done via randomization and were initially concealed from the groups. There was also low risk of attrition bias and reporting bias since all

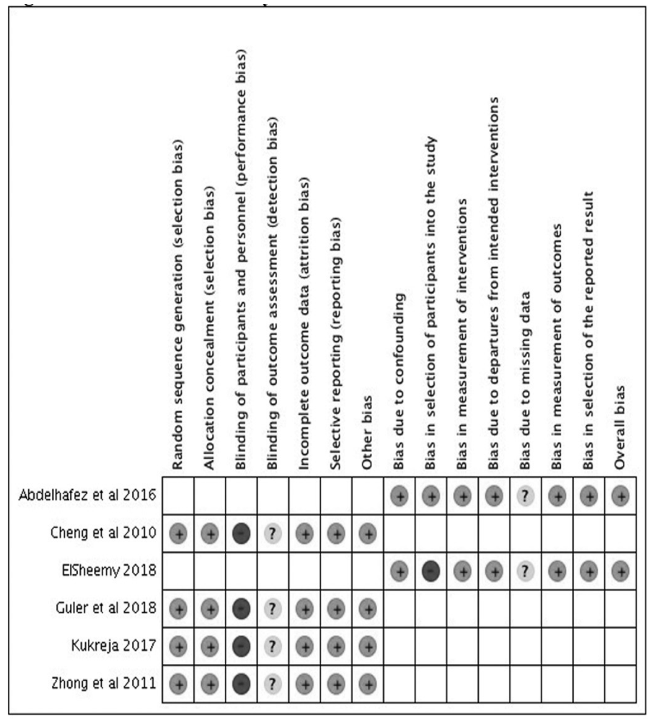

Figure 2. Risk of bias summary.

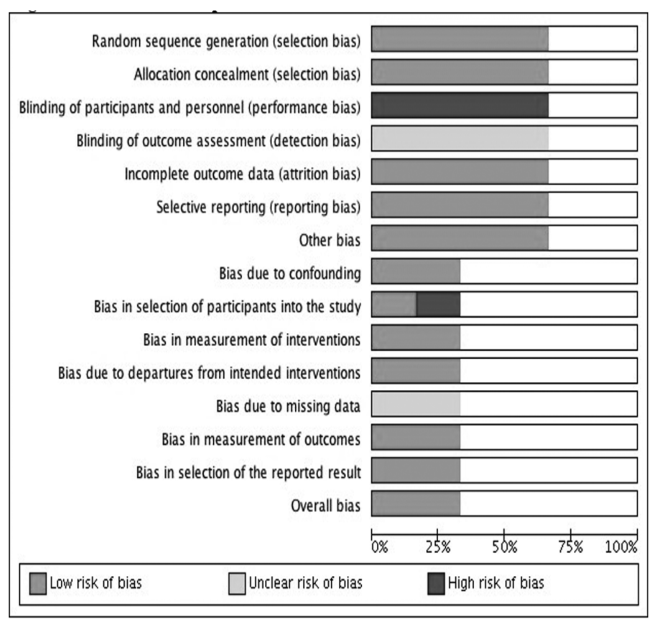

Figure 3. Risk of bias Graph

the proposed outcome measures were obtained from all the participants in the study and all of these data were reported. All of the participants underwent the surgical intervention in which they were allotted to. That is, no cases from mini-PCNL had to convert into standard PCNL. However, detection bias is unclear for this interventional study as the outcome assessment cannot be blinded. The studies could not blind the participants as the measurement of outcomes such as: hospital stay, blood transfusion, pain scales, etc. More importantly, performance bias is high for surgical intervention trials because it is not ethical to blind the participants as to which procedure they are allotted to. They will have to consent for any surgical intervention that they have to undergo.

Meta-analysis

Forest plots were created for operative time, hospital stay, postoperative hemoglobin drop, post-operative VAS pain scale, stone-free rate, blood transfusion, fever and urine leakage to show results.

Operative Time

Based on the six studies, operative time was found to be significantly favoring standard percutaneous nephrolithotomy. Standard PCNL had a shorter operative time by a difference of 8.44 minutes (MD: 8.44 min, 95% CI 6.36 – 10.52 min, $p \leq 0.00001$, Figure 4A). A subgroup analysis pooling results only from randomized controlled trials also showed that there was a significantly shorter operative time in the standard percutaneous nephrolithotomy group versus the mini-percutaneous nephrolithotomy group by 8.14 minutes (MD 8.14 95% CI 5.49 – 10.78, $p \leq 0.0001$, Figure 4A).

Length of Hospital Stay

Only 5 studies reported length of hospital stay as an outcome. One RCT did not do a subgroup analysis considering only large burden stones (>2 cm) in the analysis comparing hospital stay. Only 2 RCTs and 2 retrospective studies were included in the pooled analysis. There was a significantly lower length of hospital stay in the mini-PCNL group with a difference of 1.44 days (MD -1.44, 95% CI -1.66 – -1.22, $p \leq 0.00001$, Figure 4B). A subgroup analysis pooling results only from randomized controlled trials, the results were similar but with a much lower mean difference of 0.35 day (MD 0.35, 95% CI -0.15 – 0.84, p = 0.17). However, p-value was not <0.05, making the difference not statistically significant (Figure 4B).

