Tract Sizes in Miniaturized Percutaneous Nephrolithotomy: A Systematic Review from the European Association of Urology Urolithiasis Guidelines Panel

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Abstract

Context: Miniaturized instruments for percutaneous nephrolithotomy (PNL), utilizing tracts sized ≤22 Fr, have been developed in an effort to reduce the morbidity and increase the efficiency of stone removal compared with standard PNL (>22 Fr). Objective: We systematically reviewed all available evidence on the efficacy and safety of miniaturized PNL for removing renal calculi. Evidence acquisition: The review was performed according to the Preferred Reporting Items for Systematic Reviews and Meta-analyses statement. Since it was not possible to perform a meta-analysis, the data were summarized in a narrative synthesis. Evidence synthesis: After screening 2945 abstracts, 18 studies were included (two randomized controlled trials [RCTs], six nonrandomized comparative studies, and 10 case series). Thirteen studies were full-text articles and five were only available as congress abstracts. The size of tracts used in miniaturized procedures ranged from 22 Fr to 4.8 Fr. The largest mean stone size treated using small instruments was 980 mm². Stone-free rates were comparable in miniaturized and standard PNL procedures. Procedures performed with small instruments tended to be associated with significantly lower blood loss, while the procedure duration tended to be significantly longer. Other complications were not notably different between PNL types. Study designs and populations were heterogeneous. Study limitations included selection and outcome reporting bias, as well as a lack of information on relevant confounding factors. Conclusions: The studies suggest that miniaturized PNL is at least as efficacious and safe as standard PNL for the removal of renal calculi. However, the quality of the evidence was poor, drawn mainly from small studies, the majority of which were...
1. Introduction

Kidney stone disease is considered to be an important health issue; its incidence has increased over the years to almost 9% [1]. Despite efforts in prevention and advances in management methods, urolithiasis is still an important cause of morbidity in all age groups and carries a significant economic burden because of associated direct and indirect costs [2,3].

Percutaneous nephrolithotomy (PNL) has gained acceptance as the gold standard for the treatment of large renal calculi [4,5]. During the past 20 yr, the instruments used have been miniaturized in an effort to decrease morbidity associated with standard PNL and increase the efficiency of stone removal. Jackman et al [6] and Helal et al [7] initially used smaller instruments in 1997 for pediatric cases with the proposed advantage of lower morbidity. Today, the term mini-perc, or mini-PNL (mPNL), usually describes tract sizes between 14 Fr and 22 Fr, although a clear definition does not exist [4]. Recently, even smaller systems—ultramini-PNL (umPNL) using tracts sized 11–13 Fr and microperc (μPNL) using tracts sized 4.8–10 Fr—have been introduced as alternative modalities to reduce procedure-related morbidity [8,9].

The primary goal of PNL is to achieve stone-free status while minimizing morbidity and complications. It has been reported that tract size is one of the main parameters affecting the complication rate [10]. However, reducing the tract size may adversely affect some procedure-related factors such as operation time [11]. We performed a systematic review to assess the relative benefits and harms of different PNL tract sizes for the treatment of renal stones.

2. Evidence acquisition

2.1. Search strategy

This systematic review was performed according to the Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) statement [12] and the Cochrane Handbook for Systematic Reviews of Interventions [13]. Studies on PNL (from January 1, 2000 to October 30, 2014) were identified by highly sensitive searches of electronic databases (Embase, Medline, the Cochrane Central Register of Controlled Trials, and the Health Technology Assessment Database). Studies in languages other than English were excluded. The protocol for the review is available on PROSPERO (CRD42015023766; www.crd.york.ac.uk/PROSPERO).

single-arm case series, and only two of which were RCTs. Furthermore, the tract sizes used and types of stones treated were heterogeneous. Hence, the risks of bias and confounding were high, highlighting the need for more reliable data from RCTs.

Patient summary: Removing kidney stones via percutaneous nephrolithotomy (PNL) using smaller sized instruments (mini-PNL) appears to be as effective and safe as using larger (traditional) instruments, but more clinical research is needed.

