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Keywords:	percutaneous nephrolithotomy, tract dilatation, one-shot dilatation, meta-analysis

One-shot dilatation versus serial dilatation technique for access in percutaneous nephrolithotomy: a systematic review and meta-analysis

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Abstract:

Objective The purpose of this study was to systematically review the outcomes of one-shot dilatation (OSD) and serial tract dilatation for percutaneous nephrolithotomy (PCNL). **Methods** A systematic review and meta-analysis was conducted. Randomized clinical trials (RCTs) that were included in the study were identified from EMBASE, MEDLINE, and the Cochrane Central Register of Controlled Trials. The last date of the search was April 30, 2018. Summary effects were calculated as risk ratios (RRs) with 95% confidence interval (CIs) or mean differences (MDs) with 95% CIs. The endpoints included access time, fluoroscopy time, successful dilation rate, stone-free rate, postoperative decrease in hemoglobin levels, transfusion rate, rate of complications, and length of postoperative hospital stay. **Results** A total of 7 RCTs comparing the efficacy and safety of OSD with those of serial dilatation were included in the study, and clinical data were reported for 697 patients. The overall access time were shorter with OSD than with serial dilatation (MD, -110.14; 95% CI, -161.99 to -58.30; P<0.0001). The fluoroscopy time was shorter with OSD than with serial dilatation in all RCTs. In addition, there was less of a decrease in postoperative hemoglobin levels in patients in the OSD group than in those in the serial dilatation group (RR, -0.23; 95% CI, -0.39 to -0.07; P=0.004). There were no associations among successful dilation rate, stone-free rate, transfusion rate, complication rate or the method of tract dilatation. **Conclusion** The data from the included studies indicated that OSD is a safe and efficacious tract dilatation technique that can reduce the access time, fluoroscopy time, and postoperative decreases in hemoglobin levels.

There was no difference in the successful dilation rate, stone-free rate, transfusion rate, or rate of complications between OSD and serial dilatation. A difference in the length of postoperative hospital stay was uncertain. OSD may be a better method for tract creation for PCNL.

Keywords: percutaneous nephrolithotomy, tract dilatation, one-shot dilatation, meta-analysis

Abbreviations: AMD, Amplatz dilator; ALD, Alken telescoping dilator; MTD, Metal telescopic dilators; OSD, One-shot dilatation; NR, Not reported; PCNL, Percutaneous nephrolithotomy; RR, Risk ratio; MD, Mean difference; CI, Confidence interval; RCTs, Randomized controlled trials

Strengths and limitations of this study

This meta-analysis and systematic review was performed via a strict literature search. It was the updated meta-analysis to systematically review the outcomes of one-shot dilatation (OSD) and serial tract dilatation for percutaneous nephrolithotomy (PCNL).

The number of studies considered in the final meta-analysis was 7. This small sample size limited the potential analyses. The research did not consider the surgical skills mentioned in published studies.

Despite a systematic search strategy, the inclusion criteria excluded non-English documents and had language bias.

These limitations notwithstanding, the research can guide the choice of access

creation in PCNL.

Introduction

With the minimally invasive treatment of urinary calculi, percutaneous nephrolithotomy (PCNL) has become one of the main treatments for large kidney and ureteral stones.[1] One of the most fundamental steps of PCNL surgery is to establish safe and effective access. The most common complications in this process are failure of tract dilatation, hemorrhage, and perforation of the renal parenchyma or collection system.[2] It is especially important to find a simple, effective, and safe tract dilatation method. One-shot dilatation (OSD) and serial dilatation are two controversial tract dilatation methods. To further compare the safety and efficacy of these two methods, we conducted a systematic review and meta-analysis of previous randomized controlled trials (RCTs) comparing the outcomes of these two tract dilatation methods for PCNL.

Methods

This meta-analysis was performed according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement (**Table S1**).[3] The present meta-analysis did not need the approval because all the enrolled published studies were approved by the ethics committee in there research institute.

Literature search

We used EMBASE, Ovid MEDLINE, and the Cochrane Central Register of Controlled Trials to conduct systematic literature searches. The final date for literature

searches was April 30, 2018. Searches were performed using the keywords "percutaneous nephrolithotomy, tract dilatation" combined with free-text terms for gradual, sequential, serial, one-shot, one-step, one-stage, single-step, or single-increment dilatation. No language was restricted. **Fig. 1** shows the process of identifying RCTs.

Inclusion criteria and study outcomes

The inclusion criteria were as follows: prospective RCTs comparing OSD and serial dilatation for PCNL in adults and children. Patients may have had a history of ipsilateral surgery. Retrospective, animal, noncomparative and duplicated studies were excluded. Two authors independently reviewed the titles and abstracts, and differences were discussed with a third author to reach an agreement. The primary outcomes included access time, fluoroscopy time, successful dilation rate, and postoperative decreases in hemoglobin levels. The secondary outcomes were transfusion rate, stone-free rate, complication rate, and length of postoperative hospital stay.

Data extraction and quality assessment

Two authors independently extracted the demographic, quality and results data by reading the full-text articles. Data were extracted from RCTs that met the inclusion criteria. If there were differences in the same research report, the latest full report was used. Any differences in data extraction were resolved by discussion and consultation with senior authors. In addition, we evaluated the methodological quality of the trials according to the methods recommended by the Cochrane Collaboration.[4]

Data analysis

We used Review Manager for statistical analysis (RevMan, Version 5.3; Cochrane Collaboration, Copenhagen, Denmark). For dichotomous data, risk ratios (RRs) were used to evaluate the incidence of events, and the results were reported with 95% confidence intervals (CIs). For continuous data, mean difference (MD) with 95% CI was used. Cochrane's Q and I^2 statistics were calculated to assess the heterogeneity, and $P<0.1$ indicates significant heterogeneity. The I^2 test describes heterogeneity beyond chance. In the absence of heterogeneity, a fixed-effect meta-analysis was used in conjunction with the study.[5] If there was heterogeneity and the cause was determined by sensitivity analysis, the result of the random-effects meta-analysis was used, otherwise, only a systematic review was performed. $P<0.05$ was considered statistically significant.

Results

Based on the search strategies and selection criteria, initial literature searches identified 356 studies across all databases. We eventually included 7 RCTs comparing the outcomes of OSD and serial dilatation for PCNL in this review.[6-12] **Table 1** shows the basic characteristics of these studies. Several studies were described using only one abstract, but the results were not presented in a usable way. The authors declined to provide more information, so these articles were not included in the results.

Table. 1 Studies of characteristics of machine one-shot dilatation VS serial dilatation.

Authors	Year	Institution location	Cases (N)		Gender (M/F)		Age (Y)		Stone size (cm)		Dilators	
			One-shot	Serial	One-shot	Serial	One-shot	Serial	One-shot	Serial	One-shot	Serial
Frattini et al	2001	Italy	26	27	15/12	17/9	59	54	2.3±0.7	2.9±0.9	AMD	ALD
Amjadi et al	2008	Iran	17	14	10/7	12/2	42	44	3.7±1.0	3.2±1.1	AMD	ALD
Falahatkar et al	2009	Iran	102	112	56/46	62/50	57	51	3.9±1.6	3.4±1.2	AMD	MTD
Aminsharifi et al	2011	Iran	29	19	19/10	9/10	44.1	42.5	2.7±1.0	3.7±1.3	AMD	ALD
Nour et al	2014	Egypt	24	25	17/7	16/9	43.8	38.2	3.7±7.2	30.2±6.9	AMD	ALD
Hosseini et al	2014	Iran	31	31	22/9	18/13	3.7	3.7	2.0±0.35	1.7±0.4	AMD	ALD
Srivastava et al	2017	India	120	120	59/61	62/58	38.9	40.1	NR	NR	AMD	ALD

M, Male; F, Female; AMD, Amplatz dilator; ALD, Alken telescoping dilator; MTD, Metal telescopic dilators; NR, Not reported

Quality of the included trials

The overall quality of the included trials was acceptable, although there were some deficiencies in the reporting of methods in some trials. **Fig. 2** illustrates the risk of a bias summary. Sequence generation was adequate in six trials and unclear in the remaining one. Allocation concealment was judged to be adequate to minimize selection bias in two trials and unclear in five. Blinding of participants and personnel was judged to be adequate to prevent performance bias in two trials and unclear in five. Blinding of outcome assessment was judged to be adequate to prevent detection bias in two trials and unclear in five. The quality of outcome data reporting was adequate in six trials and unclear in one. No selective reporting of outcomes were observed, and other bias was classified as unclear in all seven trials.

Access time and fluoroscopy time

The reported access time varied between the included RCTs.[6, 7, 9, 10] Meta-analysis showed that the MD of the access time was shorter with OSD than with serial tract dilatation (random-effects analysis: MD, -110.14; 95% CI, -161.99 to -58.30; P<0.0001) **(Fig. 3A)**. Significant heterogeneity was observed (Q=21.86, P<0.0001, I^2=86%).

A sensitivity analysis was performed after Aminisharifi's study was removed from the analysis.[9] Meta-analysis of this subgroup was supportive of the overall analysis (fixed-effects analysis: MD, -77.13; 95% CI, -94.35 to -59.91; P<0.00001) (**Fig. S1**). There was no significant heterogeneity in this subgroup (Q=1.52, P=0.47,

I^2=0%).

Seven trials reported data regarding fluoroscopy time.[6-12] All of the trials showed that OSD had significantly decreased fluoroscopy time compared with serial tract dilatation. Due to the significant heterogeneity among the studies and failure to analyze the source of heterogeneity, meta-analysis was not performed. The results of a previous meta-analysis from 2013 (including 4 RCTs[9-12]) also indicated that OSD had a significantly shorter tract dilatation fluoroscopy time than serial tract dilatation.[13, 14]

Successful dilation rate and stone-free rate

Six trials reported successful dilation rates.[6-11] None of the RCTs found significant differences between OSD and serial tract dilatation. The results of the meta-analysis showed that the OSD had a slightly lower successful dilation rate than serial tract dilatation. However, there was no statistical significance (fixed-effects analysis: RR, 0.98; 95% CI, 0.96 to 1.00; P=0.07) **(Fig. 3B)**. There was no significant heterogeneity (Q=2.73, P=0.74, I^2=0%).

Seven trials reported stone-free rates.[6-12] None of them found significant differences between OSD and serial tract dilatation. The overall stone-free rate was no different between OSD and serial tract dilatation (fixed-effects analysis: RR, 0.98; 95% CI, 0.93 to 1.03; P=0.52) (**Fig. 3C**). Heterogeneity was not observed (Q=1.93, P=0.93, I^2 =0%).

Decreases in hemoglobin levels and transfusion rate

Four RCTs recorded postoperative decreases in hemoglobin levels.[6, 9, 11, 12] There was less of a decrease in hemoglobin levels with OSD than with serial tract dilatation in two RCTs but not in another. The results of the meta-analysis showed that OSD significantly reduced hemoglobin loss compared with serial tract dilatation (RR, -0.23; 95% CI, -0.39 to -0.07; P=0.004) (**Fig. 4A**). There was no heterogeneity (Q=0.66, P=0.88, I^2 =0%).

Four trials reported transfusion rates.[6, 10-12] Transfusion rates varied between the included studies. No significant difference were found in any trial. Meta-analysis showed that the RR of the successful dilation rate was similar with OSD and with serial tract dilatation (fixed-effects analysis: RR, 0.69; 95% CI, 0.29 to 1.63; P=0.40) **(Fig. 4B**). No significant heterogeneity was observed(Q = 0.25, P=0.97, I^2 = 0%).

Complication rates and length of postoperative hospital stay

Six RCTs provided complication rates.[6-8, 10-12] These RCTs found no relationship between the method of tract dilatation and complication rates. Meta-analysis showed that the overall rate of complications was lower in the OSD group than in the serial tract dilatation group (fixed-effects analysis: RR, 0.78; 95% CI, 0.48 to 1.26; P=0.31) (**Fig. 4C**). Heterogeneity was not observed (Q=1.57, P=0.81, I^2 =0%).

Four RCTs provided the length of postoperative hospital stay.[6-8, 10-12] One reported that serial tract dilatation significantly reduced the length of postoperative

hospital stay versus OSD.[12] Two studies found that OSD was more effective than serial tract dilatation in decreasing the length of postoperative hospital stay.[7-8] No significant difference was found in one trial.[6] Meta-analysis showed that the RR of postoperative hospital stay was less with OSD than with serial tract dilatation, but without statistical significance. (random-effects analysis: MD, -0.15; 95% CI, -0.93 to 0.64; P=0.71) **(Fig. 4D)**. Significant heterogeneity was observed (Q=23.64, P<0.0001, I^2=87%).

A sensitivity analysis was conducted after excluding Frattini's study.[6] However, meta-analysis of this subgroup did not support the overall analysis (fixed-effects analysis: MD, -0.48; 95% CI, -0.80 to -0.16; P=0.003) (**Fig. S2**). There was no significant heterogeneity in this subgroup (Q=2.21, P=0.33, I2=0%).

Discussion

PCNL is the main treatment for large and complex kidney stones. The creation of a nephrostomy tract is one of the most basic steps in PCNL. This systematic review of seven RCTs including 697 patients has examined the evidence for the use of OSD versus serial tract dilatation to create access for PCNL. The RCTs showed a statistically significant reduction in access time and fluoroscopy time with OSD but no difference between OSD and serial tract dilatation in terms of successful dilation rate or transfusion rate. These results are consistent with a previous systematic review performed in 2013.[13, 14] In addition, there was no difference in the stone-free rate or complication rate. However, there was less of a decrease in postoperative hemoglobin

levels with OSD than with serial tract dilatation, which was inconsistent with the results of the previous meta-analysis.[14] The difference was mainly due to an increase in the sample size.