Stone-Free Rate

All six studies analyzed data on stone-free rates. While some studies analyzed data also on the stone-free rate after a second procedure, this meta-analysis only considered the primary stone-free rates. For the

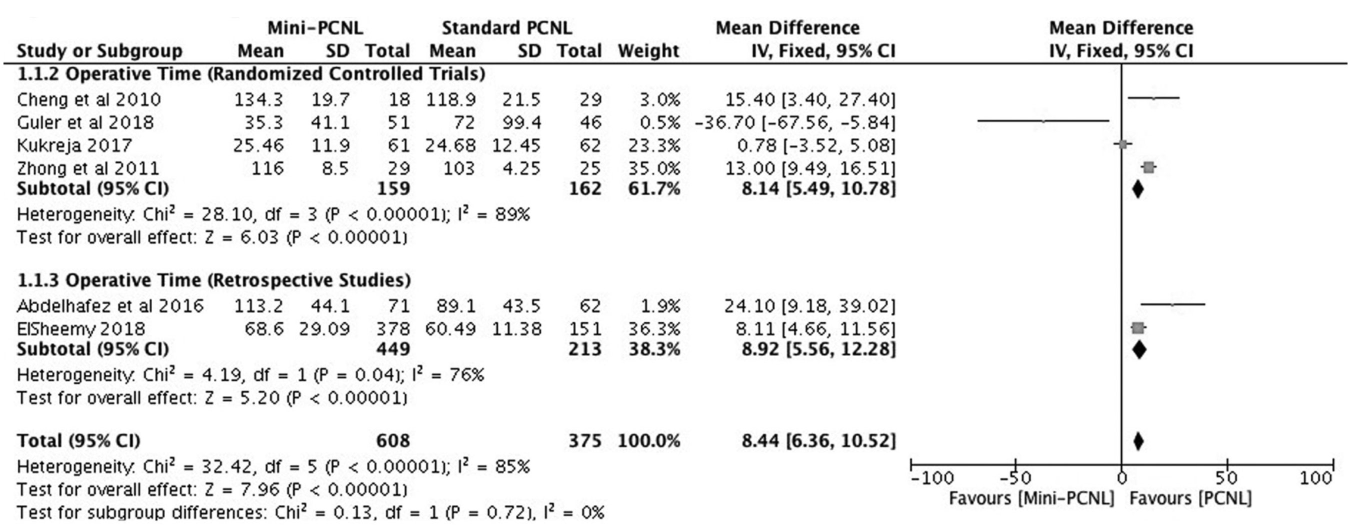

Figure 4A. Forest plot for operative time for mini-PCNL vs. standard PCNL

Study or Subgroup	Mini-PCNL Mean	Mini-PCNL SD	Mini-PCNL Total	Standard PCNL Mean	Standard PCNL SD	Standard PCNL Total	Weight	Mean Difference IV, Fixed, 95% CI
1.2.1 Length of Hospital Stay (Randomized Controlled Trials)								
Guler et al 2018	2	1.09	51	2.78	1.8	46	14.2%	-0.78 [-1.38, -0.18]
Zhong et al 2011	9.6	3.4	29	7.1	4.9	25	1.0%	2.50 [0.22, 4.78]
Subtotal (95% CI)			**80**			**71**	**15.2%**	**-0.57 [-1.15, 0.01]**
Heterogeneity: Chi² = 7.41, df = 1 (P = 0.007); I² = 86%								
Test for overall effect: Z = 1.92 (P = 0.05)								
1.2.2 Length of Hospital Stay (Retrospective Studies)								
Abdelhafez et al 2016	4.2	1.7	71	6.7	4.4	62	3.8%	-2.50 [-3.66, -1.34]
ElSheemy 2018	2.43	1.46	378	4.29	1.28	151	81.0%	-1.86 [-2.11, -1.61]
Subtotal (95% CI)			**449**			**213**	**84.8%**	**-1.89 [-2.13, -1.64]**
Heterogeneity: Chi² = 1.11, df = 1 (P = 0.29); I² = 10%								
Test for overall effect: Z = 15.05 (P < 0.00001)								
Total (95% CI)			**529**			**284**	**100.0%**	**-1.69 [-1.91, -1.46]**
Heterogeneity: Chi² = 25.36, df = 3 (P < 0.0001); I² = 88%								
Test for overall effect: Z = 14.60 (P < 0.00001)								
Test for subgroup differences: Chi² = 16.85, df = 1 (P < 0.0001), I² = 94.1%								

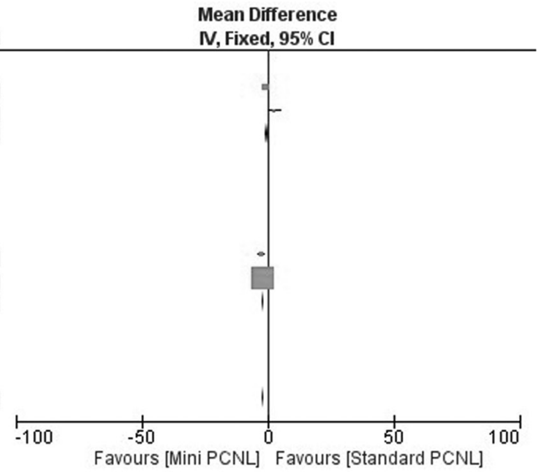

Figure 4B. Forest plot for length of post-operative hospital stay for mini-PCNL vs. standard PCNL.

pooled analysis of all studies included, there was no significant difference between the stone-free rates in standard and mini-PCNL. The pooled analysis showed only a difference of 0.97 between the two groups (MD 0.97, 95% CI 0.67 – 1.41, p = 0.88, Figure 4C). Similar results were also seen in the randomized controlled trial only subgroup (MD 1.5, 95% CI 0.85 – 2.66, p = 0.17, Figure 4C).