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re-treatment using the same modality [ie, more than one PNL session] or other modality such as shockwave lithotripsy [SWL] or transurethral endoscopic lithotripsy); need for adjunctive procedure (a procedure to deal with a complication [eg, nephrostomy or double-J stent insertion for obstruction] and procedures incidental to the stone removal process such as stent insertion and/or removal); duration of hospital stay; hospital readmission; and emergency department visit.

2.3. Data extraction

A data extraction form was developed a priori to collect information on study design, characteristics of participants and interventions, and primary and secondary outcome measures (benefits and harms).

2.4. Risk-of-bias assessment

Two reviewers (Y.R. and A.T.) independently assessed the risk of bias (RoB) for individual studies. Any disagreements were resolved by discussion or by consulting a third author (T.K.). The RoB in RCTs was assessed using the recommended tool in the Cochrane Handbook for Systematic Reviews of Interventions [13]. This included assessment of random sequence generation, allocation concealment, blinding of participants and personnel, blinding of outcome assessment, incomplete outcome data, selective reporting, and other sources of bias.

RoB in NRCSs was assessed using all seven domains above and an extra item to assess the risk of findings being explained by confounding. This is a pragmatic approach informed by methodological literature pertaining to assessing RoB in NRCSs [14,15]. A list of the most important potential confounders for harm and benefit outcomes was developed a priori with clinical content experts (European Association of Urology Urolithiasis Guidelines Panel). The potential confounding factors were stone size, stone location, obesity, previous open surgery on a kidney (eg, open nephrolithotomy), subcostal versus intercostal puncture, and calyceal access (upper vs middle vs lower calyx).

For each study, an algorithmic approach was used to assess the risk of confounding bias. The following were considered in sequence. (1) Was the prognostic confounder considered? If “no”, the study was deemed to be at “high” RoB for this confounder. If “yes”, go to the next question. (2) Was the confounder balanced between the intervention(s) and control group(s)? If “yes”, the study was at “low” RoB. If “no”, go to the next questions. (3) Was the confounder controlled for in the analysis, for example via statistical adjustment such as univariate or multivariate analysis or propensity score matching? If “yes”, the study was at “low” RoB. If “no”, the study was at “high” RoB.

The approach described above cannot be used to assess RoB in NRCSs. To address the external validity (ie, applicability of the results to different people, places, or time) of the NRCSs, we assessed whether study participants were selected consecutively or representative of a wider patient population, and whether the specified confounding factors were comparable across studies reporting on the same intervention. This too was a pragmatic approach informed by the methodological literature [16,17]. Further details on the approach outlined above are available on PROSPERO (CRD42015023766; www.crd.york.ac.uk/PROSPERO).

The key RoB and confounder assessments from the tools described above were summarized and presented graphically (Fig. 2).

2.5. Data analysis

For the purposes of this review, we refer to all procedures using smaller tract sizes (≤22 Fr) as mPNL when compared with procedures using larger instruments (unless otherwise specified). A meta-analysis for the two RCTs was not feasible because of heterogeneity in study design. Forest plots were created for the RCTs and NRCSs reporting SFRs to show the direction and magnitude of effects.

3. Evidence synthesis

3.1. Search results

The search returned 2945 abstracts (Fig. 1), of which 240 were scrutinized for eligibility. Four articles in languages other than English were excluded, as were an additional 218 studies that did not meet the remaining inclusion criteria. A total of 18 studies were eligible for final inclusion, of which 13 were full-text articles [8,11,18–28] and five were conference abstracts [29–33].