OSD involving a single dilatation of the tract with a 25- or 30-F dilator is simple and does not require gradual channel expansion.[12] This technique saves access time and X-ray exposure time for channel creation and reduces the operative time and the amount of radiation damage to patients. In addition, OSD helps reduce the operative time, thus decreasing the risk of surgery for patients.

Successful dilation and stone-free rates are important factors that influence the effectiveness of tract dilatation techniques. However, this meta-analysis did not find significant differences in the successful dilation rate or the stone-free rate in patients who underwent OSD versus serial dilatation.

The meta-analysis showed that the postoperative decrease in hemoglobin levels was less in patients who underwent OSD than in those who underwent serial dilatation. The difference was statistically significant. Kessaris et al[15] found that the amount of intraoperative blood loss caused by the tract dilatation technique accounted for half of the total blood loss. The correct puncture path and appropriate tract dilatation methods were key decisive factors that determined the amount of intraoperative blood loss. The OSD method can effectively lessen postoperative decreases in hemoglobin levels by reducing the amount of bleeding during surgery.

However, the meta-analysis did not find that one particular tract dilatation method significantly reduced the transfusion rates of patients. A possible reason is that the sample size of the included studies was not enough to detect differences between these two methods. In addition, more high-quality RCTs are required for further study.

In this study, the overall rate of complication was 12.8% in all patients, with 11.6% in the OSD group and 14.0% in the serial dilatation group. The main complications included postoperative urinary tract infections, urine leakage, hemorrhage, hematoma formation and postoperative fever. The difference in complication rates was not statistically significant between the OSD group and the serial dilatation group.

The results of the meta-analysis did not show that the OSD technique could significantly reduce the length of postoperative hospital stay. However, two recent RCTs have shown that the OSD technique significantly reduced the length of postoperative hospital stay,[6, 7] thereby reducing hospitalization costs and benefiting patients. In addition, due to the obvious heterogeneity in the included studies, after eliminating low-quality studies and those with small sample sizes, we found that the results of the analysis were changed. The result showed that OSD was more conducive to reducing the length of postoperative hospital stay than serial dilatation, which made the overall results of the analysis unstable. More high-quality RCTs are required for further study.

It should be highlighted that an RCT involving preschool children was included in

this systematic review. The results of the study showed that the access and fluoroscopy times in the OSD group were less than those in the serial dilatation group. The difference was statistically significant. These findings basically consistent with the results of RCTs involving adults. In addition, the OSD technique significantly shortened the length of postoperative hospital stay. This study indicated that the OSD method was also safe and effective for preschool children.

Some studies have demonstrated that the OSD technique is equally safe and effective for patients with a history of open surgery.[11, 16] In addition, only one dilator is needed to establish a tract with the OSD technique. The price of OSD is much lower than that of the serial dilation method, which reduces the economic burden on patients. Tonshal S et al[17] reported that the cost of OSD technique is significantly lower than that of the Amplatz sequential dilatation technique.

Some factors may influence interpretation of this meta-analysis. Many studies with small sample sizes were included in this analysis, and the methodological quality of these studies was poor or uncertain. However, in this study, we have included more RCTs than previous meta-analyses. In contrast, early systematic reviews and meta-analyses included only four RCTs, so the findings were more robust in this study.

Conclusion

The results of this meta-analysis and systematic review suggest that the OSD is a safe and efficacious tract dilatation technique that can reduce the access time, fluoroscopy time, and postoperative decreases in hemoglobin levels. There were no differences in the successful dilation rate, stone-free rate, transfusion rate, or complication rate between the two techniques. A difference in the length of postoperative hospital stay between the two techniques is uncertain. OSD may be a better method to establish tracts for PCNL. More high-quality RCTs are needed for further study.

Authors' contributions

PXP, ZSD, and GZ conceived and designed the experiments. YHH and LHZ extracted the data. PXP, ZSD, and SCL analyzed the data. YHH, XMW and LHZ contributed materials/analysis tools. PXP wrote the paper. GZ critically revised the report.

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Disclaimer

The contents of the present study are solely the responsibility of the author. The funders had no role in study design, data collection and analysis, decision to publish, or preparation of the manuscript.

Competing interests

The authors declare that no conflicts of interest exist.

Data sharing statement

Datasets used and/or analyzed in the present study are available from the corresponding author on reasonable request.

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Table File

Table. 1 Studies of characteristics of machine one-shot dilatation VS serial dilatation.

Figure Files

Fig. 1 Flowchart of study selection.

Fig. 2 Risk of bias summary: judgments about each risk of bias item for each included study.

Fig. 3 Forest plots illustrating the meta-analysis of outcomes with one-shot tract dilatation versus serial tract dilatation for PCNL. The outcomes analyzed were (A) access time, (B) successful dilation rate, and (C) stone-free rate.

Fig. 4 Forest plots illustrating the meta-analysis of outcomes with one-shot tract dilatation versus serial tract dilatation for PCNL. The outcomes analyzed were (A) postoperative decrease in hemoglobin level, (B) transfusion rate, (C) complication rate, and (D) length of postoperative hospital stay.

Fig. S1 Sensitivity analysis of access time with the aforementioned study excluded.

Fig. S2 Sensitivity analysis of the length of postoperative hospital stay with the aforementioned study excluded.

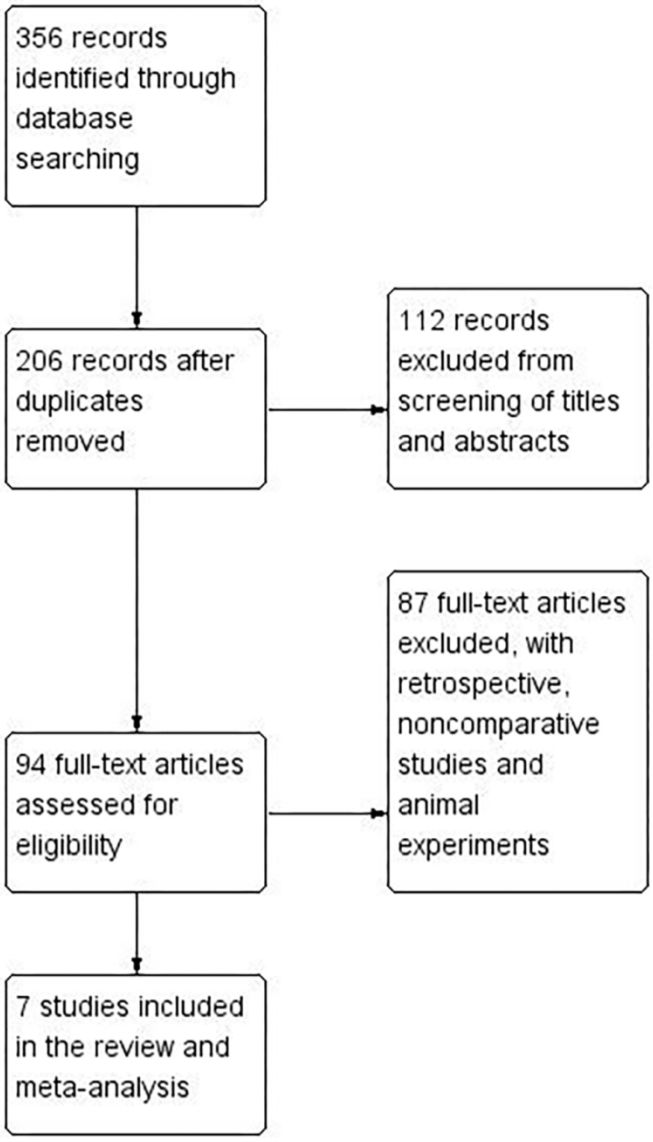

Fig. 1 Flowchart of study selection.

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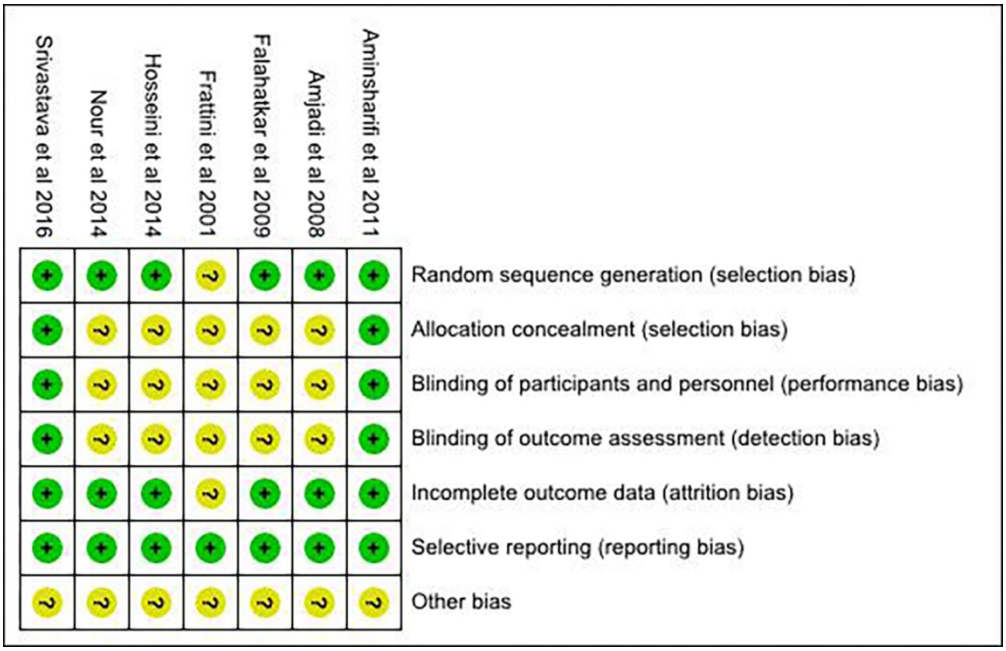

Fig. 2 Risk of bias summary: judgments about each risk of bias item for each included study.

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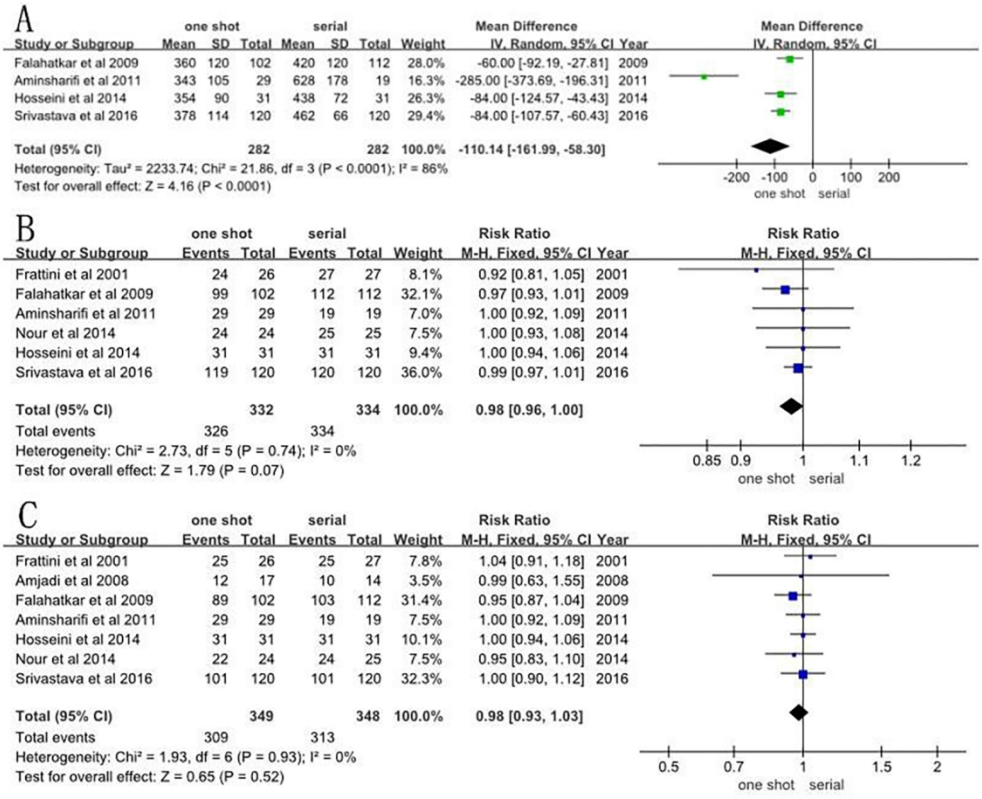

Fig. 3 Forest plots illustrating the meta-analysis of outcomes with one-shot tract dilatation versus serial tract dilatation for PCNL. The outcomes analyzed were (A) access time, (B) successful dilation rate, and (C) stone-free rate.

