REVIEW

Bali Medical Journal (*Bali MedJ*) 2022, Volume 11, Number 3: 1331-1338
P-ISSN.2089-1180, E-ISSN: 2302-2914

Comparison between mini-Percutaneous Nephrolithotomy (PCNL) and standard PCNL in pediatric patients: a systematic review and meta-analysis

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Received: 2022-06-28
Accepted: 2022-08-02
Published: 2022-09-30

ABSTRACT

Background: We conducted a systematic review and meta-analysis to determine the efficacy and safety of mini-Percutaneous Nephrolithotomy (PCNL) compared to standard PCNL in children with nephrolithiasis. Clinical trials and observational studies comparing standard PCNL and mini-PCNL in pediatric patients were identified from electronic databases in November 2021.
Method: Studies were extracted for author, year, location, design, subjects' age, sample size, objective, primary endpoint, level of evidence, and results (stone-free rates and complications). Results were subjected to qualitative analysis using the synthesis method. Adequate results were extracted and analyzed quantitatively using the fixed-effect model on homogenous data or the random-effect model on heterogeneous data for meta-analysis. Outcome variables are shown as odds ratios (ORs) with 95% confidence intervals (CIs). All statistical analyses were performed with Review Manager version 5.4.
Result: We reported that stone-free rate and residual stone vary between two studies with contrary results. However, our quantitative analysis showed an insignificant difference between both groups of stone-free rate (OR 0.75; 95% CI 0.22-2.54) and residual stone (OR 1.27; 95% CI 0.55-2.91). Complications rates were insignificantly different between mini-PCNL group and PCNL group in two studies in Clavien 1 (OR 0.65; 95% CI 0.27-1.54) and Clavien 2 grade (OR 0.48; 95% CI 0.19-1.22). In addition, pooled analysis of both complication grades was also insignificant in the difference between groups (OR 0.56; 95% CI 0.30-1.06).
Conclusion: The efficacy and safety of mini PCNL were neither superior nor inferior compared to standard PCNL in managing nephrolithiasis in pediatric patients. Moreover, mini PCNL was considered better regarding post-operative pain and tract infection; thus, mini PCNL could be considered a treatment option for pediatric patients with nephrolithiasis.

Keywords: Kidney stone, pediatric, mini-PCNL, standard PCNL, efficacy, safety, complication.
Cite This Article: Aulia, K., Atmoko, W., Birowo, P., Rastid, N. 2022. Comparison between mini-Percutaneous Nephrolithotomy (PCNL) and standard PCNL in pediatric patients: a systematic review and meta-analysis. *Bali Medical Journal* 11(3): 1331-1338. DOI: 10.15562/bmj.v11i3.3563

INTRODUCTION

Renal stones or nephrolithiasis is a common condition in adults with a lifetime prevalence of 10.6% for men and 7.1% for women.[1] However, the proportion of nephrolithiasis in pediatric patients is only 1–2% of adults' prevalence. Prevalence of nephrolithiasis in children began to increase to 50 cases per 100,000 children in 2016.[2] It has been identified that most nephrolithiasis in children is caused by metabolic imbalances such as uneven calcium, oxalate, citrate, cystine, and uric acid metabolism. It was known that hypercalciuria and hypocitraturia were the most common metabolism errors leading to nephrolithiasis in children.[3]

Thorough anamnesis, physical examination, and supporting examination should be taken to determine the presence of nephrolithiasis in children. The interventional approach was intended for children with obstruction caused by solitary kidney, serious bacterial illness, uncontrolled gastrointestinal symptoms, unrelieved pain with analgesics, high-grade obstruction, and unlikely spontaneous passage.[4]

The main aim of interventional treatment in children with nephrolithiasis is to create a stone-free experience in a single intervention without causing complications.[4] There are plenty of intervention options, such as extracorporeal shock wave lithotripsy (ESWL), percutaneous nephrolithotomy (PNCL), and retrograde intrarenal surgery (RIRS). However, PCNL was proven effective in treating larger stones and/or stones resistant to ESWL treatment.[2] European Association of Urology indicates PCNL for staghorn stones, stones larger than 20 mm, lower pole stones larger than 10 mm, cystine stones, and failure to other treatments.[2,4,5]