3.2. Study and patient characteristics

Of the 18 studies included, two were RCTs [19,28], six were NRCSs [11,21,22,24,26,27], and ten were single-arm case series on mPNL only [8,18,20,23,25,29–33]. There was one study on PNL using tract size 22 Fr [21] and one on tract sizes <20 Fr [29]. Three studies evaluated tract size 18 Fr [18,22,23], two studies 16 Fr [19,26], and two 14 Fr [11,25]. One study reported on tracts sized 14–18 Fr [24], and another on tracts ≤18 Fr [27]. There were three studies on tract sizes 11–13 Fr [8,20,30] and one on 4.8 Fr [28]. Three studies presented as conference abstracts did not explicitly state the tract size, but the procedures were termed mPNL [31–33]. No studies reported QOL outcomes. The baseline characteristics of the participants in the studies included are outlined in Table 1 and the findings are summarized in Table 2.

3.3. RCTs

Two RCTs were identified, both of which were full-text articles. Only one study investigated the benefits and harms of mPNL using “regular” (16 Fr) compared to standard PNL (24 Fr) [19]. Both blood loss and the need for blood transfusion were significantly lower in the mPNL group (both p < 0.05), although the types of stone were not fully comparable. The SFR was only significantly different for
multiple calyceal stones (85% for mPNL vs 70% for standard PNL, p < 0.05). The duration of the procedure was longer in the mPNL group for all stone types (all p < 0.05; Table 1).

The other RCT was a comparison of μPNL (4.8 Fr) and standard PNL (30 Fr) [28]. No benefit was found with respect to ISFR (p = 1), although blood loss and procedure duration were lower (p = 0.004 and 0.034, respectively) and hospital stay was shorter (p = 0.0001). Intrarenal pelvic pressure was higher in the μPNL group (p < 0.0001; Table 1).