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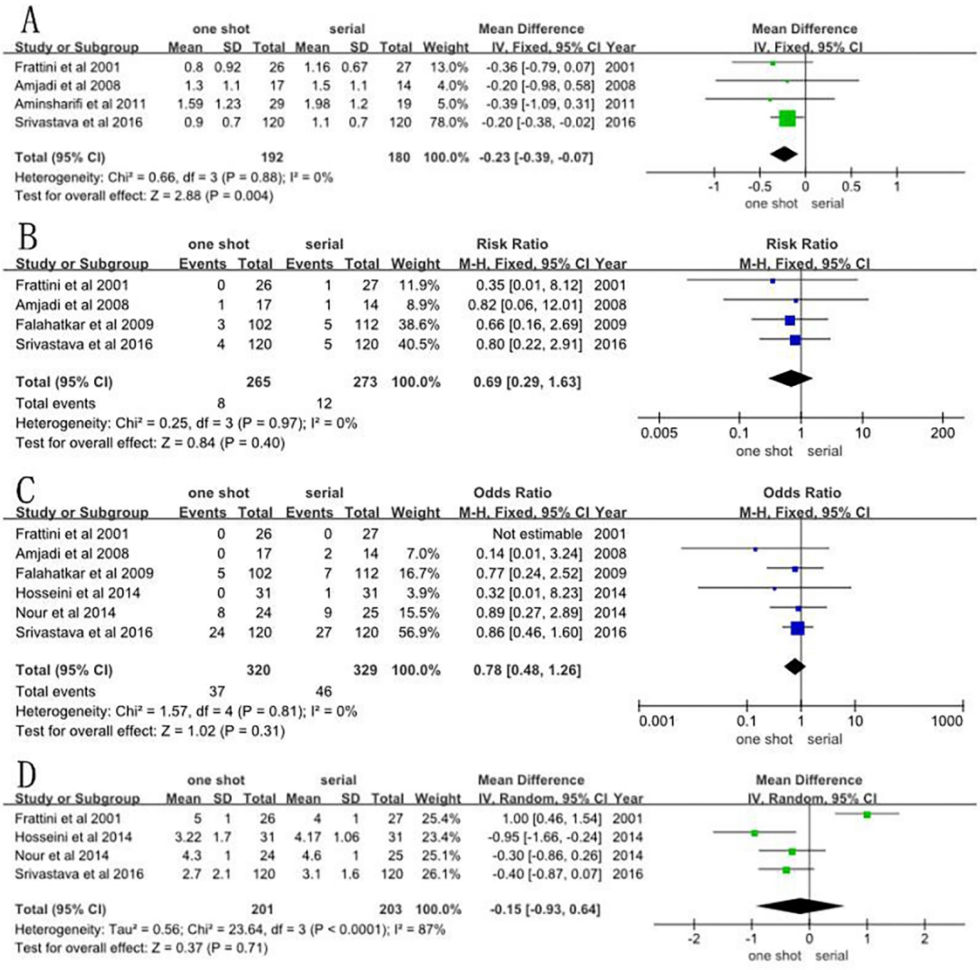

Fig. 4 Forest plots illustrating the meta-analysis of outcomes with one-shot tract dilatation versus serial tract dilatation for PCNL. The outcomes analyzed were (A) postoperative decrease in hemoglobin level, (B) transfusion rate, (C) complication rate, and (D) length of postoperative hospital stay.

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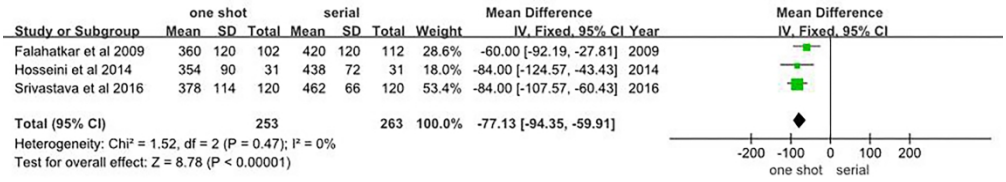

Fig. S1 Sensitivity analysis of access time with the aforementioned study excluded.

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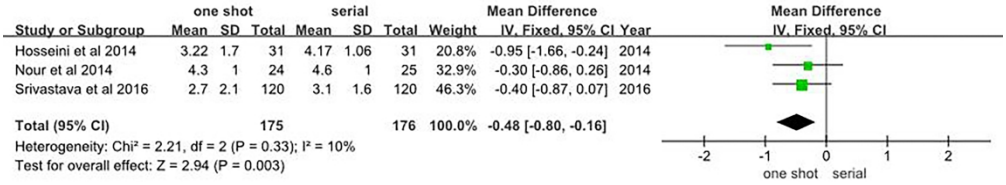

Fig. S2 Sensitivity analysis of the length of postoperative hospital stay with the aforementioned study excluded.

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One-shot dilation versus serial dilation technique for access in percutaneous nephrolithotomy: a systematic review and meta-analysis

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Abstract:

Objective The purpose of this study was to systematically review the outcomes of one-shot dilation (OSD) and serial tract dilation for percutaneous nephrolithotomy (PCNL). **Methods** A systematic review and meta-analysis was conducted. Randomized clinical trials (RCTs) that were included in the study were identified from EMBASE, MEDLINE, and the Cochrane Central Register of Controlled Trials. The last date of the search was April 30, 2018. Summary effects were calculated as risk ratios (RRs) with 95% confidence interval (CIs) or mean differences (MDs) with 95% CIs. The endpoints included access time, fluoroscopy time, successful dilation rate, stone-free rate, postoperative decrease in hemoglobin levels, transfusion rate, rate of complications, and length of postoperative hospital stay. **Results** A total of 7 RCTs were included in the study, and clinical data were reported for 697 patients. For overall access time, OSD groups were about 110 seconds shorter than serial dilation groups (MD, -110.14; 95% CI, -161.99 to -58.30; $P < 0.0001$). The fluoroscopy time was shorter with OSD in all RCTs. In addition, there was about 0.23g/dl less of a decrease in postoperative hemoglobin levels in patients in the OSD group than in those in the serial dilation group (MD, -0.23; 95% CI, -0.39 to -0.07; $P = 0.004$). There were no associations among successful dilation rate, stone-free rate, transfusion rate, complication rate or the method of tract dilation. **Conclusion** OSD is a safe and efficacious tract dilation technique that can reduce the access time, fluoroscopy time, and postoperative decreases in hemoglobin levels. There was no difference in the successful dilation rate, stone-free rate, transfusion rate, or rate of complications between OSD and serial dilation. A difference in the length of postoperative hospital stay was uncertain. OSD may be a better method for tract creation for PCNL.

Keywords: percutaneous nephrolithotomy, tract dilatation, one-shot dilation, meta-analysis

Abbreviations: AMD, Amplatz dilator; ALD, Alken telescoping dilator; MTD, Metal telescopic dilators; OSD, One-shot dilatation; NR, Not reported; PCNL, Percutaneous nephrolithotomy; RR, Risk ratio; MD, Mean difference; CI, Confidence interval; RCTs, Randomized controlled trials

Strengths and limitations of this study

This meta-analysis and systematic review was performed via a strict literature search. It was the updated meta-analysis to systematically review the outcomes of one-shot dilation (OSD) and serial tract dilation for percutaneous nephrolithotomy (PCNL).

The number of studies considered in the final meta-analysis was 7 and some small sample size limited the potential analyses.

Despite a systematic search strategy, the article language was restricted to English which may result in language bias.

These limitations notwithstanding, the research can guide the choice of access creation in PCNL.

Introduction

With the development of minimally invasive treatment of urinary calculi, percutaneous nephrolithotomy (PCNL) has become one of the main treatments for large kidney and upper ureteral stones.[1] To our best of knowledge, One of the most fundamental steps of PCNL surgery is to establish safe and effective access. However,

complications in this process such as failure of tract dilation, hemorrhage, and perforation of the renal parenchyma or collecting system were not uncommon.[2] Consequently, it is especially important to find a simple, effective, and safe tract dilation method in our clinical work. Currently, the primary dilation methods of access creation in PCNL can be classified as one-shot dilation (OSD) and serial dilation. Whereas, the current evidence regarding the efficacy and safety of these two methods were still controversial. In recent years, more and more studies showed that OSD was associated with more advantageous than serial dilation, which attracted the attention of urologists a lot. To further compare the safety and efficacy of these two methods, we conducted an updated systematic review and meta-analysis of previous randomized controlled trials (RCTs) comparing the outcomes of these two tract dilation methods for PCNL.

Methods

Patient and Public Involvement statement

This study was a systematic review and meta-analysis. Ethics committee approval was not necessary because all the data was carefully extracted from existing literature, and this article was not involving handling of individual patient data. In addition, no patients and or public were involved.

Literature search

To assess the clinical efficacy and safety of OSD and serial dilation technique for PCNL, a comprehensive literature search was performed using EMBASE, MEDLINE, and the Cochrane Central Register of Controlled Trials in April 30, 2018. The following MeSH terms and free text words were used: percutaneous nephrolithotomy, PCNL, tract dilation, one-

shot, one-step, sequential, serial. These search terms were used singly and combination. The following search strategy was adopted for each database: ("percutaneous nephrolithotomy"[Mesh] OR "PCNL") AND ("tract dilatation"[Mesh] OR "tract dilation" OR "access creation") AND ("one-shot "[Mesh] OR " one-step" OR " single-step" OR " one-stage" OR " gradual" OR " sequential" OR " serial") (**File. S1**). For the literature selection, the search strategy was applied based upon the Preferred Reporting Items for Systematic Reviews and Meta-analysis statement.[3] **Fig. 1** showed the process of identifying RCTs.

Inclusion criteria and study outcomes

The following criteria are included: (1) All prospective RCTs of comparing OSD and serial dilation for PCNL in any age and gender; (2) All patients were in good general condition before surgery and had no coagulopathy; (3) The article language was restricted to English and full text or related data can be obtained in the included studies; Two authors independently reviewed the titles and abstracts, and differences were discussed with a third author to reach an agreement. The primary outcomes included access time, fluoroscopy time, successful dilation rate, and postoperative decreases in hemoglobin levels. The secondary outcomes were transfusion rate, stone-free rate, complication rate, and length of postoperative hospital stay.

Data extraction and quality assessment

Two authors independently extracted the demographic, quality and results data by reading the full-text articles. Data were extracted from RCTs that met the inclusion criteria. If there were differences in the same research report, the latest full report was used. Any differences in data extraction were resolved by discussion and consultation

with senior authors. In addition, we evaluated the methodological quality of the trials according to the methods recommended by the Cochrane Collaboration.[4]

Data analysis

We used Review Manager for statistical analysis (RevMan, Version 5.3; Cochrane Collaboration, Copenhagen, Denmark). For dichotomous data, risk ratios (RRs) were used to evaluate the incidence of events, and the results were reported with 95% confidence intervals (CIs). For continuous data, mean difference (MD) with 95% CI was used. Cochrane's *Q* and I^2 statistics were calculated to assess the heterogeneity. When I^2<50%, heterogeneity was considered to be low. When 50% ⩽ I^2 <75%, there was moderate heterogeneity. When I^2 ⩾75%, high heterogeneity was considered. When there was low heterogeneity(I^2 <50%), a fixed-effect meta-analysis was used in conjunction with the study.[5] If there was significant heterogeneity（50%⩽I^2<75% or I^2 ⩾75%）, the result of the random-effects meta-analysis was used and we deleted the study one by one to determine source of significant heterogeneity and analyzed the causes of significant heterogeneity in detail. Otherwise, only a systematic review was performed. P<0.05 was considered statistically significant.

Results

Based on the search strategies and selection criteria, initial literature searches identified 356 studies across all databases. We eventually included 7 RCTs comparing the outcomes of OSD and serial dilation for PCNL in this review.[6-12] **Table 1** showed the basic characteristics of these studies. Several studies were described using only one abstract, but the results were not presented in a usable way. The authors declined to provide more

information, so these articles were not included in the results. In all studies, the groups were similar in stone location, size, and shape, and no flexible uretroscopy was used. Only single tract was used in all included studies.

Table. 1 Studies of characteristics of machine one-shot dilation VS serial dilation.

			Cases (N)		Gender (M/F)		Age (Y)		Stone size (cm)		Staghorn%		Type and size of dilator		Size of access sheath	
Authors	Year	Institution location	One-shot	Serial	One-shot	Serial	One-shot	Serial	One-shot	Serial	One-shot	Serial	One-shot	Serial	One-shot	Serial
Frattini et al[12]	2001	Italy	26	27	15/12	17/9	59	54	2.3±0.7	2.9±0.9	NR	NR	AMD 25/30F	ALD 10 to 30F	34F	34F
Amjadi et al[11]	2008	Iran	17	14	10/7	12/2	42	44	3.7±1.0	3.2±1.1	7(41%)	4(29%)	AMD 27F	ALD 12 to 27F	28F	28F
Falahatkar et al[10]	2009	Iran	102	112	56/46	62/50	57	51	3.9±1.6	3.4±1.2	NR	NR	AMD 28F	MTD 10 to 28F	30F	30F
Aminsharifi et al[9]	2011	Iran	29	19	19/10	9/10	44.1	42.5	2.7±1.0	3.7±1.3	6 (20.7%)	5 (26.3%)	AMD 28F	ALD 10 to28F	30F	30F
Nour et al[8]	2014	Egypt	24	25	17/7	16/9	43.8	38.2	3.7±7.2	30.2±6.9	NR	NR	AMD 30F	ALD 10 to 30F	NR	NR
Hosseini et al[7]	2014	Iran	31	31	22/9	18/13	3.7	3.7	2.0±0.35	1.7±0.4	NR	NR	AMD 24/26F	ALD 10 to 24/26F	24F or 26F	24F or 26F
Srivastava et al[6]	2017	India	120	120	59/61	62/58	38.9	40.1	NR	NR	34(28.3%)	33(27.5%)	AMD 28F	ALD 12 to 28F	30F	30F

M, Male; F, Female; AMD, Amplatz dilator; ALD, Alken telescoping dilator; MTD, Metal telescopic dilators; NR, Not reported

Quality of the included trials

The overall quality of the included trials was acceptable, although there were some deficiencies in the reporting of methods in some trials. **Fig. 2** illustrates the risk of a bias summary. Random sequence generation was adequate in six trials and unclear in the remaining one. Allocation concealment was judged to be adequate to minimize selection bias in two trials and unclear in four, inadequate in one. Blinding of participants and personnel was judged to be adequate to prevent performance bias in two trials and unclear in four, inadequate in one. Blinding of outcome assessment was judged to be adequate to prevent detection bias in two trials and unclear in five. The quality of outcome data reporting was adequate in six trials and unclear in one. No selective reporting of outcomes were observed. Other bias was classified as unclear in two, inadequate in five.