Hemoglobin Decrease and Blood Transfusion

All of the randomized controlled trials reported hemoglobin drop. However, one RCT did not do a subgroup analysis on large burden stones and this was not included in the pooled analysis. The retrospective studies did not report hemoglobin decrease as an outcome and were not included in this pooled analysis. The pooled data from three studies showed a significantly lower hemoglobin drop in mini-percutaneous nephrolithotomy compared to standard percutaneous nephrolithotomy with a difference of 0.48 g/dL (MD -0.48, 95% CI – 0.66 – 0.30, p < 0.00001, Figure 4D).

Three randomized controlled trials reported the need for blood transfusion as an outcome, but one RCT did not do a subgroup analysis specifically on large burden stones and was not included the pooled analysis. One retrospective study reported blood transfusion as an outcome and was included in the analysis separately from a subgroup analysis containing the randomized controlled trials. If only the RCTs are considered, there is no significant difference in the requirement for blood transfusion between mini-PCNL and standard PCNL (MD 0.25, 95% CI 0.05 – 1.41, p = 0.12, Figure 4E). However, when the retrospective study was included, there was a significantly lower incidence of blood transfusion in mini-PCNL with a difference of 0.40 (MD 0.40, 95% CI 0.20 – 0.99, p = 0.01, Figure 4E).

Postoperative Pain Score

Postoperative pain scores were reported as VAS (Visual Analogue Scale) scores from 1 – 10 in increasing pain intensity. Although two RCTs were able to report postoperative pain scores, the study by Cheng et al reported pain scores for all stone sizes. Only Kukreja, et al. was able to report postoperative pain scores within the first 24 hours of surgery for stones 2 cm and above. Figure 4F shows that post-operative pain scores in mini-PCNL was lower but there was no significant difference from the pain scores in standard PCNL (MD 0.19, %CI 0.16 – 0.54, p = 0.29, Figure 4F).

Intraoperative and Postoperative Complications

Total Complications and Clavien-Dindo Grade >2 complications

Five studies reported intraoperative and post-operative complications. However, one RCT did not

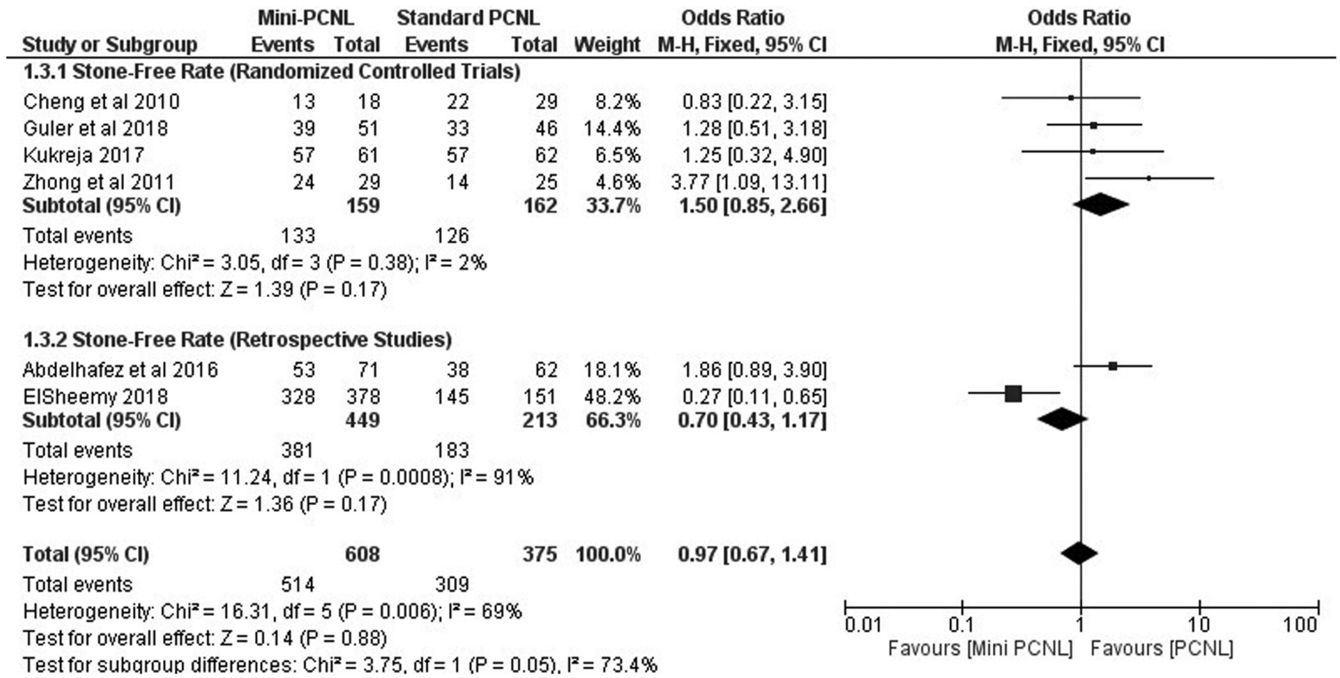

Figure 4C. Forest plot for stone-free rate for mini-PCNL vs. standard PCNL.

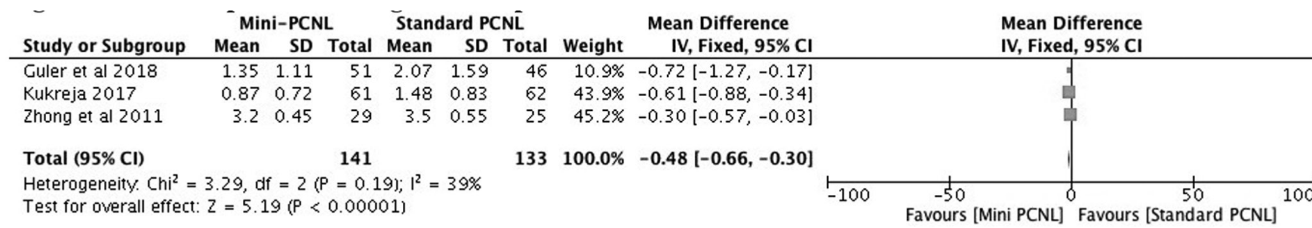

Figure 4D. Forest plot for hemoglobin drop for mini-PCNL vs. standard PCNL.