3.4. NRCSs

Six NRCSs were included, all of which were full-text articles. One study compared five groups with successively increasing PNL tract size (22, 24, 26, 28, and 30 Fr) [21]. Blood loss increased with the tract size (p < 0.05) but the procedure duration did not significantly differ between the groups (Table 2). Another study using the PNL Global Study database of The Clinical Research Office of the Endourological Society (CROES) reported data for four groups (≤18, 24–26, 27–30, and ≥32 Fr) [27]. The only relevant outcomes were blood loss and blood transfusion rates, which significantly increased with the tract size (p = 0.00016 and <0.0001). Four comparative studies comprised two main comparator groups (mPNL vs standard PNL). In one of the studies [11], the control arm (30 Fr) was further divided into two groups: patients who received a nephrostomy tube and patients who did not (tubeless). SFR was lower in the mPNL group (14 Fr) than in either of the standard PNL groups (tube p = 0.016 and tubeless p = 0.009). Blood loss was lower than in the tube standard PNL group (p = 0.021) but not the tubeless standard PNL group (p = 0.041). Tubeless standard PNL was also superior in terms of analgesic requirement, pain (VAS), and duration of procedure and hospital stay (Table 2). Xu et al [26] compared 16 Fr mPNL with 24 Fr PNL, and observed lower blood loss in the mPNL group (p = 0.015), although the stones treated were also smaller. ISFR, complication rates, procedure duration, and hospital stay did not differ (Table 2). Mishra et al [24] compared mPNL (14–18 Fr) with standard PNL (24–28 Fr), but interpretation of the results is obscured by the use of different energy sources for stone fragmentation: laser in the mPNL group and pneumatic in the standard PNL group [24]. The study reported similar SFR (p = 0.49) and analgesic requirement (p = 0.28), but lower blood loss (p = 0.0098) and procedure duration (p = 0.0008), and shorter hospital stay (p < 0.00001) in the mPNL group. A greater proportion of procedures were tubeless in the mPNL (78%) than in the standard PNL group (14%; p < 0.001). Knoll et al [22] compared mPNL (18 Fr) and standard PNL (26 Fr) and found similar ISFR in both groups (p = 1.00). However, stones were significantly larger in the standard PNL group (p = 0.042). The study also revealed similar blood loss, complication rates, procedure duration, and analgesic requirements for both groups (all p > 0.05). However pain scores (VAS) were lower (p = 0.048) and hospital stay was shorter (p = 0.021) among mPNL patients. All mPNL procedures were tubeless if uncomplicated and the patient was rendered stone-free, otherwise a nephrostomy tube was placed. All patients undergoing standard PNL received a nephrostomy tube.
Fig. 2 – Risk of bias and confounding assessment summary. (A) Risk of bias assessment for randomized controlled trials. (B) Risk of bias and confounding assessment for non-randomized comparative studies. (C) Risk of bias assessment for case series. Green circle = low risk of bias or confounding; red circle = high risk of bias or confounding; yellow circle = unclear risk of bias or confounding.
<table>
<thead>
<tr>
<th>Study ID, design, country, recruitment period</th>
<th>Intervention</th>
<th>N</th>
<th>FU (mo), mean ± SD, median [range]</th>
<th>Age (yr), mean ± SD, median [range]</th>
<th>Gender M/F</th>
<th>BMI (kg/m²), mean ± SD, median [range]</th>
<th>Inclusion criteria</th>
<th>Exclusion criteria</th>
<th>Stone size in mm or mm², mean ± SD, [range]</th>
<th>Stone location in UC, MC, LC, P or UPJ if available</th>
<th>Stone laterality RL</th>
<th>Outcomes measured</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tepeler 2014, RCT, Turkey, 2012–2013 [28]</td>