Access time and fluoroscopy time

The reported access time varied between the included RCTs.[6, 7, 9, 10] Meta-analysis showed that the access time in OSD group was about 110 seconds shorter (random-effects analysis: MD, -110.14; 95% CI, -161.99 to -58.30; $P < 0.0001$) **(Fig. 3A**). Significant heterogeneity was observed ($Q = 21.86$, $P < 0.0001$, $I^2 = 86\%$).

A sensitivity analysis was performed after Aminisharifi's study[9] was removed from the analysis. Meta-analysis of this subgroup was supportive of the overall analysis (fixed-effects analysis: MD, -77.13; 95% CI, -94.35 to -59.91; $P < 0.00001$) (**Fig. S1**). There was no significant heterogeneity in this subgroup ($Q = 1.52$, $P = 0.47$, $I^2 = 0\%$).

Seven trials reported data regarding fluoroscopy time.[6-12] All of the trials showed that OSD had significantly decreased fluoroscopy time, compared with serial tract dilation[6-12]. Due to the significant heterogeneity among the studies and failure to analyze the source of heterogeneity, meta-analysis was not performed.

Successful dilation rate and stone-free rate

Six trials reported successful dilation rates.[6-11] None of the RCTs found significant differences between OSD and serial tract dilatation. The results of the meta-analysis showed that the OSD had a slightly lower successful dilation rate than serial tract dilation. However, there was no statistical significance (fixed-effects analysis: RR, 0.98; 95% CI, 0.96 to 1.00; $P = 0.07$) **(Fig. 3B**). There was no significant heterogeneity ($Q = 2.73$, $P = 0.74$, $I^2 = 0\%$).

Seven trials reported stone-free rates.[6-12] None of them found significant differences between OSD and serial tract dilation. The overall stone-free rate was no different between OSD and serial tract dilation (fixed-effects analysis: RR, 0.98; 95% CI, 0.93 to 1.03; $P = 0.52$) (**Fig. 3C**). Heterogeneity was not observed ($Q = 1.93$, $P = 0.93$, $I^2 = 0\%$).

Decreases in hemoglobin levels and transfusion rate

Four RCTs recorded postoperative decreases in hemoglobin levels.[6, 9, 11, 12] There was less of a decrease in hemoglobin levels with OSD than with serial tract dilation in two RCTs but not in another. The results of the meta-analysis showed that OSD significantly reduced hemoglobin loss compared with serial tract dilation (MD, -0.23; 95% CI, -0.39 to -0.07; $P = 0.004$) (**Fig. 4A**). There was no heterogeneity ($Q = 0.66$, $P =$

0.88, I^2 = 0%).

Four trials reported transfusion rates.[6, 10-12] Transfusion rates varied between the included studies. No significant difference were found in any trial. Meta-analysis showed that the RR of the successful dilation rate was similar with OSD and with serial tract dilation (fixed-effects analysis: RR, 0.69; 95% CI, 0.29 to 1.63; *P* = 0.40) **(Fig. 4B**). No significant heterogeneity was observed(Q = 0.25, *P* = 0.97, I^2 = 0%).

Complication rates and length of postoperative hospital stay

Six RCTs provided complication rates.[6-8, 10-12] These RCTs found no relationship between the method of tract dilation and complication rates. Meta-analysis showed that the overall rate of complications was lower in the OSD group than in the serial tract dilation group (fixed-effects analysis: RR, 0.82; 95% CI, 0.56 to 1.20; *P* = 0.31) (**Fig. 4C**). Heterogeneity was not observed (*Q* = 1.63, *P* = 0.80, I^2 = 0%).

Four RCTs provided the length of postoperative hospital stay.[6-8, 10-12] One reported that serial tract dilation significantly reduced the length of postoperative hospital stay versus OSD.[12] Two studies found that OSD was more effective than serial tract dilation in decreasing the length of postoperative hospital stay.[7-8] No significant difference was found in one trial.[6] Meta-analysis showed that the RR of postoperative hospital stay was less with OSD than with serial tract dilation, but without statistical significance. (random-effects analysis: MD, -0.15; 95% CI, -0.93 to 0.64; *P* = 0.71) **(Fig. 4D**). Significant heterogeneity was observed (*Q* = 23.64, *P* < 0.0001, I^2 = 87%).

A sensitivity analysis was conducted after excluding Frattini's study.[12] However, meta-analysis of this subgroup did not support the overall analysis (fixed-effects

analysis: MD, -0.48; 95% CI, -0.80 to -0.16; $P = 0.003$) (**Fig. S2**). There was no significant heterogeneity in this subgroup (Q = 2.21, P = 0.33, I^2=0%).

Discussion

PCNL is the main treatment for large and complex kidney stones. The creation of a nephrostomy tract is one of the most basic steps in PCNL. This systematic review of seven RCTs including 697 patients has examined the evidence for the use of OSD versus serial tract dilation to create access for PCNL. The RCTs showed a statistically significant reduction in access time and fluoroscopy time with OSD but no difference between OSD and serial tract dilatation in terms of successful dilation rate or transfusion rate. These results are consistent with a previous systematic review performed in 2013.[13, 14] In addition, there was no difference in the stone-free rate or complication rate. However, there was less of a decrease in postoperative hemoglobin levels with OSD than with serial tract dilation, which was inconsistent with the results of the previous meta-analysis.[14] The difference was mainly due to an increase in the sample size.

For access time, the results of the sensitivity analysis did not change when a study causing significant heterogeneity was deleted.[9] Possible causes of heterogeneity included small sample size and surgeon's experience in this study. OSD involving a single dilation of the tract with a 25- or 30-F dilator is simple and does not require gradual tract dilation.[12] It saves access time and X-ray exposure time for tract creation, thus reducing the operative time and decreasing the risk of radiation damage to patients and operators. In addition, simple surgical procedures make it easier for surgeons to master the technique.

To our knowledge, successful dilation and stone-free rates are important factors that influence the effectiveness of tract dilation techniques. According to our analysis, the successful dilation rate and stone-free rate of OSD group were slightly lower than the serial group (98.2 vs 100% and 88.5 vs 89.9% respectively), however, our meta-analysis results did not find significant differences regarding the successful dilation rate or the stone-free rate between these two methods. Factors influencing the successful dilation rate may be related to the patient's body mass index (BMI), a previous history of kidney surgery, and the surgeon's experience.

The meta-analysis showed that the postoperative decrease in hemoglobin levels was less in patients who underwent OSD than in those who underwent serial dilation. The difference was statistically significant. Kessaris et al[15] found that the amount of intraoperative blood loss caused by the tract dilation technique accounted for half of the total blood loss. The correct puncture path and appropriate tract dilation methods were key decisive factors that determined the amount of intraoperative blood loss. The OSD method may effectively lessen postoperative decreases in hemoglobin levels by reducing the amount of bleeding during surgery. However, the meta-analysis did not find that one particular tract dilation method significantly reduced the transfusion rates of patients. A possible reason is that the sample size of the included studies was not enough to detect differences between these two methods. In addition, more high-quality RCTs are required for further study.

In this study, the overall rate of complication was 12.8% in all patients, with 11.6% in the OSD group and 14.0% in the serial dilation group. The main complications included postoperative urinary tract infections, urine leakage, hemorrhage,

hematoma formation and postoperative fever. The difference in complication rates was not statistically significant between the OSD group and the serial dilation group.

The results of the meta-analysis did not show that the OSD technique could significantly reduce the length of postoperative hospital stay. However, after deleting the study published by Frattini et al[12], we found that the statistical results changed significantly. The results showed that OSD was more conducive to reducing the length of postoperative hospital stay than serial dilation. The publication date may be a main source of heterogeneity. In 2001， OSD was a novel method to dilate the nephrostomy Access for PCNL. Due to lack of surgical experience, OSD might cause more parenchymal damage than the serial dilation technique. This may prolonged the patient's recovery time. With the maturity of the OSD technique, the damage was reduced, thereby shortening the hospital stay. More high-quality RCTs are required for further study.

It should be highlighted that an RCT involving preschool children was included in this systematic review. The results of the study showed that the access and fluoroscopy times in the OSD group were less than those in the serial dilation group. The difference was statistically significant. These findings basically consistent with the results of RCTs involving adults. In addition, the OSD technique significantly shortened the length of postoperative hospital stay. This study indicated that the OSD method was also safe and effective for preschool children.

Some studies have demonstrated that the OSD technique is equally safe and effective for patients with a history of open surgery.[11, 16] In addition, only one dilator is needed to establish a tract with the OSD technique. The price of OSD is much lower

than that of the serial dilation method, which reduces the economic burden on patients.[12] Tonshal S et al[17] reported that the cost of OSD technique is significantly lower than that of the Amplatz sequential dilation technique. Two recent studies have shown that OSD can significantly shorten the length of hospital stay,[7-8] which could also reduce the cost of hospitalization for patients. Reduction in treatment costs can optimize the allocation of medical resources. It is vital to evaluate the cost effectiveness of the two tract dilation techniques in clinical practice, especially for developing countries.

Limitations of this study

However, this study still had some limitations. Firstly, only seven studies were included in this analysis, and the methodological quality of several studies with small sample size was poor or uncertain. All these factors might have led to heterogeneity. secondly, the experience of the surgeons has not been considered which might add to bias. Thirdly, due to inadequate number of studies included, we did not perform a funnel plots for further analysis of publication bias. Despite a systematic search strategy, the article language was restricted to English which may result in language bias.

Conclusion

The results of this meta-analysis and systematic review suggest that the OSD is a safe and efficacious tract dilation technique that can reduce the access time, fluoroscopy time, and postoperative decreases in hemoglobin levels. There were no differences in the successful dilation rate, stone-free rate, transfusion rate, or complication rate

between the two techniques. A difference in the length of postoperative hospital stay between the two techniques is uncertain. OSD may be a better method to establish tracts for PCNL. More high-quality RCTs are needed for further study.

Authors' contributions

PXP, SCL, and GZ conceived and designed the experiments. YHH and LHZ extracted the data. PXP, ZSD and SCL analyzed the data. ZSD, YHH, XMW and LHZ contributed materials/analysis tools. PXP and SCL wrote the paper. GZ critically revised the report.

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Disclaimer

The contents of the present study are solely the responsibility of the author. The funders had no role in study design, data collection and analysis, decision to publish, or preparation of the manuscript.

Competing interests

The authors declare that no conflicts of interest exist.

Data sharing statement

Datasets used and/or analyzed in the present study are available from the

corresponding author on reasonable request.

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Table File

Table. 1 Studies of characteristics of machine one-shot dilation VS serial dilation.

Figure Files

Fig. 1 Flowchart of study selection.

Fig. 2 Risk of bias summary: judgments about each risk of bias item for each included study.

Fig. 3 Forest plots illustrating the meta-analysis of outcomes with one-shot tract dilation versus serial tract dilation for PCNL. The outcomes analyzed were (A) access time, (B) successful dilation rate, and (C) stone-free rate.

Fig. 4 Forest plots illustrating the meta-analysis of outcomes with one-shot tract dilation versus serial tract dilation for PCNL. The outcomes analyzed were (A) postoperative decrease in hemoglobin level, (B) transfusion rate, (C) complication rate, and (D) length of postoperative hospital stay.

Fig. S1 Sensitivity analysis of access time with the aforementioned study excluded.

Fig. S2 Sensitivity analysis of the length of postoperative hospital stay with the aforementioned study excluded.

Supplementary Files

File. S1 Electronic search strategy in EMBASE.

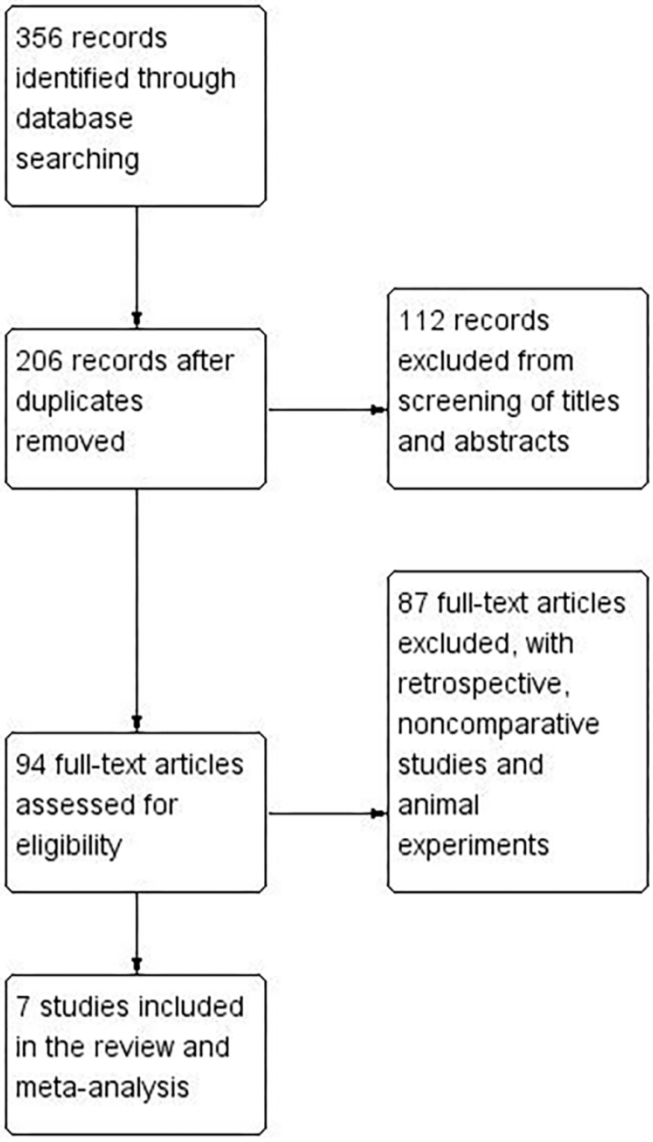

Fig. 1 Flowchart of study selection.