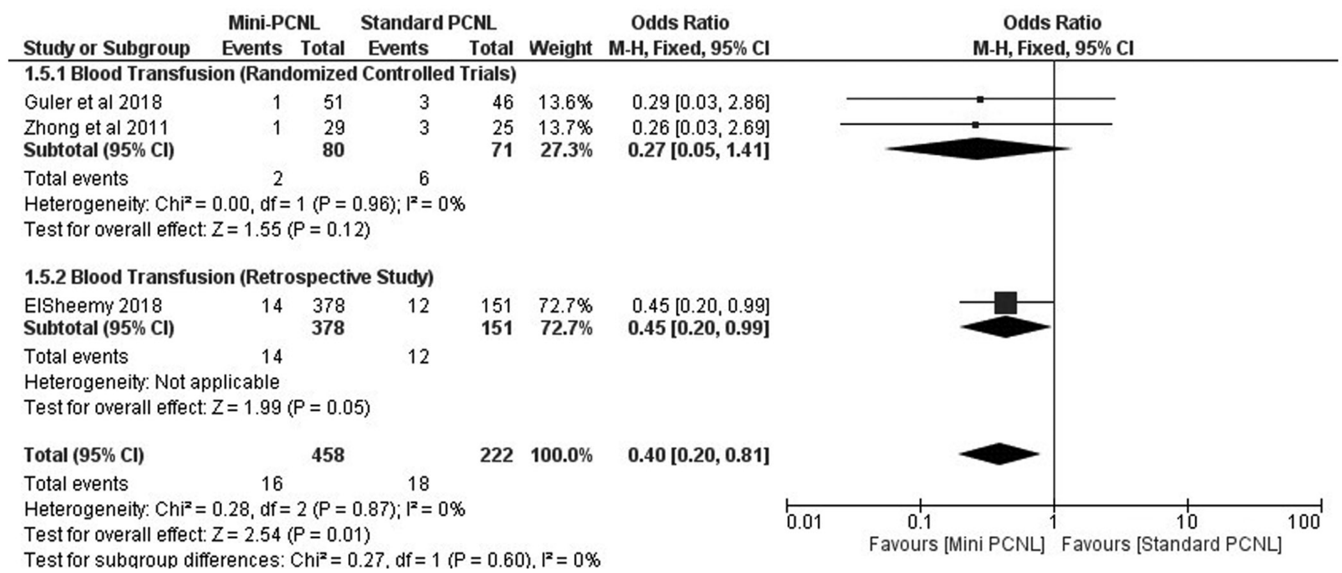

Figure 4E. Forest plot for blood transfusion requirement for mini-PCNL vs. standard PCNL.

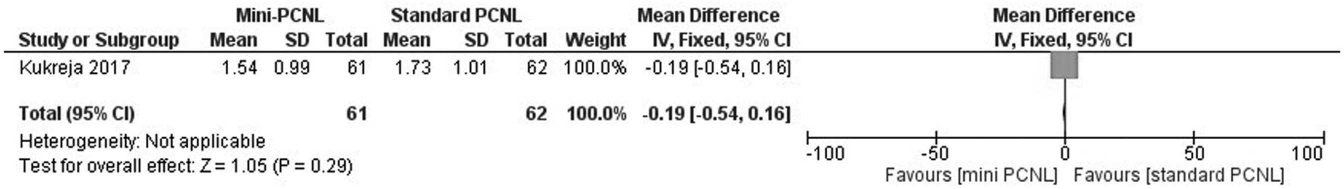

Figure 4F. Forest plot for postoperative pain scores for mini-PCNL vs. standard PCNL.

do a subgroup analysis for larger stones (ex: staghorn calculi). Three studies have reported complications in the Clavien-Dindo classification. While one study reported complications but not classified accordingly. Further analysis of complications classified as Clavien-Dindo grade more than II was done for these studies, the significance of which is further explained in the discussion.

Figure 4G shows the comparison of the total number of complications seen in mini-PCNL compared to that in standard PCNL. The odds ratio obtained in the pooled analysis of all RCTs and retrospective studies showed a significantly lower rate of complications in mini-PCNL with an odds ratio of 0.42 (OR 0.42, 95% CI 0.28 – 0.62, p <0.0001, Figure 4G). Similar results were obtained in the retrospective study subgroup with an odds ratio of 0.38 (OR 0.38, 95% CI 0.24 – 0.60, p < 0.0001). In the RCT subgroup, there was also lower rate of complications in mini PCNL but the difference from standard PCNL was not statistically significant (OR 0.53, %CI 0.25 – 1.13, p = 0.89, Figure 4G).

In comparing complications with Clavien-Dindo classification more than grade II, no significant difference was found between those in the mini-PCNL and standard PCNL groups in the RCT subgroup (OR 1.07, 95% CI 0.31 – 3.67, p = 0.91, Figure 4H). However, in the retrospective study subgroup and the pooled analysis, there was significantly lower grade II above complications in mini-PCNL. In the retrospective study subgroup, there was 0.10 times the risk of complications in mini PCNL (OR 0.10, % CI 0.04 – 0.26, p < 0.00001, Figure 4H. In the pooled analysis, there was 0.24 times the risk of complications (OR 0.24, 95% CI 0.12 – 0.47, p < 0.0001, Figure 4H).