PCNL was proven to be an effective approach towards large and complicated kidney stones in adult and pediatric patients. However, due to the large nephroscope and amplatz size of 24–30 F, standard PCNL has caused several complications, such as depletion of hemoglobin, the need for transfusion, disintegration of renal parenchyma, and

post-operative pain in pediatric patients.[2,6] Therefore, PCNL was developed to be done in a smaller nephroscope and amplatz, sized 14–20 F. This is called mini-PCNL or miniperc. The stone-free rate of mini-PCNL was 84.7% after one month of intervention with mean hospitalization period of 3.8 days, compared to stone-free rate of standard PCNL of 70.1% in another study.[7,8] However, accurate interpretation of comparison between mini-PCNL and standard PCNL in terms of efficacy in pediatric patients is not yet known. In addition, a comparison of the stone-free rate above was made based on different studies, thus subject to biases. Some studies described limitations in mini-PCNL, such as longer operative time, decreased visibility, difficulty in stone retrieval, increased intraoperative renal pressures, and higher rates of infectious complications, but its comparison in terms of safety compared to standard PCNL is yet to be known.[9,10] Therefore, we conducted a systematic review and meta-analysis to determine the efficacy and safety of mini-PCNL compared to standard PCNL in children with nephrolithiasis.

MATERIAL AND METHODS

We conducted a systematic review and meta-analysis complied to Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) Guideline, using a search strategy on three databases: PubMed, Scopus, and ProQuest. Four authors (A, B, C, D) conducted search on PubMed using keywords ((“Nephrolithotomy, Percutaneous”[Mesh] AND “mini”) OR (mini PCNL)) AND ((((((“Child”[Mesh]) OR “Child, Preschool”[Mesh]) OR (Children)) OR (Child)) OR (Pediatric)) OR (Paediatric)), on Scopus and ProQuest using keywords ((mini percutaneous nephrolithotomy) OR (mini PCNL)) AND ((children) OR (pediatric) OR (paediatric) OR (child) OR (adolescent) OR (toddler) OR (infant) OR (newborn)).[11] All searching was done on November 4th, 2021. The authors also looked for ongoing trials on *Clinicaltrial.gov* and emailed two experts with expertise on mini-PCNL and further recommendations.

Authors set inclusion criteria: (1) observational study or clinical trial; (2) studying pediatric patients; (3) mini-PCNL as intervention or independent variable; (4) PCNL as control; (5) Stone-free rate, complication, or mortality as the outcome; (6) Full text written in English. Authors excluded editorial/review articles, case reports or other articles discussing indirect relationships within variables. All studies were searched by four authors independently, with different results discussed by authors for the final decision.

Included studies will be assessed for validity, importance, and applicability using Oxford Center for Evidence-Based Medicine’s tool for critical appraisal.[12] In addition, studies will be assessed for risk of bias using Cochrane’s tool for risk of bias.[13] Studies will be extracted for the author, year, location, design, subjects’ age, sample size, objective, the primary endpoint, level of evidence, and results. Results will undergo qualitative analysis using the synthesis method. Adequate results will be extracted and analyzed quantitatively using a fixed- or random-effect model for meta-analysis. Results also will be assessed for heterogeneity and significance on the same model. The result will be considered heterogeneous if the p-value is equal to or lesser than 0.05 and/or the I-squared statistic value is more than 50%, and homogenous if the I-squared statistic value is equal or less than 50% and/or the p-value is lesser than 0.05. The fixed-effect model will be used on homogenous data, and the random-effect model will be used on heterogeneous data.[14,15]

RESULTS

We found 254 articles after duplication removal from searching in PubMed, Scopus, and ProQuest. After screening, we found 12 studies suitable for inclusion and exclusion criteria. After the full-text assessment, we found three studies eligible for qualitative analysis.[16–18] However, only two studies provided sufficient data for meta-analysis (**Figure 1**).[16,17,19] Two studies originated from Asia, and one study originated from Europe. All studies were done in retrospective analysis with level evidence of 3, involving children with mean ages ranging from 5.9 to 10.8 years old.[16–18,20] There were 317 subjects involved