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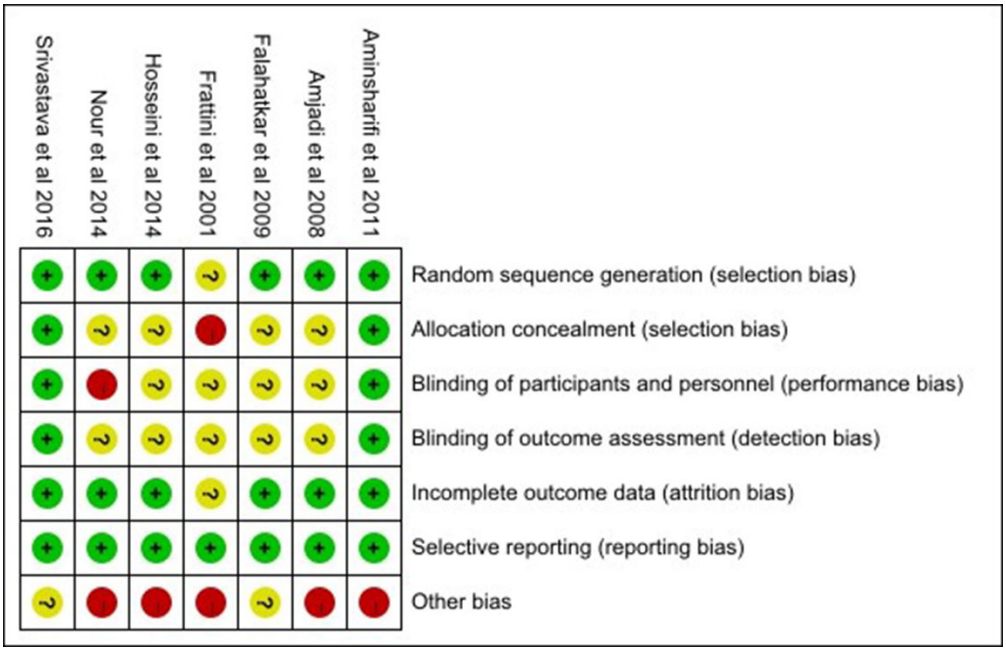

Fig. 2 Risk of bias summary: judgments about each risk of bias item for each included study.

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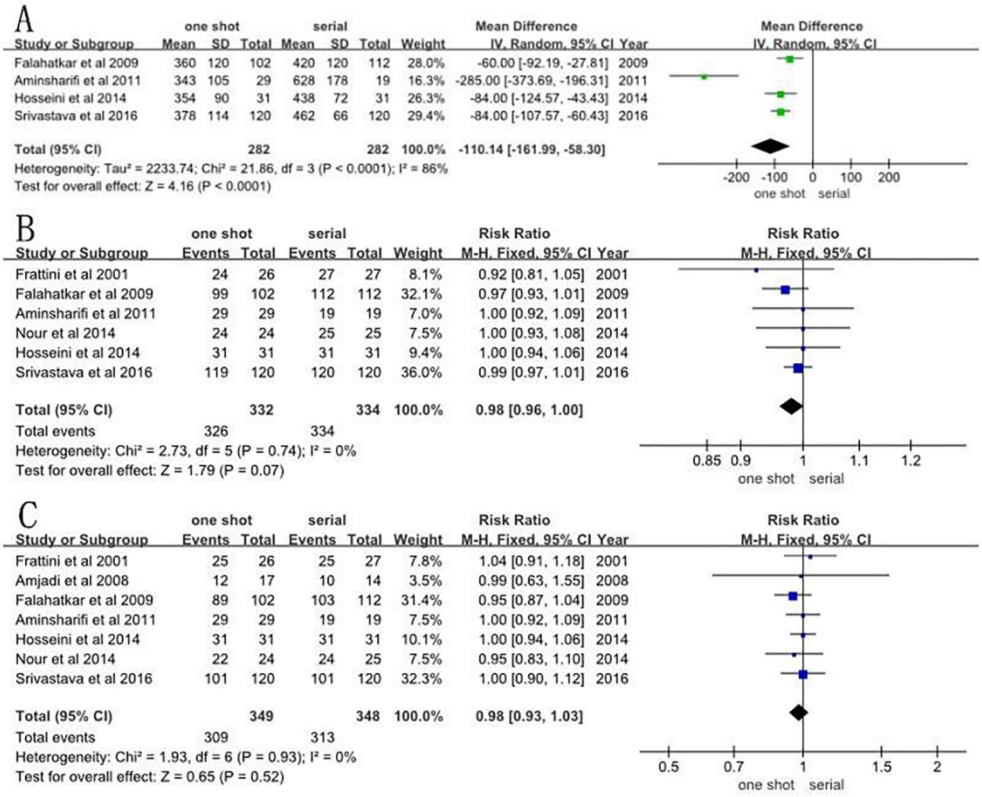

Fig. 3 Forest plots illustrating the meta-analysis of outcomes with one-shot tract dilation versus serial tract dilation for PCNL. The outcomes analyzed were (A) access time, (B) successful dilation rate, and (C) stone-free rate.

144x116mm (300 x 300 DPI)

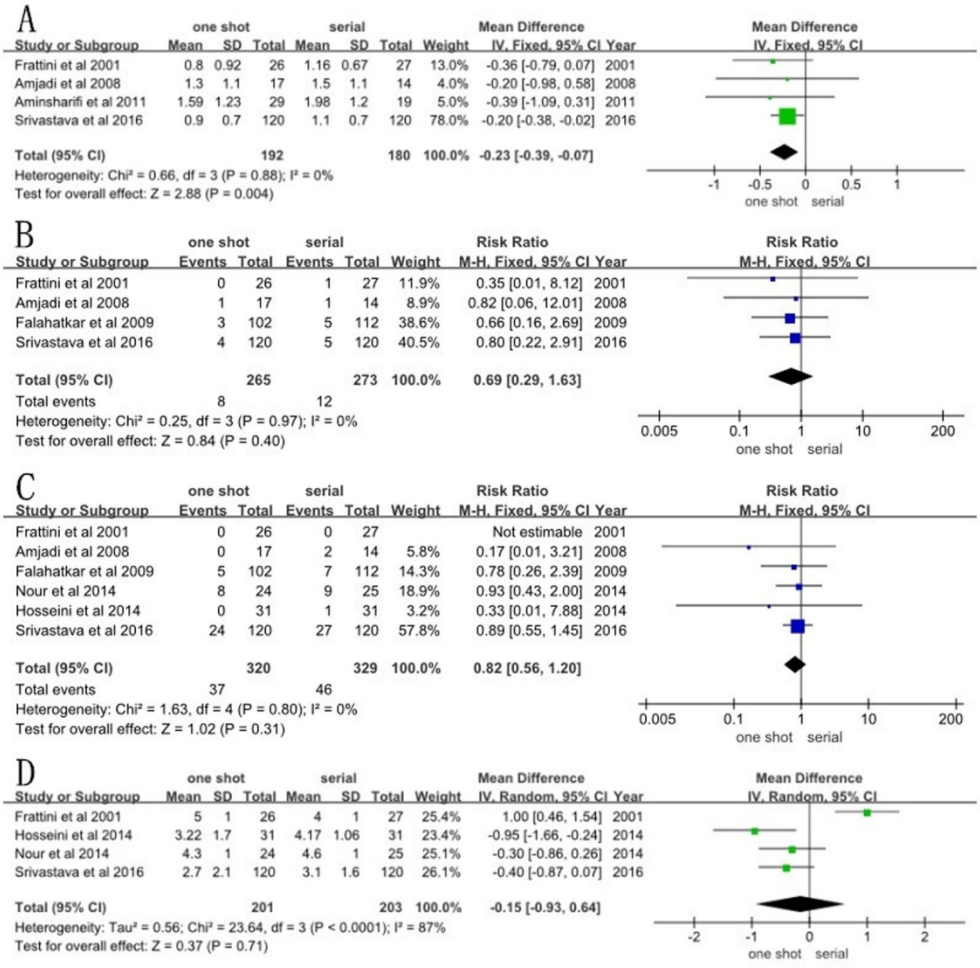

Fig. 4 Forest plots illustrating the meta-analysis of outcomes with one-shot tract dilation versus serial tract dilation for PCNL. The outcomes analyzed were (A) postoperative decrease in hemoglobin level, (B) transfusion rate, (C) complication rate, and (D) length of postoperative hospital stay.

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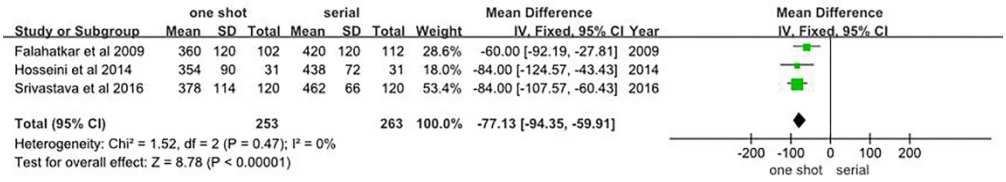

Fig. S1 Sensitivity analysis of access time with the aforementioned study excluded.

488x90mm (300 x 300 DPI)

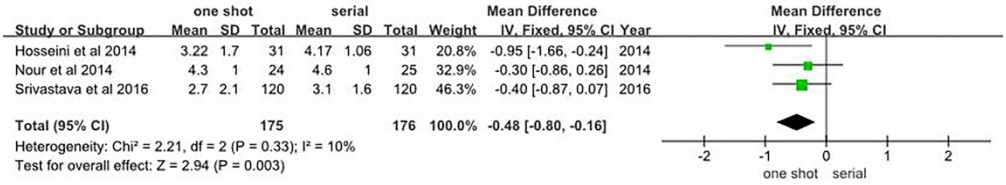

Fig. S2 Sensitivity analysis of the length of postoperative hospital stay with the aforementioned study excluded.

471x90mm (300 x 300 DPI)

One-shot dilation versus serial dilation technique for access in percutaneous nephrolithotomy: a systematic review and meta-analysis

Search strategy in EMBASE.

The last quest was updated on April 30, 2018.

#1 Search “percutaneous nephrolithotomy” [Mesh]

#2 Search PCNL

#3 Search (#1 or #2)

#4 Search "tract dilatation" [Mesh]

#5 Search tract dilation

#6 Search access creation

#7 Search (#4 or #5 or #6)

#8 Search "one-shot" [Mesh]

#9 Search one-step

#10 Search single-step

#11 Search one-step

#12 Search one-stage

#13 Search gradual

#14 Search sequential

#15 Search serial

#16 Search (#8 or #9 or #10 or #11or #12 or #13 or #14 or #15)

#17 Search (#3 and #7 and #16)

PRISMA 2009 Checklist

Section/topic	#	Checklist item	Reported on page #
TITLE			
Title	1	Identify the report as a systematic review, meta-analysis, or both.	1
ABSTRACT			
Structured summary	2	Provide a structured summary including, as applicable: background; objectives; data sources; study eligibility criteria, participants, and interventions; study appraisal and synthesis methods; results; limitations; conclusions and implications of key findings; systematic review registration number.	3
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of what is already known.	4-5
Objectives	4	Provide an explicit statement of questions being addressed with reference to participants, interventions, comparisons, outcomes, and study design (PICOS).	5
METHODS			
Protocol and registration	5	Indicate if a review protocol exists, if and where it can be accessed (e.g., Web address), and, if available, provide registration information including registration number.	None
Eligibility criteria	6	Specify study characteristics (e.g., PICOS, length of follow-up) and report characteristics (e.g., years considered, language, publication status) used as criteria for eligibility, giving rationale.	5-6
Information sources	7	Describe all information sources (e.g., databases with dates of coverage, contact with study authors to identify additional studies) in the search and date last searched.	5-6
Search	8	Present full electronic search strategy for at least one database, including any limits used, such that it could be repeated.	5-6
Study selection	9	State the process for selecting studies (i.e., screening, eligibility, included in systematic review, and, if applicable, included in the meta-analysis).	6
Data collection process	10	Describe method of data extraction from reports (e.g., piloted forms, independently, in duplicate) and any processes for obtaining and confirming data from investigators.	6
Data items	11	List and define all variables for which data were sought (e.g., PICOS, funding sources) and any assumptions and simplifications made.	6-7
Risk of bias in individual studies	12	Describe methods used for assessing risk of bias of individual studies (including specification of whether this was done at the study or outcome level), and how this information is to be used in any data synthesis.	7
Summary measures	13	State the principal summary measures (e.g., risk ratio, difference in means).	7
Synthesis of results	14	Describe the methods of handling data and combining results of studies, if done, including measures of consistency (e.g., I^2) for each meta-analysis.	7