Fever

Comparison of the incidence of postoperative fever was also done in these studies. One RCT lacked data on larger stones and was not included in this analysis. Two RCTs and one retrospective study reported this outcome. In the pooled analysis, there was no significant difference in the occurrence of postoperative fever in mini-PCNL compared to standard PCNL (OR 0.33, 95% CI 0.18 – 0.61, p = 0.06, Figure 4I). Similarly, no significant difference was seen in the RCT subgroup analysis (OR 1.13, 95% CI 0.26 – 4.89, p = 0.87, Figure 4I). The significant difference was only seen in the retrospective study in favor of mini-PCNL (OR 0.24, 95% CI 0.12 – 0.48, p < 0.0001, Figure 4I).

Urine Leakage

Only two studies had urine leakage as an outcome, one was a retrospective study and another was a randomized controlled study. Pooled analysis showed a significantly lower rate of urine leakage in the mini-PCNL group with an odds ratio of 0.11 (OR 0.11, 95% CI 0.03 – 0.39, p = 0.0008, Figure 4J).

Discussion

Although mini-percutaneous nephrolithotomy was developed as a technique to decrease morbidity of stone removal in pediatric patients, it has been recently adopted for stone clearance in the adult population. However, there was initial hesitation among urologists in adopting this new technology. The proposed advantage of nephron-sparing in mini-PCNL compared to standard PCNL was disproved in an animal study by Traxer et al, which showed no difference in scar tissue between the two interventions in pigs.[9] Another reason for choosing mini-PCNL over standard PCNL is that it is hypothesized to have a lower blood loss. However, initial studies found conflicting results. While a large-scale study by Zeng, et al. showed a lower blood transfusion rate

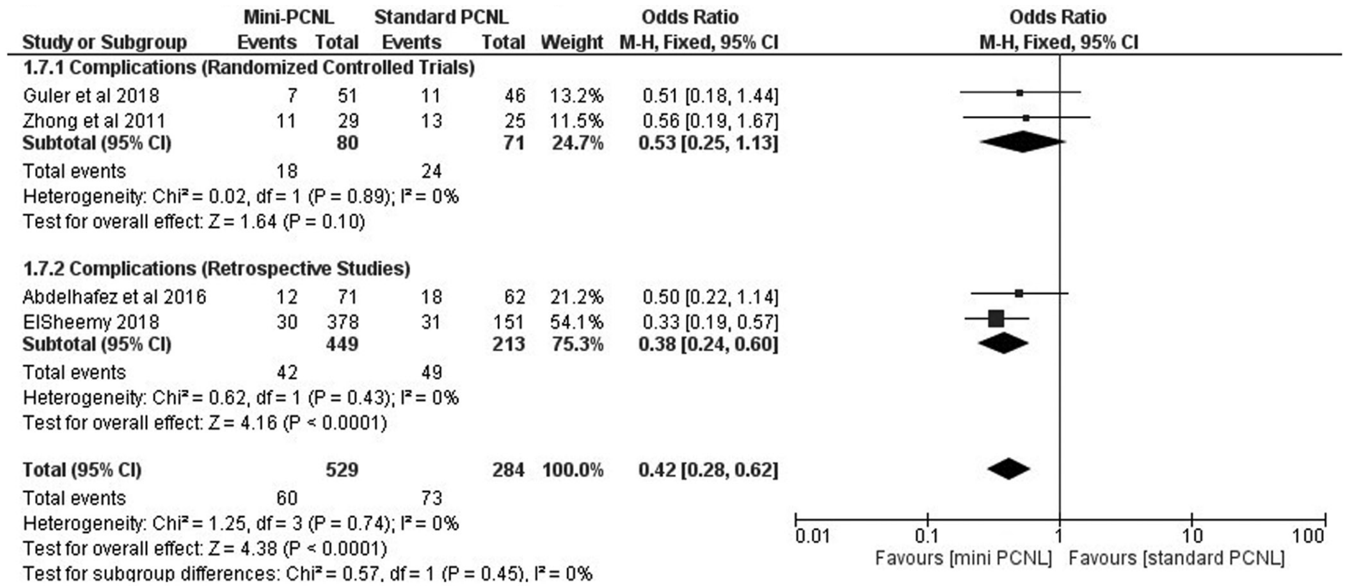

Figure 4G. Forest plot for intra-op and post-operative complications for mini-PCNL and standard PCNL.