<td>tPNL 4.8 Fr</td>
<td>10</td>
<td>42 ± 15.1 [26–66] 27.5 ± 3.6 (21.8–43.5) 27.8 ± 2.8 (23.7–33.1)</td>
<td>4/6</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>19 ± 5.0 (12–30) mm Renal NR</td>
<td>Renal NR</td>
<td>Benefits: EFR</td>
<td>Harms: CG, BL, Secondary outcomes: DP, DHS Other: pelvic pressure</td>
</tr>
<tr>
<td></td>
<td>PNL 30 Fr</td>
<td>10</td>
<td>44.3 ± 10.1 [27–62] 25.9 ± 3.6 27.8 ± 3.4 (21.8–33.5)</td>
<td>1.2 NR</td>
<td></td>
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<td>21.9 ± 4.8 (15–30) mm Renal</td>
<td>Renal</td>
<td>Benefits: EFR</td>
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<tr>
<td></td>
<td>PNL 24 Fr</td>
<td>115</td>
<td>30.6 (27–72)</td>
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<td></td>
<td></td>
<td>1010 mm²</td>
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<td></td>
<td>PNL 26 Fr</td>
<td>26</td>
<td>45.94 ± 14.09 [24–72] (11) 8</td>
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<td>37.47 ± 10.35 (17–53) mm Renal</td>
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<td></td>
<td>PNL 28 Fr</td>
<td>18</td>
<td>41.88 ± 16.53 (22–69) (10)</td>
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<td>37.84 ± 14.14 (15–55) mm Renal</td>
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<td></td>
<td>PNL 30 Fr</td>
<td>32</td>
<td>45.37 ± 13.80 (24–72) (11)</td>
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<td>36.49 ± 11.33 (25–50) mm Renal</td>
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<td>Xu 2014, comparative study, China, 2011–2013 [26]</td>
<td>mPNL 16 Fr</td>
<td>37</td>
<td>50.3 ± 14.8 45.3 ± 13.5</td>
<td>13/24 22.7 ± 4 13/21 22.8 ± 1.5</td>
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<td>33.4 ± 10.3 mm 41.4 ± 10.9 mm Renal</td>
<td></td>
<td>Benefits: EFR</td>
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<tr>
<td></td>
<td>PNL 24 Fr</td>
<td>34</td>
<td></td>
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<tr>
<td>Yamaguchi 2011, comparative study, global, 2007–2009 [27]</td>
<td>mPNL 22 Fr</td>
<td>271</td>
<td></td>
<td>21/10 42.2 NR</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>260 ± 30 mm²</td>
<td>2 (8%) UC 1 (4%) MC 15 (58%) LC 9 (35%) P 3 (125) UC 2 (8%) MC 10 (38%) LC 13 (50%) P</td>
<td></td>
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<td></td>
<td>PNL 24 Fr</td>
<td>371</td>
<td></td>
<td>18/8 23.8 ± 2.6</td>
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<td></td>
<td>PNL 24-28 Fr</td>
<td>26</td>
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<tr>
<td></td>
<td>PNL 26 Fr</td>
<td>25</td>
<td>48 ± 15.5 [23–73]</td>
<td>20 ± 20.6</td>
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<td></td>
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<td></td>
<td>22 ± 4.4 [15–29] (11)</td>
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<tr>
<td></td>
<td>PNL 30 Fr</td>
<td>67</td>
<td>51.3 ± 19.78</td>
<td>30/31.6</td>
<td>14/13.2</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>310 mm²</td>
<td>320 mm²</td>
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<td></td>
<td>TL PNL 30 Fr</td>
<td>27</td>
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<tr>
<td>Miller 2014, case series, UK, 2009–2013, abstract [32]</td>
<td>mPNL 16.5 Fr</td>
<td>116</td>
<td>63.2 ± 10.5</td>
<td>60/56 NR</td>
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<tr>
<td>Bhattu 2014, case series, India, mPNL (±20Fr)</td>
<td>2002–2013, abstract [29]</td>
<td>301</td>
<td>42 NR</td>
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<tr>
<td>Karatag 2014, case series, Turkey, 2013, abstract [34]</td>
<td>mPNL 4 Fr</td>
<td>68</td>
<td>41.4 NR</td>