PRISMA 2009 Checklist

Section/topic	#	Checklist item	Reported on page #
Risk of bias across studies	15	Specify any assessment of risk of bias that may affect the cumulative evidence (e.g., publication bias, selective reporting within studies).	7
Additional analyses	16	Describe methods of additional analyses (e.g., sensitivity or subgroup analyses, meta-regression), if done, indicating which were pre-specified.	7
RESULTS			
Study selection	17	Give numbers of studies screened, assessed for eligibility, and included in the review, with reasons for exclusions at each stage, ideally with a flow diagram.	7-8
Study characteristics	18	For each study, present characteristics for which data were extracted (e.g., study size, PICOS, follow-up period) and provide the citations.	9
Risk of bias within studies	19	Present data on risk of bias of each study and, if available, any outcome level assessment (see item 12).	10
Results of individual studies	20	For all outcomes considered (benefits or harms), present, for each study: (a) simple summary data for each intervention group (b) effect estimates and confidence intervals, ideally with a forest plot.	10-13
Synthesis of results	21	Present results of each meta-analysis done, including confidence intervals and measures of consistency.	10-13
Risk of bias across studies	22	Present results of any assessment of risk of bias across studies (see Item 15).	10-13
Additional analysis	23	Give results of additional analyses, if done (e.g., sensitivity or subgroup analyses, meta-regression [see Item 16]).	10，12-13
DISCUSSION			
Summary of evidence	24	Summarize the main findings including the strength of evidence for each main outcome; consider their relevance to key groups (e.g., healthcare providers, users, and policy makers).	13-16
Limitations	25	Discuss limitations at study and outcome level (e.g., risk of bias), and at review-level (e.g., incomplete retrieval of identified research, reporting bias).	16
Conclusions	26	Provide a general interpretation of the results in the context of other evidence, and implications for future research.	16-17
FUNDING			
Funding	27	Describe sources of funding for the systematic review and other support (e.g., supply of data); role of funders for the systematic review.	17

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Secondary Subject Heading:	Urology
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One-shot dilation versus serial dilation technique for access in percutaneous nephrolithotomy: a systematic review and meta-analysis

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Abstract

Objective The purpose of this study was to systematically review the outcomes of the use of one-shot dilation (OSD) and serial tract dilation for percutaneous nephrolithotomy (PCNL). **Methods** A systematic review and meta-analysis was conducted. The randomized controlled trials (RCTs) included in the study were identified from EMBASE, MEDLINE, and the Cochrane Central Register of Controlled Trials. The last search was performed on April 30, 2018. Summary effects were calculated as risk ratios (RRs) with 95% confidence intervals (CIs) or mean differences (MDs) with 95% CIs. The endpoints included access time, fluoroscopy time, successful dilation rate, stone-free rate, postoperative decrease in hemoglobin levels, transfusion rate, complication rate, and length of postoperative hospital stay. **Results** A total of 7 RCTs were included in the study, with clinical data reported for 697 patients. The overall access time was approximately 110 seconds shorter in the OSD group than in the serial dilation group (MD, -110.14; 95% CI, -161.99 to -58.30; *P*<0.0001). The fluoroscopy time was shorter with OSD in all RCTs. In addition, the decrease in postoperative hemoglobin levels was approximately 0.23 g/dl less in patients in the OSD group than in those in the serial dilation group (MD, -0.23; 95% CI, -0.39 to -0.07; *P*=0.004). No relationship was found between the successful dilation rate, stone-free rate, transfusion rate, or complication rate and the method of tract dilation. **Conclusion** OSD is a safe and efficacious tract dilation technique that can reduce the access time, fluoroscopy time, and postoperative decrease in hemoglobin level. No difference was found in the successful dilation rate, stone-free rate, transfusion rate, or rate of complications between the OSD and serial dilation groups. The difference in the length of postoperative hospital stay was uncertain. OSD may be a better method of tract

creation for PCNL.

Keywords: percutaneous nephrolithotomy, tract dilatation, one-shot dilation, meta-analysis

Abbreviations: AMD, Amplatz dilator; ALD, Alken telescoping dilator; MTD, Metal telescopic dilators; OSD, One-shot dilatation; NR, Not reported; PCNL, Percutaneous nephrolithotomy; RR, Risk ratio; MD, Mean difference; CI, Confidence interval; RCTs, Randomized controlled trials

Strengths and limitations of this study

This meta-analysis and systematic review was performed via a strict literature search. It was an updated meta-analysis to systematically review the outcomes of one-shot dilation (OSD) and serial tract dilation for percutaneous nephrolithotomy (PCNL).

Seven studies were considered in the final meta-analysis, and several studies with small sample sizes limited the potential analyses.

Although a systematic search strategy was used, the article language was restricted to English, which may have a resulted in language bias.

Due to a lack of sufficient data, an age-sex adjusted meta-analysis was not conducted.

Introduction

With the development of minimally invasive treatment of urinary calculi, percutaneous nephrolithotomy (PCNL) has become one of the main treatments for large kidney and upper ureteral stones.[1] One of the most fundamental steps of PCNL surgery is to establish safe and effective access. However, complications in this process such as tract

dilation failure, hemorrhage, and perforation of the renal parenchyma or collecting system are not uncommon.[2] Consequently, it is especially important to identify a simple, effective, and safe tract dilation method for clinical application. Currently, the primary dilation methods of access creation in PCNL can be classified as one-shot dilation (OSD) and serial dilation. Although the related systematic reviews were conducted in 2013, only four randomized controlled trials (RCTs) were included in the previous systematic reviews, and the comparison of the two tract dilation methods was not sufficiently comprehensive; therefore, additional RCTs are needed for verification. Currently, the evidence regarding the efficacy and safety of these two methods is still controversial. In recent years, an increasing number of studies have shown that OSD is associated with more advantages than serial dilation, which attracted much attention from urologists. To further compare the safety and efficacy of these two methods, we conducted an updated systematic review and meta-analysis of previous RCTs comparing the outcomes of these two tract dilation methods for PCNL.

Methods

Patient and public involvement statement

This study was a systematic review and meta-analysis. Ethics committee approval was not necessary because all data were carefully extracted from existing literature, and this article did not involve handling of individual patient data. In addition, neither patients nor the public were involved in the design and planning of the study.

Literature search

To assess the clinical efficacy and safety of OSD and the serial dilation technique for

PCNL, a comprehensive literature search was performed using EMBASE, MEDLINE, and the Cochrane Central Register of Controlled Trials on April 30, 2018. The following MeSH terms and free text words were used: percutaneous nephrolithotomy, PCNL, tract dilation, one-shot, one-step, sequential, and serial. These search terms were used alone and in combination. The following search strategy was adopted for each database: ("percutaneous nephrolithotomy"[Mesh] OR "PCNL") AND ("tract dilatation"[Mesh] OR "tract dilation" OR "access creation") AND ("one-shot"[Mesh] OR "one-step" OR "single-step" OR " one-stage" OR " gradual" OR "sequential" OR "serial") (**File S1**). For the study selection, the search strategy was applied based on the Preferred Reporting Items for Systematic Reviews and Meta-analysis statement.[3] **Fig. 1** shows the process of identifying RCTs.

Inclusion criteria and study outcomes

The following inclusion criteria were used: (1) all prospective RCTs compared OSD and serial dilation for PCNL in patients of any age and sex; (2) all patients were in good general condition before surgery and did not have coagulopathy; and (3) the article language was restricted to English, and full text or related data could be obtained from the studies. Two authors independently reviewed the titles and abstracts, and differences were discussed with a third author to reach an agreement. The primary outcomes included access time, fluoroscopy time, successful dilation rate, and postoperative decreases in hemoglobin levels. The secondary outcomes were transfusion rate, stone-free rate, complication rate, and length of postoperative hospital stay.

Data extraction and quality assessment

Two authors independently extracted the demographic, quality, and results data by reading the full-text articles. Data were extracted from the RCTs that met the inclusion criteria. If duplicate research reports were found, the most recent full report was used. Any discrepancies regarding data extraction were resolved by discussion and consultation with senior authors. In addition, we evaluated the methodological quality of the trials according to the methods recommended by the Cochrane Collaboration.[4]

Data analysis

We used Review Manager (RevMan, Version 5.3; Cochrane Collaboration, Copenhagen, Denmark) for the statistical analysis. For dichotomous data, risk ratios (RRs) were used to evaluate the incidence of events, and the results were reported with 95% confidence intervals (CIs). For continuous data, mean differences (MDs) with 95% CIs were used. Cochrane's Q and the I^2 statistic were calculated to assess the heterogeneity. When I^2<50%, heterogeneity was considered to be low. When 50%≤I^2<75%, heterogeneity was considered moderate. When I^2≥75%, heterogeneity was considered high. In cases of low heterogeneity (I^2<50%), a fixed-effect meta-analysis was used in conjunction with the study.[5] In cases of significant heterogeneity （50%≤I^2 <75% or I^2≥75%), a random-effects meta-analysis was used, and studies were individually removed to determine the source of significant heterogeneity. Then, the causes of significant heterogeneity were analyzed in detail. Otherwise, only a systematic review was performed. A value of P<0.05 was considered statistically significant.

Results

Based on the search strategies and selection criteria, initial literature searches

identified 356 studies across all databases. We eventually included 7 RCTs comparing the outcomes of OSD and serial dilation for PCNL in this review.[6-12] **Table 1** shows the basic characteristics of these studies. Several studies were described using only one abstract, but the results were not presented in a usable manner, and the authors declined to provide additional information; therefore, these articles were not included in the results. In all studies, the groups were similar regarding stone location, size, and shape, and flexible uretroscopy was not used in any studies. Only a single tract was used in all included studies.

Table. 1 Studies of the characteristics of mechanical one-shot dilation vs serial dilation.

			Cases (N)		Sex (M/F)		Age (y)		Stone size (cm)		Staghorn %		Type and size of dilator		Size of access sheath	
Authors	Year	Institution location	One-shot	Serial	One-shot	Serial	One-shot	Serial	One-shot	Serial	One-shot	Serial	One-shot	Serial	One-shot	Serial
Frattini et al[12]	2001	Italy	26	27	15/12	17/9	59	54	2.3±0.7	2.9±0.9	NR	NR	AMD 25/30F	ALD 10 to 30F	34F	34F
Amjadi et al[11]	2008	Iran	17	14	10/7	12/2	42	44	3.7±1.0	3.2±1.1	7 (41%)	4 (29%)	AMD 27F	ALD 12 to 27F	28F	28F
Falahatkar et al[10]	2009	Iran	102	112	56/46	62/50	57	51	3.9±1.6	3.4±1.2	NR	NR	AMD 28F	MTD 10 to 28F	30F	30F
Aminsharifi et al[9]	2011	Iran	29	19	19/10	9/10	44.1	42.5	2.7±1.0	3.7±1.3	6 (20.7%)	5 (26.3%)	AMD 28F	ALD 10 to 28F	30F	30F
Nour et al[8]	2014	Egypt	24	25	17/7	16/9	43.8	38.2	3.7±7.2	30.2±6.9	NR	NR	AMD 30F	ALD 10 to 30F	NR	NR
Hosseini et al[7]	2014	Iran	31	31	22/9	18/13	3.7	3.7	2.0±0.35	1.7±0.4	NR	NR	AMD 24/26F	ALD 10 to 24/26F	24F or 26F	24F or 26F
Srivastava et al[6]	2017	India	120	120	59/61	62/58	38.9	40.1	NR	NR	34 (28.3%)	33 (27.5%)	AMD 28F	ALD 12 to 28F	30F	30F

M, Male; F, Female; AMD, Amplatz dilator; ALD, Alken telescoping dilator; MTD, Metal telescopic dilators; NR, Not reported

Quality of the included trials

The overall quality of the included trials was acceptable, although there were some deficiencies in the reporting of methods in some trials. **Fig. 2** illustrates the risk of bias summary. Random sequence generation was adequate in six trials and unclear in the remaining trial. Allocation concealment was judged to be adequate to minimize selection bias in two trials, unclear in four trials, and inadequate in one trial. Blinding of participants and personnel was judged to be adequate to prevent performance bias in two trials, unclear in four trials, and inadequate in one trial. Blinding of outcome assessment was judged to be adequate to prevent detection bias in two trials and unclear in five trials. The quality of outcome data reporting was adequate in six trials and unclear in one trial. No selective reporting of outcomes was observed. Other bias was classified as unclear in two and inadequate in five trials.

Access time and fluoroscopy time

The reported access time varied among the included RCTs.[6, 7, 9, 10] The meta-analysis showed that the access time in the OSD group was approximately 110 seconds shorter than that in the serial dilation group (random-effects analysis: MD, -110.14; 95% CI, -161.99 to -58.30; P<0.0001) **(Fig. 3A**). However, significant heterogeneity was observed (Q=21.86, P<0.0001, I^2=86%).

A sensitivity analysis was performed after Aminisharifi's study[9] was removed from the analysis. Meta-analysis of this subgroup was supportive of the overall analysis (fixed-effects analysis: MD, -77.13; 95% CI, -94.35 to -59.91; P<0.00001) (**Fig. S1**). No significant heterogeneity was found in this subgroup (Q=1.52, P=0.47, I^2=0%).

Seven trials reported data regarding fluoroscopy time.[6-12] All of the trials showed that OSD was associated with significantly decreased fluoroscopy time compared to serial tract dilation.[6-12] Due to the significant heterogeneity among the studies and the failure to identify the source of heterogeneity, a meta-analysis was not performed.

Successful dilation rate and stone-free rate

Six trials reported successful dilation rates.[6-11] None of the RCTs found significant differences between OSD and serial tract dilatation. The results of the meta-analysis showed that OSD had a slightly lower successful dilation rate than serial tract dilation. However, no significant difference was found (fixed-effects analysis: RR, 0.98; 95% CI, 0.96 to 1.00; P=0.07) **(Fig. 3B**). No significant heterogeneity was observed (Q=2.73, P=0.74, I^2=0%).

Seven trials reported stone-free rates,[6-12] and none found significant differences between OSD and serial tract dilation. The overall stone-free rate was not different between OSD and serial tract dilation (fixed-effects analysis: RR, 0.98; 95% CI, 0.93 to 1.03; P=0.52) (**Fig. 3C**). Heterogeneity was not observed (Q=1.93, P=0.93, I^2=0%).

Decreases in hemoglobin levels and transfusion rate

Four RCTs recorded postoperative decreases in hemoglobin levels.[6, 9, 11, 12] The hemoglobin levels decreased less in the OSD group than in the serial tract dilation group in two RCTs, but no difference was found in another trial. The results of the meta-analysis showed that OSD significantly reduced hemoglobin decrease compared to serial tract dilation (MD, -0.23; 95% CI, -0.39 to -0.07; P=0.004) (**Fig. 4A**). No heterogeneity was observed (Q=0.66, P=0.88, I^2=0%).