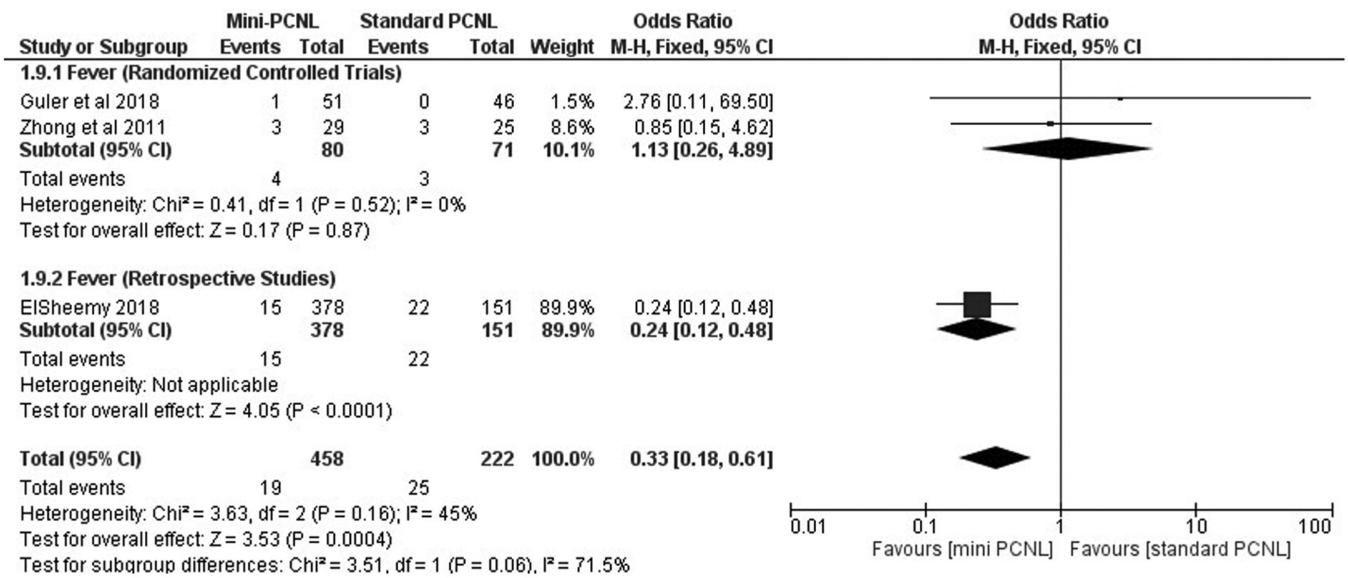

Figure 4H. Forest plot for complications Clavien-Dindo Grade >2 for mini-PCNL and standard PCNL.

and hemoglobin drop in mini-PCNL[10], another study by Zhong, et al. showed no significant difference in severe bleeding and the blood transfusion rate in mini-PCNL and standard PCNL.[11]

More recently, mini-percutaneous nephrolithotomy has been recommended for smaller stones. It has been found that the procedure is safe and effective in small burden stones < 2 cm. This is due to the high stone-free rate, less blood loss and shorter hospital stay.[5]

For smaller stones, standard percutaneous nephrolithotomy has been replaced by less invasive procedures for smaller stones owing to a comparable operative time, stone-free rate but with a lower complication rate. A recent meta-analysis of stones of all sizes showed less bleeding, fewer transfusion, less postoperative pain and shorter operating time. However, no subgroup analysis on large burden stones or stones 2 cm and above was done to compare outcomes from mini-PCNL and standard PCNL.[12]

Study or Subgroup	Mini-PCNL Events	Mini-PCNL Total	Standard PCNL Events	Standard PCNL Total	Weight	Odds Ratio M-H, Fixed, 95% CI
1.9.1 Fever (Randomized Controlled Trials)						
Guler et al 2018	1	51	0	46	1.5%	2.76 [0.11, 69.50]
Zhong et al 2011	3	29	3	25	8.6%	0.85 [0.15, 4.62]
Subtotal (95% CI)		**80**		**71**	**10.1%**	**1.13 [0.26, 4.89]**
Total events	4		3			
Heterogeneity: Chi² = 0.41, df = 1 (P = 0.52); I² = 0%						
Test for overall effect: Z = 0.17 (P = 0.87)						
1.9.2 Fever (Retrospective Studies)						
ElSheemy 2018	15	378	22	151	89.9%	0.24 [0.12, 0.48]
Subtotal (95% CI)		**378**		**151**	**89.9%**	**0.24 [0.12, 0.48]**
Total events	15		22			
Heterogeneity: Not applicable						
Test for overall effect: Z = 4.05 (P < 0.0001)						
Total (95% CI)		**458**		**222**	**100.0%**	**0.33 [0.18, 0.61]**
Total events	19		25			
Heterogeneity: Chi² = 3.63, df = 2 (P = 0.16); I² = 45%						
Test for overall effect: Z = 3.53 (P = 0.0004)						
Test for subgroup differences: Chi² = 3.51, df = 1 (P = 0.06), I² = 71.5%						

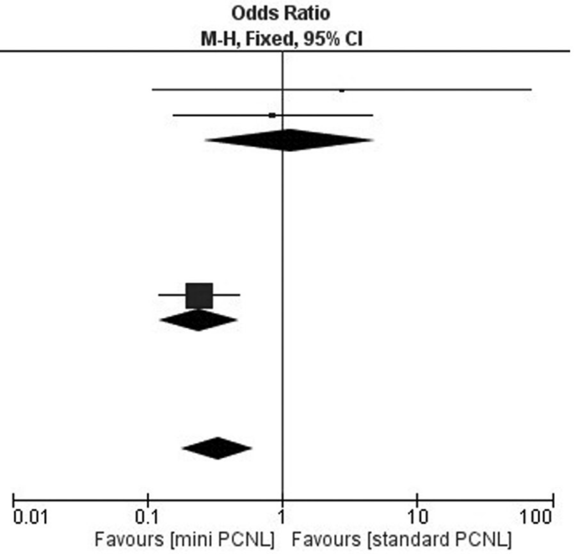

Figure 4I. Forest plot of postoperative fever in mini-PCNL vs. standard PCNL.

Study or Subgroup	Mini-PCNL Events	Mini-PCNL Total	Standard PCNL Events	Standard PCNL Total	Weight	Odds Ratio M-H, Fixed, 95% CI
ElSheemy 2018	1	378	12	151	97.1%	0.03 [0.00, 0.24]
Zhong et al 2011	1	29	0	25	2.9%	2.68 [0.10, 68.87]
Total (95% CI)		**407**		**176**	**100.0%**	**0.11 [0.03, 0.39]**
Total events	2		12			
Heterogeneity: Chi² = 5.21, df = 1 (P = 0.02); I² = 81%						
Test for overall effect: Z = 3.36 (P = 0.0008)						

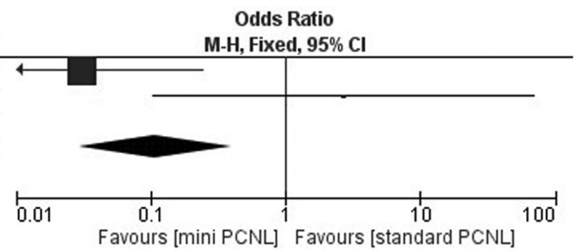

Figure 4J. Forest plot of postoperative urine leakage in mini-PCNL vs. standard PCNL.