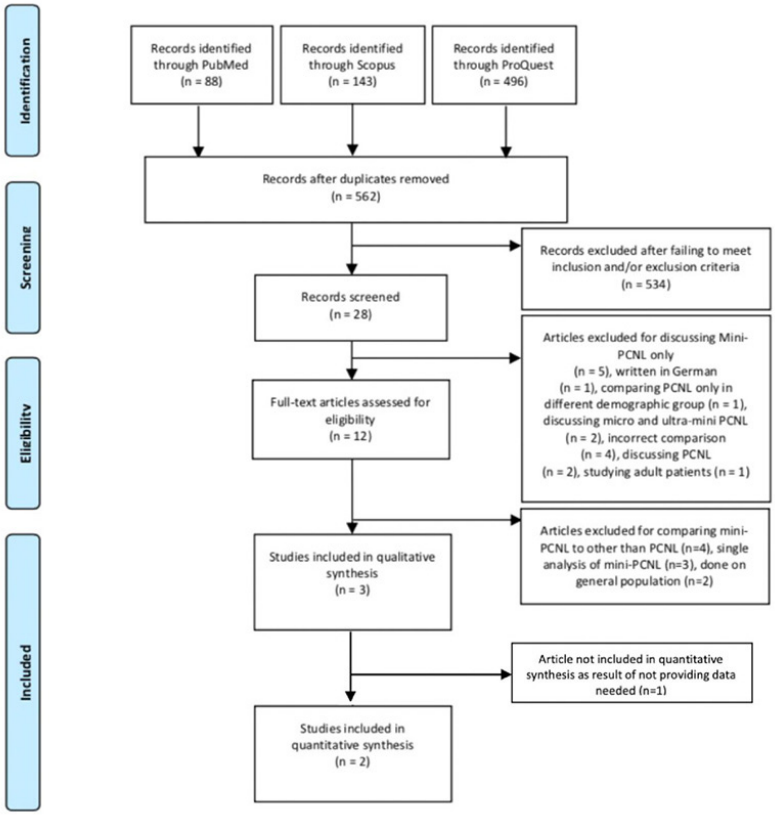


Figure 1. PRISMA diagram of search strategy.[9]

Table 1. Study characteristics.[12–14]

Study	Year	Location	Design	Age (years) Mini-PCNL	Age (years) PCNL	Sample size Mini-PCNL	Sample size PCNL	Objective	Primary endpoint	Level of evidence*
Celik H, *et al*	2016	Turkey	Retrospective study	9.52	10.8	89	82	Determine morbidity and success rates among different groups of pediatric patients undergoing PCNL	Stone-free rate	3
Mahmood S, *et al*	2019	Iraq	Retrospective study	6.91±4 .98	6.20±4. 14	59	75	Evaluate relative effectiveness and safety of mini-PCNL compared with standard PCNL in renal stones treatment in pediatric age-groups	Stone-free rate	3
Hasegan A, *et al*	2017	Romania	Retrospective study	5.9±3. 5	7.2±3.9	7	5	Analyze efficacy and safety of PCNL and mini-PCNL in pediatric patients	Intra-operative and post-operative complication	3

*Level of evidence according to The OCEBM.[18]

Table 2. Result of critical appraisal of studies.[10,12–14]

Author	Validity					Applicability			
	PICO	Randomization	Similar entry point	Equal treatment	Intention-to-treat	Objective / blinding	Similarity	Feasibility	Benefits
Celik H, *et al*	Yes	No	Yes	Yes	Yes	Yes	Yes	Yes	No
Mahmood S, *et al*	Yes	No	Yes	Yes	Yes	Yes	Yes	Yes	No
Hasegan A, *et al*	Yes	No	Yes	Unclear	Yes	Yes	Yes	Yes	Yes

in the qualitative analysis and 305 subjects involved in the meta-analysis (Table 1).[12–14] Based on critical appraisal, all studies were not randomized but clear regarding the rest of the validity criteria. Two studies could not determine the superiority of benefits, and one study could determine (Table 2).[12,16–18] We found out that all studies were at high risk of selection bias but a low risk of performance bias, detection bias, attrition, and other bias. Two studies reported unclear reporting bias in their study, with one study reporting low risk (Table 3).[13,16–18]

We reported that stone-free rate and residual stone vary between two studies with contrary results (Table 4).[16,17] However, our quantitative analysis showed that there was an insignificant difference in stone-free rate and residual stone between both groups (p>0.05) (Figure 2). Complications rates, both in Clavien 1 and Clavien 2 grades, were shown to be insignificantly different between the mini-PCNL group and standard PCNL group in the two studies.[16,17] Pooled odds ratio also showed an insignificant difference between both groups in quantitative analysis (p>0.05). Three studies reported insignificant differences in hospitalization period between both groups.[16–18] One study suggested no difference in bleeding and duration of procedure within groups but a lesser proportion of post-operative pain and tract infection pyelonephritis in the mini-PCNL group.[16] In terms of homogeneity, analysis varied between homogenous and heterogenous data distribution (Figure 2).[16,17]