Four trials reported transfusion rates.[6, 10-12] Transfusion rates varied among the included studies. No significant difference was found for any trial. Meta-analysis showed that the RR of successful dilation was similar for OSD and serial tract dilation (fixed-effects analysis: RR, 0.69; 95% CI, 0.29 to 1.63; *P*=0.40) **(Fig. 4B**). No significant heterogeneity was observed (Q=0.25, *P*=0.97, I^2=0%).

Complication rates and length of postoperative hospital stay

Six RCTs provided complication rates.[6-8, 10-12] These RCTs found no relationship between the method of tract dilation and complication rates. A meta-analysis showed that the overall rate of complications was lower in the OSD group than in the serial tract dilation group (fixed-effects analysis: RR, 0.82; 95% CI, 0.56 to 1.20; *P*=0.31) (**Fig. 4C**). Heterogeneity was not observed (*Q*=1.63, *P*=0.80, I^2=0%).

Four RCTs provided the length of postoperative hospital stay.[6-8, 12] One trial reported that serial tract dilation significantly reduced the length of the postoperative hospital stay vs OSD.[12] Two studies found that OSD was more effective than serial tract dilation in decreasing the length of postoperative hospital stay.[7-8] No significant difference was found in one trial.[6] The meta-analysis showed that the RR of postoperative hospital stay was lower with OSD than with serial tract dilation, but without statistical significance (random-effects analysis: MD, -0.15; 95% CI, -0.93 to 0.64; *P*=0.71) **(Fig. 4D**). Significant heterogeneity was observed (*Q*=23.64, *P*<0.0001, I^2 = 87%).

A sensitivity analysis was conducted after excluding Frattini's study.[12] However, the meta-analysis of this subgroup did not support the overall analysis (fixed-effects

analysis: MD, -0.48; 95% CI, -0.80 to -0.16; *P*=0.003) (**Fig. S2**). No significant heterogeneity was found in this subgroup (Q=2.21, P=0.33, I^2=0%).

Discussion

PCNL is the main treatment method for large and complex kidney stones. The creation of a nephrostomy tract is one of the most basic steps of PCNL. This systematic review of seven RCTs including 697 patients examined the evidence for the use of OSD vs serial tract dilation to create access for PCNL. The RCTs showed a statistically significant reduction in access time and fluoroscopy time with OSD but no difference between OSD and serial tract dilatation in terms of the successful dilation rate or transfusion rate. These results are consistent with a previous systematic review performed in 2013.[13, 14] In addition, no difference was observed in the stone-free rate or complication rate. However, postoperative hemoglobin levels decreased less with OSD than with serial tract dilation, which was inconsistent with the results of the previous meta-analysis.[14] This difference was mainly due to an increased sample size.

Regarding access time, the results of the sensitivity analysis did not change when a study responsible for significant heterogeneity was omitted.[9] The possible causes of heterogeneity included a small sample size and the surgeon's experience in this study. OSD involving a single dilation of the tract with a 25- or 30-F dilator is simple and does not require gradual tract dilation.[12] It saves access time and X-ray exposure during tract creation, thus reducing the operative time and decreasing the risk of radiation damage to patients and operators. In addition, the simple surgical procedures allow surgeons to easily master the technique.

In our experience, successful dilation and stone-free rates are important factors that influence the effectiveness of tract dilation techniques. According to our analysis, the successful dilation rate and stone-free rate of the OSD group were slightly lower than those of the serial group (98.2 vs 100% and 88.5 vs 89.9%, respectively); however, our meta-analysis results did not show significant differences regarding the successful dilation rate or the stone-free rate between these two methods. Factors that influence the successful dilation rate may be related to the patient's body mass index (BMI), a previous history of kidney surgery, and the surgeon's experience.

The meta-analysis showed that the postoperative hemoglobin levels decreased significantly less in patients who underwent OSD than in those who underwent serial dilation. Kessaris et al[15] found that the amount of intraoperative blood loss caused by the tract dilation technique accounted for half of the total blood loss. The correct puncture path and appropriate tract dilation methods were key decisive factors that determined the amount of intraoperative blood loss. The OSD method may effectively lessen postoperative decreases in hemoglobin levels by reducing the amount of bleeding during surgery. However, the meta-analysis did not find that one particular tract dilation method significantly reduced the transfusion rates of patients, possibly because the sample size of the included studies was not sufficient to detect differences between these two methods. In addition, more high-quality RCTs are required for further study.

In this study, the overall complication rate was 12.8% in all patients (11.6% in the OSD group and 14.0% in the serial dilation group). The main complications included postoperative urinary tract infections, urine leakage, hemorrhage, hematoma

formation, and postoperative fever. The difference in complication rates was not statistically significant between the OSD group and the serial dilation group.

The results of the meta-analysis did not show that the OSD technique could significantly reduce the length of the postoperative hospital stay. However, after omitting the study published by Frattini et al[12], we found that the statistical results were significantly changed. The results showed that OSD was more conducive to reducing the length of the postoperative hospital stay than serial dilation. The publication date may be the main source of heterogeneity. In 2001, OSD was a novel method used to dilate the nephrostomy access for PCNL. Due to lack of surgical experience, OSD might have caused more parenchymal damage than the serial dilation technique. This damage could prolong the patient's recovery time. With the maturity of the OSD technique, the damage was reduced, thereby shortening the hospital stay. More high-quality RCTs are required for further study.

The inclusion criteria of our systematic review specified inclusion of all prospective RCTs comparing the two methods for PCNL for patients of any age or sex; an RCT involving preschool children was also included in the analysis. The results of the study showed that the access and fluoroscopy times in the OSD group were significantly shorter than those in the serial dilation group. These findings are consistent with the results of RCTs involving adults. In addition, the OSD technique significantly shortened the length of the postoperative hospital stay. This study indicated that the OSD method was also safe and effective for preschool children.

It is likely that age and sex caused bias in this study. The age-sex adjusted RR or MD should have been reported in addition to our results. Use of an age-sex adjusted

RR or MD in this meta-analysis would have resulted in more appropriate interpretation of our results. However, not all of the 7 studies included in our meta-analysis conducted a multivariate analysis. Moreover, the authors of all trials were contacted to obtain the original data to facilitate an in-depth meta-analysis. However, no response was received. Therefore, it is impossible for us to report an age-sex adjusted RR or MD in our manuscript. We hope that further RCTs with detailed data will be available to confirm our conclusions.

Regarding the safety and effectiveness of the OSD technique, some studies have demonstrated that it is equivalent to the serial dilation method for patients with a history of open surgery.[11, 16] Furthermore, other important clinical implications of this technique may lie in its cost-effectiveness and cost-savings. Of note, only one dilator is needed to establish a tract with the OSD technique. The cost of OSD is much lower than that of the serial dilation method, which reduces the economic burden on patients.[12] Tonshal S et al[17] reported that the cost of the OSD technique is significantly lower than that of the Amplatz sequential dilation technique. Two recent studies have shown that OSD can significantly shorten the length of hospital stay,[7-8] which could also reduce the cost of hospitalization for patients. Reduction in treatment costs can optimize the allocation of medical resources. It is vital to evaluate the cost-effectiveness of the two tract dilation techniques in clinical practice, especially for developing countries.

Limitations of this study

This study had some limitations. First, only seven studies were included in this analysis, and the methodological quality of several studies with small sample sizes was

poor or uncertain. These factors might have led to heterogeneity. Second, the experience of the surgeons was not considered, which might have added to the bias. Third, due to the inadequate number of studies included, we did not perform funnel plots for further analysis of publication bias. Despite a systematic search strategy, the article language was restricted to English, which may have resulted in language bias.

Conclusion

The results of this meta-analysis and systematic review suggest that the OSD is a safe and efficacious tract dilation technique that can reduce the access time, fluoroscopy time, and postoperative decreases in hemoglobin levels. No differences were observed in the successful dilation rate, stone-free rate, transfusion rate, or complication rate between the two techniques. The difference in the length of postoperative hospital stay between the two techniques is uncertain. OSD may be a better method than serial dilation to establish tracts for PCNL. More high-quality RCTs are needed for further study.

Authors' contributions

PXP, SCL, and GZ conceived and designed the experiments. YHH and LHZ extracted the data. PXP, ZSD and SCL analyzed the data. ZSD, YHH, XMW and LHZ contributed materials/analysis tools. PXP and SCL wrote the paper. GZ critically revised the report.

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Disclaimer

The contents of the present study are solely the responsibility of the author. The funders had no role in study design, data collection and analysis, decision to publish, or preparation of the manuscript.

Competing interests

The authors declare that no conflicts of interest exist.

Data sharing statement

Data available from the Dryad Digital Repository: https://doi.org/10.5061/dryad.d5279d1

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17. Tonshal, S., B. Arun Kumar and M. Venkatraman, One Shot Versus Amplatz Sequential Fascial Dilatation Technique for Tract Creation in PCNL. Urology, 2011. 78(3): S108

Table File

Table. 1 Studies of characteristics of machine one-shot dilation VS serial dilation.

Figure Files

Fig. 1 Flowchart of study selection.

Fig. 2 Risk of bias summary: judgments about each risk of bias item for each included study.

Fig. 3 Forest plots illustrating the meta-analysis of outcomes with one-shot tract dilation versus serial tract dilation for PCNL. The outcomes analyzed were (A) access time, (B) successful dilation rate, and (C) stone-free rate.

Fig. 4 Forest plots illustrating the meta-analysis of outcomes with one-shot tract dilation versus serial tract dilation for PCNL. The outcomes analyzed were (A) postoperative decrease in hemoglobin level, (B) transfusion rate, (C) complication rate, and (D) length of postoperative hospital stay.

Fig. S1 Sensitivity analysis of access time with the aforementioned study excluded.

Fig. S2 Sensitivity analysis of the length of postoperative hospital stay with the aforementioned study excluded.

Supplementary Files

File. S1 Electronic search strategy in EMBASE.

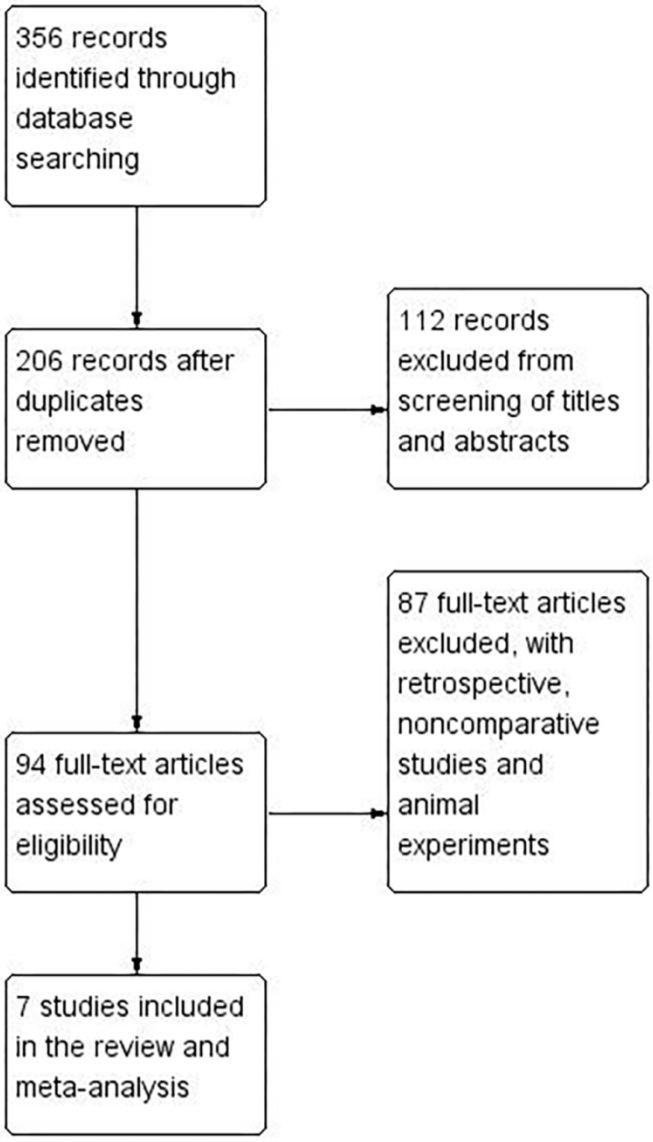

Fig. 1 Flowchart of study selection.

90x150mm (300 x 300 DPI)

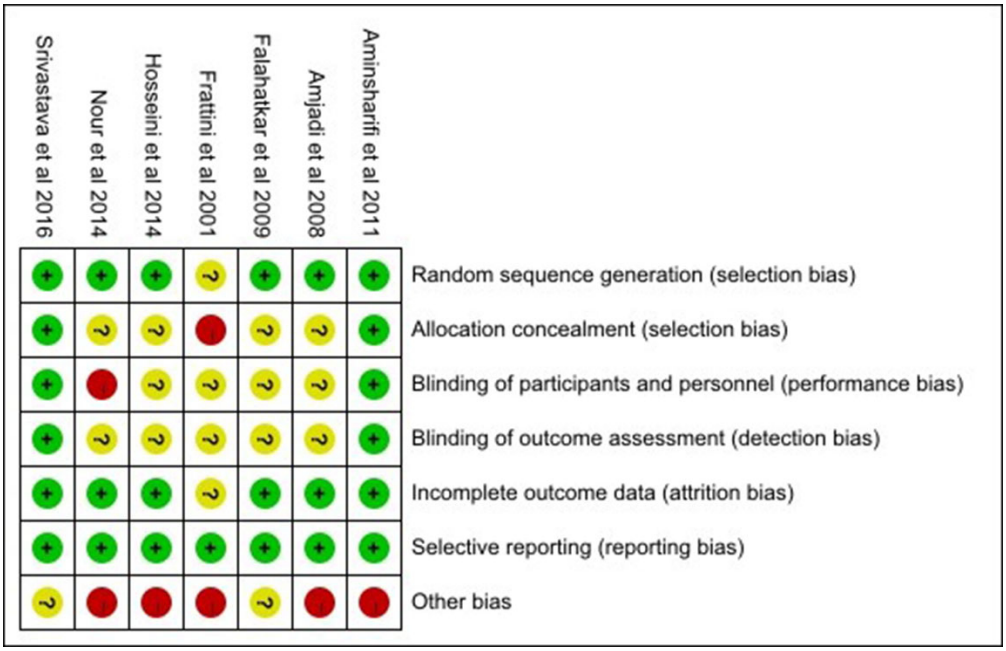

Fig. 2 Risk of bias summary: judgments about each risk of bias item for each included study.