The American Urological Association (AUA) recommends percutaneous nephrolithotomy for renal stones > 2 cm in adults owing to a higher stone free rate than other modalities. However, the guidelines recommend weighing the benefit of standard PCNL against the risk of increased invasiveness and the complication rate which was found to be higher compared to other modalities. It has not also specified a recommended tract size in managing these large burden stones.[13] The European Association of Urology (EAU) Guidelines also recommend standard percutaneous nephrolithotomy for the management of renal stones >2 cm. More recently, they performed a systematic review for tract sizes in miniaturized percutaneous nephrolithotomy, for which they concluded that mini-percutaneous nephrolithotomy is as safe and efficacious as standard PCNL, but there was no subgroup analysis dedicated for minipercutaneous nephrolithotomy for larger stones.[14] For those with a larger stone burden, specifically > 2 cm, however, standard percutaneous nephrolithotomy, is still the recommended intervention of choice.

More recent studies have supported the use of mini-PCNL for large burden stones. A more recent study done by Emiliani in 2017 has shown lesser parenchymal injury in mini-percutaneous nephrolithotomy versus standard nephrolithotomy. Although scarring in both interventions were the same, there was significantly smaller parenchymal fissures and reduced capsule rupture in the mini-PCNL group.[15] A comparative retrospective study showed shorter hospital stay and lower complication rates in mini-PCNL vs. standard PCNL even for stones >2 cm. However, they found longer operative time and lower stone-free rate in mini-PCNL for these larger stones.[16] Another retrospective study comparing mini and standard PCNL for large-sized calculi showed a shorter hospital stay but a longer operative time for mini-PCNL but achieved no significant difference in the stone-free rate.[17]

Such was the improvement in the recent results that the Urological Association of Asia has already recommended mini-percutaneous nephrolithotomy in stones > 2 cm, specifically for stones < 3.5 cm.[18] Initial results of a large scale randomized controlled trial in China by Zeng, et al. showed positive results for mini-percutaneous nephrolithotomy over standard percutaneous nephrolithotomy for kidney stones 20-40 mm in size. It showed similar stone-free rate to standard PCNL despite the smaller access size with less postoperative complications and shorter hospital stay.[18]

This meta-analysis showed that standard PCNL has an advantage over mini-PCNL only in terms of having a shorter operative time for larger stones. No difference was found in the outcomes of postoperative pain scores, postoperative fever and the stone-free rate. Mini-percutaneous nephrolithotomy has advantage over standard percutaneous nephrolithotomy for large-burden stones in terms of shorter length of postoperative hospital stay, lower hemoglobin drop, lower rate of transfusion, lower rate of urine leakage and an overall lower occurrence of complications.

A longer operative time with mini-percutaneous nephrolithotomy was found to be statistically significant but a difference of 8.44 minutes may not be clinically significant. Probable sources of a longer operative time would be the limitation of the field of view especially in multiple calyceal stones or staghorn calculi. The randomized controlled trial done by Cheng, et al. compared the operative time for 3 different subgroups, staghorn calculi, simple renal pelvis stones, and multiple calyceal stones for both mini and standard percutaneous nephrolithotomy.[19] They found a significantly shorter operative time in standard PCNL for staghorn calculi, while a significantly shorter operative time in mini PCNL for simple renal pelvis stones, suggesting that the difference in operative time is affected by stone burden.[19]

The length of hospital stay is one of primary outcomes that showed significantly better results for mini-PCNL than standard PCNL. With this, the patient will be benefited in both early resume of regular activities and lower hospital costs. The amount of decrease in hemoglobin and requirement for blood transfusion are two parameters to quantitatively represent the amount of blood loss during percutaneous nephrolithotomy. In this meta-analysis, there was a significantly lower drop in hemoglobin for patients who underwent mini-PCNL compared to those who underwent standard PCNL. The pooled analysis for blood transfusion requirement also favors mini-PCNL, which was significantly lower. This is also congruent with the findings in comparing mini-PCNL and standard PCNL for smaller stones. This supports the hypothesis that the smaller tract size decreased perioperative blood loss, even with a larger stone burden.

A lower overall complication rate and specific complication rates in mini-percutaneous nephrolithotomy supports its safety of utilization in larger stones.

In this meta-analysis, standard PCNL did not offer a significant advantage in the stone-free rate over mini-PCNL. This favors mini-PCNL in the sense that the procedure can be done to larger stones and deliver a comparable stone clearance rate to the current gold standard.

Conclusion

Mini-percutaneous nephrolithotomy has advantage over standard percutaneous nephrolithotomy for large-burden stones in terms of shorter length of postoperative hospital stay, lower hemoglobin drop, lower rate of transfusion, lower rate of urine leakage and an overall lower occurrence of complications. Standard percutaneous nephrolithotomy has an advantage over mini-percutaneous nephrolithotomy only in terms of having a shorter operative time for larger stones. Otherwise postoperative pain scores, postoperative fever and the stone-free rate are comparable. This supports the recent thrust into more minimally invasive procedures in the treatment of larger stones. Mini-percutaneous nephrolithotomy can be recommended as an alternative to standard percutaneous nephrolithotomy even in large-burden stones.