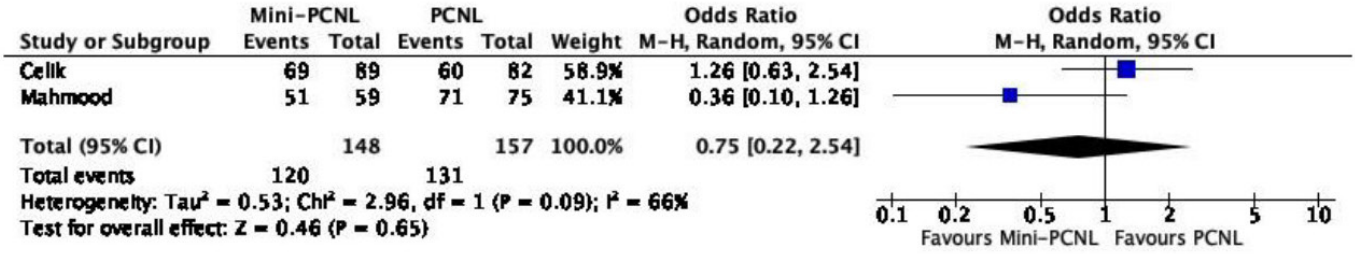
Table 3. Results of Cochrane's risk of bias assessment of studies.[11–14]

Study	Aspect of bias	Risk	Description
Celik H, *et al*	Random sequence generation (selection bias)	High	Choice of clinician or participant
	Allocation concealment (selection bias)	High	Non-random, predictable sequence
	Blinding of participants and personnel (performance bias)	Low	No blinding, but outcome unlikely to be influenced
	Blinding of outcome assessments (detection bias)	Low	No blinding, measurement unlikely to be influenced
	Incomplete outcome data (attrition bias)	Low	No missing data
	Selective reporting (reporting bias)	Unclear	Protocol is available
	Other bias	Low	Study appears to be free of other sources of risk
Mahmoo d S, *et al*	Random sequence generation (selection bias)	High	Choice of clinician or participant
	Allocation concealment (selection bias)	High	Non-random, predictable sequence
	Blinding of participants and personnel (performance bias)	Low	No blinding, but outcome unlikely to be influenced
	Blinding of outcome assessments (detection bias)	Low	No blinding, measurement unlikely to be influenced
	Incomplete outcome data (attrition bias)	Low	No missing data
	Selective reporting (reporting bias)	Unclear	Protocol not mentioned
	Other bias	Low	Study appears to be free of other sources of risk
Hasegan A, *et al*	Random sequence generation (selection bias)	High	Choice of clinician or participant
	Allocation concealment (selection bias)	High	Non-random, predictable sequence
	Blinding of participants and personnel (performance bias)	Low	No blinding, but outcome unlikely to be influenced
	Blinding of outcome assessments (detection bias)	Low	No blinding, measurement unlikely to be influenced
	Incomplete outcome data (attrition bias)	Low	No missing data
	Selective reporting (reporting bias)	Unclear	Protocol not mentioned
	Other bias	Low	Study appears to be free of other sources of risk

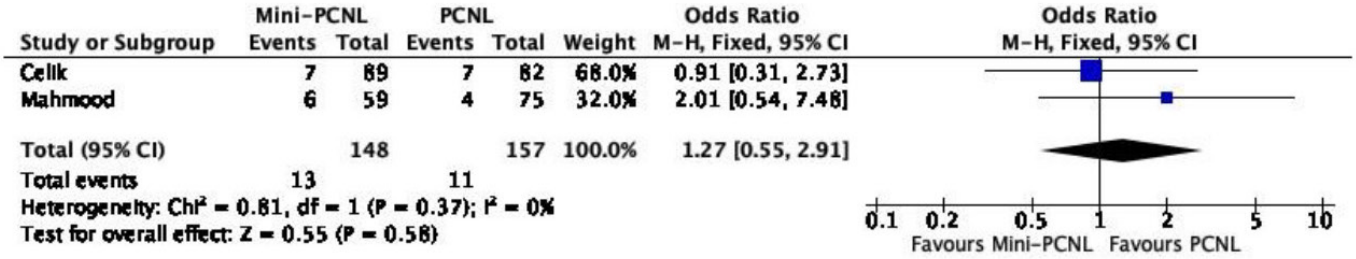
Table 4. **Results of qualitative analysis of studies.**