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<tr>
<td>Study/Duration, Country, Recruitment Period</td>
<td>Intervention</td>
<td>N</td>
<td>Recruitment Period</td>
<td>FU (mo), mean ± SD, median [range]</td>
<td>Gender M/F</td>
<td>BMI (kg/m²), mean ± SD, median [range]</td>
<td>Inclusion Criteria</td>
<td>Exclusion Criteria</td>
<td>Stone Size in mm or mm², mean ± SD, range + IQR</td>
<td>Stone Location in UC, MC, LC, PU or UPJ if available</td>
<td>Stone Laterality R/L</td>
<td>Outcomes Measured</td>
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<tr>
<td>Desai 2013, case series, India, recruitment period NR, abstract</td>
<td>umPNL 12 Fr</td>
<td>74</td>
<td>1</td>
<td>NR</td>
<td>4 (5%) pediatric cases</td>
<td>umPNL</td>
<td>NR</td>
<td>16.6 mm</td>
<td>NR</td>
<td>Benefits: SFR, Harms: CG, BL, Secondary outcomes: DHS Other outcomes: conversion to mPNL due to bleeding</td>
<td></td>
<td></td>
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<tr>
<td>Desai 2013, case series, India, recruitment period NR</td>
<td>umPNL 13 Fr</td>
<td>62</td>
<td>1</td>
<td>NR</td>
<td>4 (7%) pediatric cases</td>
<td>Renal stones</td>
<td>umPNL</td>
<td>16.8 mm</td>
<td>NR</td>
<td>Benefits: SFR, Harms: CG, BL, Secondary outcomes: DHS Other outcomes: conversion to mPNL due to bleeding</td>
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<td></td>
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<tr>
<td>Desai 2013, case series, India, 2012</td>
<td>umPNL 11–13 Fr</td>
<td>36</td>
<td>1</td>
<td>48.2 ± 15.7 [2–79]</td>
<td>Renal stone &lt; 20 mm</td>
<td>umPNL</td>
<td>NR</td>
<td>14.9 ± 4.1 [6–20] mm Area: 160.6 ± 82.7 [10–380] mm²</td>
<td>7 (19%) UC 8 (22%) MC 10 (28%) LC 3 (7%) Multiple C 5 (14%) P 3 (8%) UUr</td>
<td>21 / 15</td>
<td></td>
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<tr>
<td>Abdelhafiz 2013, case series, Germany, 2012</td>
<td>mPNL 18 Fr</td>
<td>98</td>
<td>1</td>
<td>49.6 ± 15.9</td>
<td>Consecutive patients with stones &gt; 15 mm or lower calyx stones &gt; 8 mm, or any previously failed SWL and URS</td>
<td>umPNL</td>
<td>NR</td>
<td>13.6 ± 3.4 mm</td>
<td>NR</td>
<td>Benefits: ISFR, SFR, Harms: CG, BL, BT Secondary outcomes: DP, SP, DHS Other outcomes: Puncture locations</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Zimmermann 2012, case series, Germany, abstract</td>
<td>All patients, all stone sizes Stones ≥500 mm²</td>
<td>91</td>
<td>1</td>
<td>48.8 ± 17.6</td>
<td>Access not possible</td>
<td>mPNL</td>
<td>NR</td>
<td>37.5 ± 22.9 mm</td>
<td>NR</td>
<td>Benefits: ISFR, SFR, Harms: CG, BL, BT Secondary outcomes: DP, SP, DHS</td>
<td></td>
<td></td>
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<tr>
<td>Lu 2012, case series, China, 2009–2010</td>
<td>Tubeless mPNL Standard mPNL (with 16 Fr nephrostomy tube)16</td>
<td>16</td>
<td>0.5</td>
<td>43.81 ± 18.89</td>
<td>Pelvic stone &lt; 40 mm</td>
<td>umPNL</td>
<td>NR</td>
<td>32.9 ± 6.2 mm</td>
<td>NR</td>
<td>Benefits: ISFR, SFR, Harms: CG, BL, Secondary outcomes: DHS, DP, pain</td>
<td></td>
<td></td>
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<tr>
<td>Sung 2006, case series, Korea, 1999–2002</td>
<td>mPNL 14 Fr</td>
<td>72</td>
<td>7.2 ± 8.3 [0.5–37]</td>
<td>Failed SWL and/or URS (n = 19), large stone burden (&lt;600 mm²) (n = 25), P and/or LC stones, (n = 62), UC stones (n = 2), calyceal diverticulum stone (n = 4), 1 pediatric case 31/72 patients had &gt;2 indications</td>
<td>umPNL</td>
<td>NR</td>
<td>34.2 ± 19.9 [6–102] mm 62 (86%) P and/or UC 2 (25%) UC 1 (13%) calyceal diverticulum</td>
<td>31/41</td>
<td>Benefits: ISFR, SFR, Harms: fever, BL Secondary outcomes: SP, DHS</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