97x62mm (300 x 300 DPI)

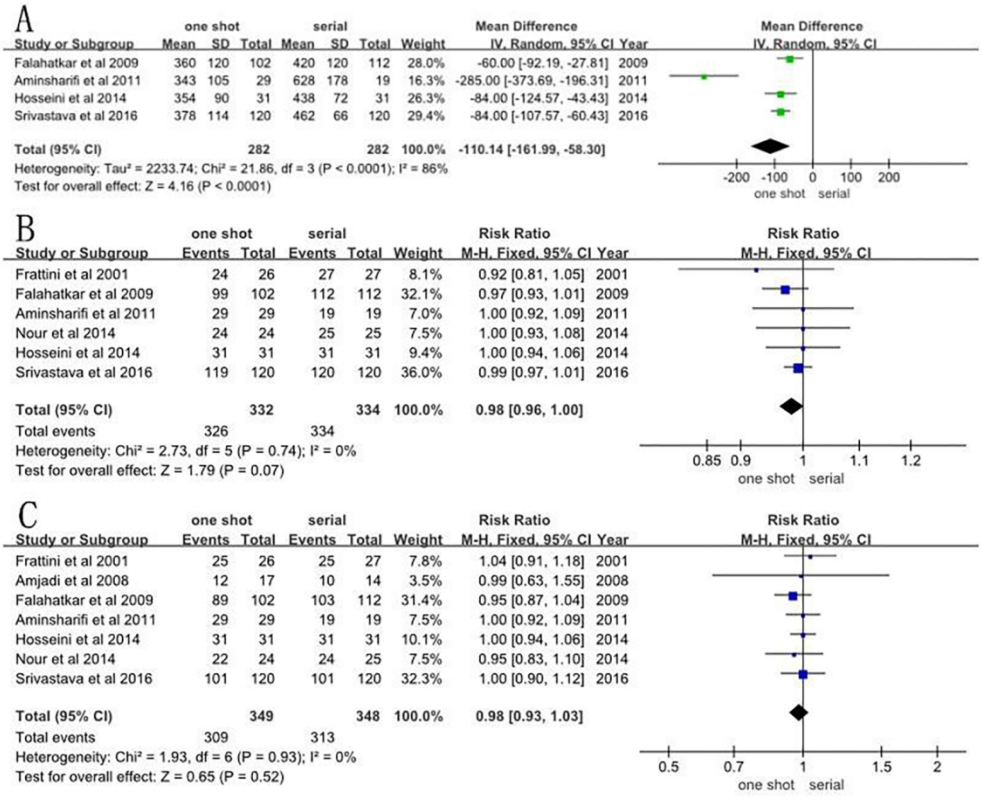

Fig. 3 Forest plots illustrating the meta-analysis of outcomes with one-shot tract dilation versus serial tract dilation for PCNL. The outcomes analyzed were (A) access time, (B) successful dilation rate, and (C) stone-free rate.

144x116mm (300 x 300 DPI)

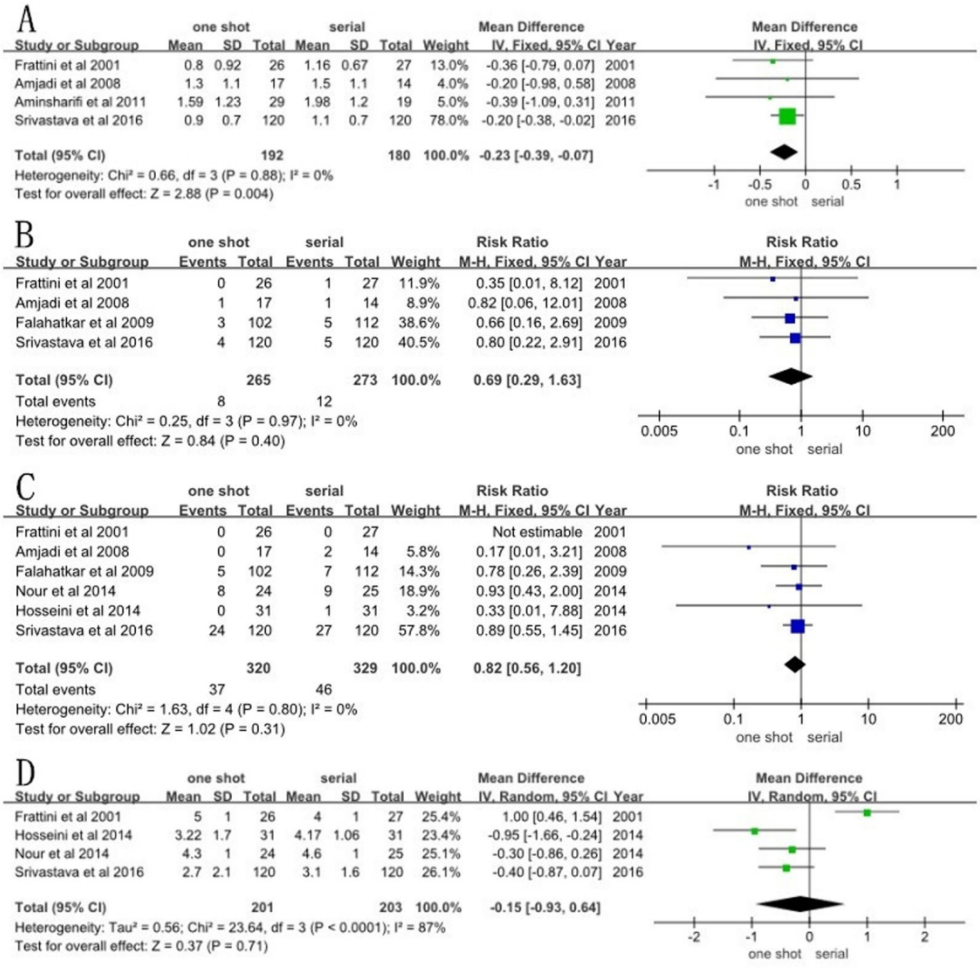

Fig. 4 Forest plots illustrating the meta-analysis of outcomes with one-shot tract dilation versus serial tract dilation for PCNL. The outcomes analyzed were (A) postoperative decrease in hemoglobin level, (B) transfusion rate, (C) complication rate, and (D) length of postoperative hospital stay.

143x140mm (300 x 300 DPI)

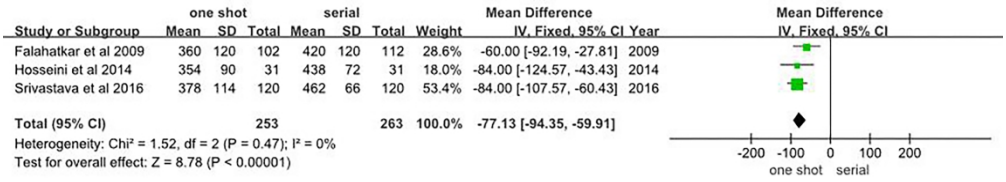

Fig. S1 Sensitivity analysis of access time with the aforementioned study excluded.

488x90mm (300 x 300 DPI)

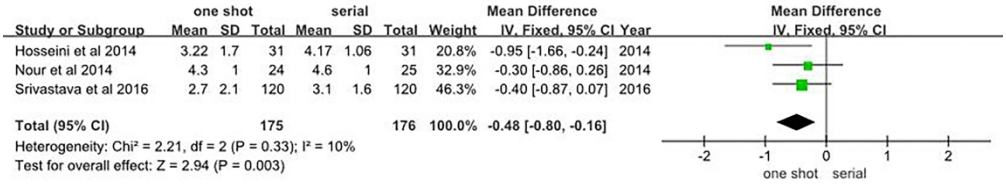

Fig. S2 Sensitivity analysis of the length of postoperative hospital stay with the aforementioned study excluded.

471x90mm (300 x 300 DPI)

One-shot dilation versus serial dilation technique for access in percutaneous nephrolithotomy: a systematic review and meta-analysis

Search strategy in EMBASE.

The last quest was updated on April 30, 2018.

#1 Search “percutaneous nephrolithotomy” [Mesh]

#2 Search PCNL

#3 Search (#1 or #2)

#4 Search "tract dilatation" [Mesh]

#5 Search tract dilation

#6 Search access creation

#7 Search (#4 or #5 or #6)

#8 Search "one-shot" [Mesh]

#9 Search one-step

#10 Search single-step

#11 Search one-step

#12 Search one-stage

#13 Search gradual

#14 Search sequential

#15 Search serial

#16 Search (#8 or #9 or #10 or #11or #12 or #13 or #14 or #15)

#17 Search (#3 and #7 and #16)

PRISMA 2009 Checklist

Section/topic	#	Checklist item	Reported on page #
TITLE			
Title	1	Identify the report as a systematic review, meta-analysis, or both.	1
ABSTRACT			
Structured summary	2	Provide a structured summary including, as applicable: background; objectives; data sources; study eligibility criteria, participants, and interventions; study appraisal and synthesis methods; results; limitations; conclusions and implications of key findings; systematic review registration number.	3
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of what is already known.	4-5
Objectives	4	Provide an explicit statement of questions being addressed with reference to participants, interventions, comparisons, outcomes, and study design (PICOS).	5
METHODS			
Protocol and registration	5	Indicate if a review protocol exists, if and where it can be accessed (e.g., Web address), and, if available, provide registration information including registration number.	None
Eligibility criteria	6	Specify study characteristics (e.g., PICOS, length of follow-up) and report characteristics (e.g., years considered, language, publication status) used as criteria for eligibility, giving rationale.	5-6
Information sources	7	Describe all information sources (e.g., databases with dates of coverage, contact with study authors to identify additional studies) in the search and date last searched.	5-6
Search	8	Present full electronic search strategy for at least one database, including any limits used, such that it could be repeated.	5-6
Study selection	9	State the process for selecting studies (i.e., screening, eligibility, included in systematic review, and, if applicable, included in the meta-analysis).	6
Data collection process	10	Describe method of data extraction from reports (e.g., piloted forms, independently, in duplicate) and any processes for obtaining and confirming data from investigators.	6-7
Data items	11	List and define all variables for which data were sought (e.g., PICOS, funding sources) and any assumptions and simplifications made.	7
Risk of bias in individual studies	12	Describe methods used for assessing risk of bias of individual studies (including specification of whether this was done at the study or outcome level), and how this information is to be used in any data synthesis.	7
Summary measures	13	State the principal summary measures (e.g., risk ratio, difference in means).	7
Synthesis of results	14	Describe the methods of handling data and combining results of studies, if done, including measures of consistency (e.g., I^2) for each meta-analysis.	7

PRISMA 2009 Checklist

Section/topic	#	Checklist item	Reported on page #
Risk of bias across studies	15	Specify any assessment of risk of bias that may affect the cumulative evidence (e.g., publication bias, selective reporting within studies).	7
Additional analyses	16	Describe methods of additional analyses (e.g., sensitivity or subgroup analyses, meta-regression), if done, indicating which were pre-specified.	7
RESULTS			
Study selection	17	Give numbers of studies screened, assessed for eligibility, and included in the review, with reasons for exclusions at each stage, ideally with a flow diagram.	7-8
Study characteristics	18	For each study, present characteristics for which data were extracted (e.g., study size, PICOS, follow-up period) and provide the citations.	9
Risk of bias within studies	19	Present data on risk of bias of each study and, if available, any outcome level assessment (see item 12).	10
Results of individual studies	20	For all outcomes considered (benefits or harms), present, for each study: (a) simple summary data for each intervention group (b) effect estimates and confidence intervals, ideally with a forest plot.	10-13
Synthesis of results	21	Present results of each meta-analysis done, including confidence intervals and measures of consistency.	10-13
Risk of bias across studies	22	Present results of any assessment of risk of bias across studies (see Item 15).	10-13
Additional analysis	23	Give results of additional analyses, if done (e.g., sensitivity or subgroup analyses, meta-regression [see Item 16]).	10，12-13
DISCUSSION			
Summary of evidence	24	Summarize the main findings including the strength of evidence for each main outcome; consider their relevance to key groups (e.g., healthcare providers, users, and policy makers).	13-16
Limitations	25	Discuss limitations at study and outcome level (e.g., risk of bias), and at review-level (e.g., incomplete retrieval of identified research, reporting bias).	16-17
Conclusions	26	Provide a general interpretation of the results in the context of other evidence, and implications for future research.	17
FUNDING			
Funding	27	Describe sources of funding for the systematic review and other support (e.g., supply of data); role of funders for the systematic review.	17-18

From: Moher D, Liberati A, Tetzlaff J, Altman DG, The PRISMA Group (2009). Preferred Reporting Items for Systematic Reviews and Meta-Analyses: The PRISMA Statement. PLoS Med 6(7): e1000097. doi:10.1371/journal.pmed1000097

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