								Surgical complications according to the modified Clavien grading system									
	Sample size		Stone-free rate stone		Residual stone		Hospitalization period (days)		1		2		3		Mortality		Other notable results
Author	Mini PCNL	PCNL	Mini-PCNL	PCNL	Mini -PCNL	PCNL	Mini-PCNL	PCNL	Mini -PCNL	PCNL	Mini -PCNL	PCNL	Mini-PCNL	PCNL	Mini-PCNL	PCNL	
Celik H, *et al*	89	82	69	60	7	7	5.22±1.85	5.67±2.15	4	5	1	4	0	0	0	**0**	
Mahmood S, *et al*	59	75	51	71	6	4	1.91±1.15	2.41±1.14	5	10	6	12	0	0	0	**0**	
Hasegan A, *et al*	7	5	-	-	-	-	3.0±1.2	4.0±1.5	-	-		-					No significant difference of mean hospital stay, bleeding, and mean duration of procedure within groups.Less post-operative pain (8.33% vs 16.60%), less tract infection pyelonephritis (0.00% vs 8.33%) in Mini-PCNL group.

Stone-Free Rate



Residual Stone



Complication Rate

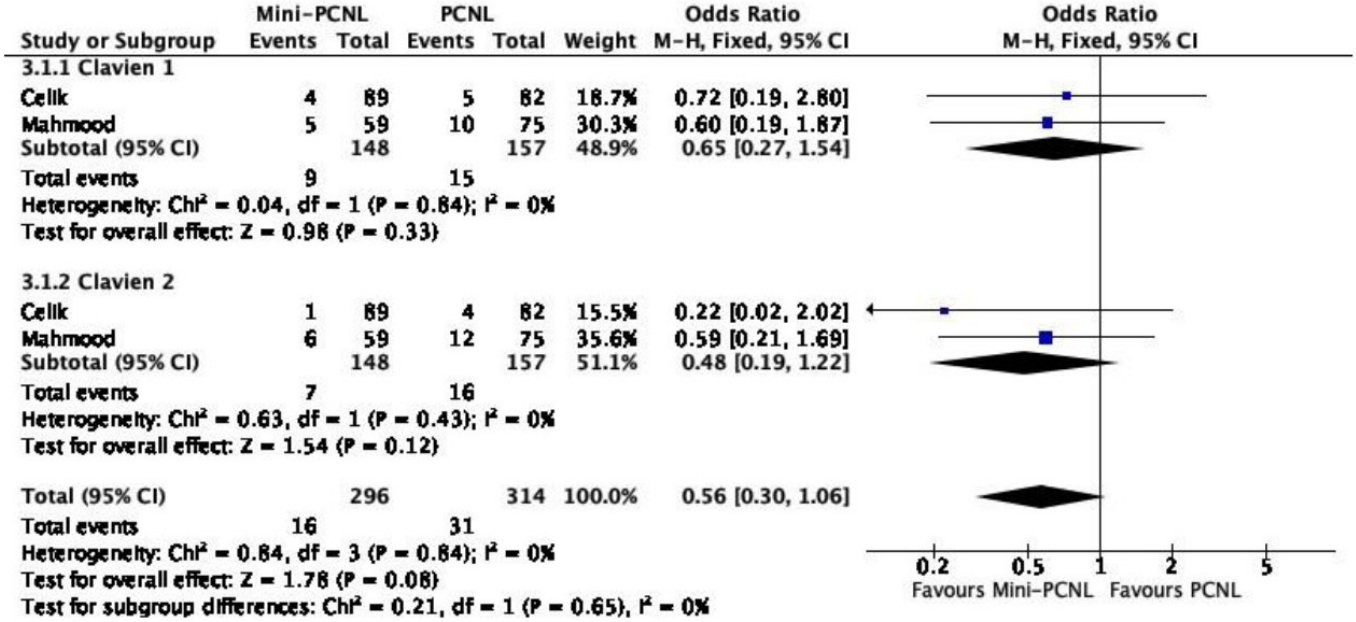


Figure 2. Analysis of selected studies.