References

1. Pietropaolo A, Proietti S, Geraghty R, et al. 2017. Trends of urolithiasis: interventions, simulation, and laser technology' over the last 16 years (2000-2015) as published in the literature (PubMed): a systematic review from European Section of Uro-technology (ESUT). World J Urol 2017; 35(11): 1651-8. doi: 10.1007/s00345-017-2055-z. Epub 2017 Jun 7.
2. Taylor E, Miller J, Chi T, Stoller M. Complications associated with percutaneous nephrolithotomy. Translational Andrology and Urology. Transl Androl Urol 2012; 1(4): 223-8. doi: 10.3978/j.issn.2223-4683.2012.12.01. Dec 2012 1(4); 223-8.
3. Ruhayel T, Tepeler A, Debastani S, et al. Tract sizes in miniaturized percutaneous nephrolithotomy: a systematic review from the European Association of Urology Urolithiasis Guidelines Panel. Eur Urol 2017; 72(2): 220-35. doi: 10.1016/j.eururo.2017.01.046. Epub 2017 Feb 23.
4. Jackman S, Docimo S, Cadeddu J, et al. The "mini-perc" technique: A less invasive alternative to percutaneous nephrolithotomy. World J Urol 1998; 16(6): 371-4.
5. Ferakis N, Stavropoulos M. Mini percutaneous nephrolithotomy in the treatment of renal and upper ureteral stones: lessons learned from a review of the literature. Urol Ann 2015; 7(2): 141-8. doi: 10.4103/0974-7796.152927.
6. Howick J, Phillips B, Ball C, et al. [Internet]. Oxford Center for Evidence-Based Medicine – Levels of Evidence (March 2009). Oxford, England: Center for evidence-based medicine; 2009 [updated 2020, cited 2020 April]. Available from: https://www.cebm.net/2009/06/oxford-centreevidence-based-medicine-levels-evidence-march-2009/
7. Wells GA, Shea B, O'Connell D, et al. Newcastle-Ottawa Scale (NOS) for assessing the quality of non-randomised studies in meta-analyses [Internet]. Ottawa Hospital Research Institute: Canada; [updated 2019, cited 2020 April]. Available from: http://www.ohri.ca/programs/clinical_epidemiology/oxford.asp.
8. Jadad AR, Moore RA, Carroll D, et al. Assessing the quality of reports of randomized clinical trials: is blinding necessary? Control Clin Trials 1996; 17(1): 1-12.
9. Traxer O, Smith T, Pearle M, Corwin S, Saboorian H, Cadeddu J. Renal parenchymal injury after standard and mini percutaneous nephrostolithotomy. J Urol 2001; 165(5): 1693-5.
10. Zeng G, Mai Z, Zhao, et al. Treatment of upper urinary calculi with Chinese minimally invasive percutaneous nephrolithotomy: a single-center experience with 12,482 consecutive patients over 20 years. Urolithiasis. 2013; 41(3): 225-9. doi: 10.1007/s00240-013-0561-z. Epub 2013 Apr 25.
11. Zhong W, Zeng G, Wu W, Chen W, Wu W. Minimally invasive percutaneous nephrolithotomy with multiple mini tracts in a single session in treating staghorn calculi. Urol Res 2011; 39(2): 117-22. doi: 10.1007/s00240-010-0308-z. Epub 2010 Sep 7.
12. Zhu W, Liu L, Liu Y and Lei M. Minimally invasive vs standard percutaneous nephrolithotomy a meta-analysis. Urolithiasis. 2015; 43(6): 563-70. doi: 10.1007/s00240-015-0808-y. Epub 2015 Aug 5.
13. American Urological Association [Internet]. USA: American Urological Association. Surgical management of stones: AUA/Endourology Society Guideline (2016); 2016 [cited 2020 April]. Available from: https://www.auanet.org/guidelines/kidney-stones-surgical-management-guideline.
14. Emiliani E, Talso M, Baghdadi M, Traxer O. Renal parenchyma injury after percutaneous nephrolithotomy tract dilatations in pig and cadaveric kidney models. Cent Euro J Urol 2017; 70(1): 69-75. doi: 10.5173/ceju.2017.930. Epub 2017 Mar 14.
15. Elsheemy M, Elmarakbi A, Hytham M, Ibrahim H, Khadgi S and Kandari A. Mini vs standard percutaneous nephrolithotomy for renal stones: a comparative study. Urolithiasis 2019; 47(2): 207-14. doi: 10.1007/s00240-018-1055-9. Epub 2018 Mar 16.
16. Abdhelhafez M, Wendt-Nordahi, Kruck S, et al. Minimally invasive versus conventional large-bore percutaneous nephrolithotomy in the treatment of large-sized renal calculi: Surgeon's preference? Scand J Urol 2016; 50(3): 2112-5.
17. Chao C, Zeng G. Mini-PCNL versus standard-PCNL for the management of 20-40 mm size kidney stones: The initial result of a multi-center randomized controlled trial [Abstract]. J Urol 2018 [cited 2020 April]. Available from: 10.1016/j.juro.2018.02.1787.
18. Cheng F, Yu W, Xhang C, Yang S, Xia Y and Ruan Y. Minimally invasive tract in percutaneous nephrolithotomy for renal stones. J Endourol. 2010; 24(10): 1579-82.
19. Guler A, Erbin A, Ucpinar B, Savun M, Sarilar O, Akbulut M. Comparison of miniaturized percutaneous nephrolithotomy and standard percutaneous nephrolithotomy for the treatment of large kidney stones: a randomized prospective study. Urolithiasis 2019; 47(3): 289-95.
20. Kukreja R. Should mini percutaneous nephrolithotomy (MiniPNL/Miniperc) be the ideal tract for medium-sized renal calculi (15-30mm)? World J Urol 2018; 36(2): 285-91.