DISCUSSION

It was known from this study that the stone-free rate event of mini-PCNL was 0.75 times (95% CI 0.22; 2.54) of standard PCNL in children. In addition, the residual stone event of mini PCNL was 1.27 times (95% CI 0.55; 2.91) more likely to occur than in standard PCNL. However, these statistics of mini PCNL safety were not significantly different (p>0.05). In terms of safety, mini PCNL provided complication risk in Clavien grade I and grade II 0.65 times (95% CI 0.27; 1.54) and 0.48 times (95% CI 0.19; 1.22), respectively. In addition, pooled analysis of both complication grades was insignificant in the difference between groups. These findings were similar to another study that did not put into the quantitative analysis, which stated that there was no significant difference in mean hospital stay, intraoperative and post-operative bleeding, and mean duration of procedure within groups. However, the same study reported less post-operative pain and less tract infection pyelonephritis in the mini PCNL group.[18]

Despite the insignificant results, mini PCNL was considered good in efficacy and safety in several studies. One study assessing mini PCNL done on 234 patients under 3 years old showed that the stone-free rate was 97.2%.[21] Another study reported a stone-free rate of 90.8% in pediatric patients with stone diameters>20 mm.[22] Four studies also reported stone-free rates ranging from 85%, 95%, 86%, and 85%, respectively.[23–26] Stone-free rate was an important factor to ensure that no residual stone could lead to a stone-related event.[3] Residual stone size <5 mm could evoke an increase in stone size with the probability of 69%, according to a study.[27] Therefore, reaching an optimal stone-free rate was an important prognostic factor of stone recurrence in the future.[28]

The same four studies mentioned above have reported an overall complication rate ranging from 15% to 25%, with a total of 253 renal units examined.[23–26] They were mainly distributed in Clavien grade I–II, with 4% of cases in Clavien grade III, as stated by one study.[23] Two studies studied 69 renal units with a diameter of 2.3–2. 4 cm reported an overall complication rate of 10.6% and 36.3%, respectively.[29,30] Complications in Clavien grade I usually do not need special therapy. Clavien grade II usually needs blood transfusion and/or parenteral antibiotics. In contrast, Clavien grade III needs angiographic embolization and ureteral stent insertion, which could interrupt the quality of life of the patients.[31] Pediatric patients experiencing mini PCNL have the risk of hemoglobin drop ranging from 0.4% to 24.0%.[5] However, a study stated that the incidence was only notifiable if the tract size exceeded 22 F.[32] Mini PCNL was associated with less post-operative pain and less tract infection pyelonephritis.[18] Less pain means less interruption in sleep, social activities, and daily performance, which could contribute to a better quality of life for children who underwent mini PCNL.[33] Less infection could mean less uroepithelial disruption, which could cause nidus, the surface that promotes the growth and formation of urinary stones.[6] Therefore, it was fair enough to say that mini PCNL was not inferior in efficacy and safety compared to standard PCNL and was proven to provide less pain and infection to pediatric patients. Two recent studies have also confirmed mini PCNL's efficacy and safety to be done towards children with urinary tract stones.[34–35]

This study was a pilot meta-analysis on the efficacy and safety of mini PCNL for pediatric nephrolithiasis. A limitation of this study is that it lacked sufficient resources, including only two studies for all quantitative analysis. Thus, more high-quality randomized controlled trials comparing mini PCNL and standard PCNL should be made to make systematic review and meta-analysis results more significant and applicable. This study also reports moderate heterogeneity in stone-free rates between both groups. This result might be due to a difference in how these studies measured, documented, or reported at a stone-free rate. Unfortunately, sensitivity analysis cannot be conducted due to lack of research data.

CONCLUSION

The efficacy and safety of mini PCNL were neither superior nor inferior compared to standard PCNL in managing nephrolithiasis in pediatric patients. However, some individual studies showed the superiority of mini PCNL over standard PCNL in terms of complications and effectiveness. Moreover, mini PCNL was considered better in terms of post-operative pain and urinary tract infection, thus, mini PCNL could be considered a treatment option for pediatric patients with nephrolithiasis. More randomized controlled studies should be made to improve the significance and applicability of this meta-analysis.

DISCLOSURE

Conflict of Interest: The author reports no conflicts of interest in this work.

AUTHOR CONTRIBUTIONS

KA contributed to literature searching, data acquisition, data and statistical analysis, manuscript preparation and editing. WA, PB, and NR contributed to the concept, design, definition of intellectual content, data and statistical analysis, and manuscript review.

FUNDINGS

None

ETHICAL CONSIDERATION

None

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