AP = adjunctive procedure; BL = blood loss; BT = blood transfusion; C = calyx; CG = Clavien grade; CIRFR = clinically insignificant residual fragment rate; DB = database; DHS = duration of hospital stay; DP = duration of procedure; EDV = emergency department visit; FU = follow-up (here meaning time point for delayed assessment of stone status, if applicable); HR = hospital readmission; ISFR = immediate SFR; ICIRFR = immediate CIRFR; LC = lower calyceal; MC = middle calyceal; mPNL = mini-PNL; NR = not reported; P = pelvis; PNL = percutaneous nephrolithotomy; QOL = quality of life; RCT = randomized controlled trial; SFR = stone-free rate; SP = secondary procedure; UC = upper calyceal; umPNL = ultra-mini-PNL; UPJ = ureteropelvic junction; URS = ureteroscopy; US = urosepsis; UUr = upper ureteral; VI = visceral injury.
<table>
<thead>
<tr>
<th>Study ID, design, country, recruitment period, Subgroups (of mPNL group)</th>
<th>Intervention</th>
<th>Comparator</th>
<th>Outcomes measured</th>
<th>n at baseline</th>
<th>Outcomes</th>
<th>Reported p values</th>
<th>Notes</th>
<th>Summary</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tepeler 2014, RCT, Turkey, 2012–2013 [28]</td>
<td>NA</td>
<td>mPNL 16 Fr</td>
<td>PNL Fr</td>
<td>Benefits: ISFR, Harms: CG, BL</td>
<td>ISFR: 9 (90%)</td>
<td>1</td>
<td>BL reported as percent drop in hematurit</td>
<td>mPNL vs PNL showed no ISFR benefit, although BL and DP were lower. DP was higher in the mPNL group</td>
</tr>
<tr>
<td>Cheng 2010, RCT, China, 2004–2007 [19]</td>
<td>Total</td>
<td>mPNL 16 Fr</td>
<td>PNL 24 Fr</td>
<td>Benefits: ISFR, Harms: CG, BL</td>
<td>BL: 0.53 ± 0.79 g/dL</td>
<td>&lt;0.05</td>
<td>BL and need for BT were lower in mPNL group, however stones were not fully comparable. mPNL results most favorable for multiple calyceal stones. DP was longer in mPNL group.</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Staghorn stones (SS)</td>
<td></td>
<td></td>
<td>Secondary outcomes: DHS, DP, analgesic requirement</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Simple renal pelvic stones (SRPS)</td>
<td></td>
<td></td>
<td></td>
<td></td>
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<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Multiple calyceal stones (MCS)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Secondary outcomes: DP</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Other outcomes: preop vs postop creatinine</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Xue 2014, comparative study, China, 2011–2013 [26]</td>
<td>NA</td>
<td>mPNL 16 Fr</td>
<td>PNL 24 Fr</td>
<td>Benefits: ISFR, Harms: CG, BL</td>
<td>ISFR: 27/34 (79%)</td>
<td>0.915</td>
<td>Not randomized: selection of technique based on joint decision by surgeons and patients. Stones in PNL group significantly larger</td>
<td>BL was significantly lower in mPNL group, however stones treated were smaller.</td>
</tr>
<tr>
<td>Study ID, design, country, recruitment period (of mPNL group)</td>
<td>Subgroups measured</td>
<td>Intervention Comparator</td>
<td>Outcomes at baseline</td>
<td>Outcomes Reported (\text{at} ) BL, BT</td>
<td>Factors predictive of bleeding complications included bladder perforation, pelvic perforation, energy source for stone treatment, dilatation methods. Data for BT are described in Table 2.</td>
<td>Notes Summary</td>
<td></td>
<td></td>
</tr>
<tr>
<td>---</td>
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<td>---</td>
<td>---</td>
<td>---</td>
<td>---</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
| Yamaguchi 2011, NA | NA | NA | NA | NA | NA | Shorter operation time, mPNL had shorter DHS and higher tubeless rate related to less bleeding. Lower stone burden and size24–26 Fr and hemoglobin (p = 0.042) in PNL group. Otherwise, 16 Fr tube was placed. All PNL had 22 Fr tube. BL reported as percent drop in hematocrit. Analgesic substance included DFA (tramadol): 55.4 mg, 50 mg, 10 mg. AR (piritramide): 73.8 mg, 25 mg, 37 mg. Mean values.

| Mishra 2011, India, 2009–2010 [24] | NA | NA | NA | NA | NA | Despite longer operation time, mPNL had shorter DHS and higher tubeless rate related to less bleeding. Lower stone burden and size24–26 Fr and hemoglobin (p = 0.042) in PNL group. Otherwise, 16 Fr tube was placed. All PNL had 22 Fr tube. BL reported as percent drop in hematocrit. Analgesic substance included DFA (tramadol): 55.4 mg, 50 mg, 10 mg. AR (piritramide): 73.8 mg, 25 mg, 37 mg. Mean values.

| Knoll 2010, comparative study, Germany, 2007–2009 [22] | NA | NA | NA | NA | NA | Despite longer operation time, mPNL had shorter DHS and higher tubeless rate related to less bleeding. Lower stone burden and size24–26 Fr and hemoglobin (p = 0.042) in PNL group. Otherwise, 16 Fr tube was placed. All PNL had 22 Fr tube. BL reported as percent drop in hematocrit. Analgesic substance included DFA (tramadol): 55.4 mg, 50 mg, 10 mg. AR (piritramide): 73.8 mg, 25 mg, 37 mg. Mean values.

| Giusti 2007, Italy, 1999–2004 [11] | NA | NA | NA | NA | NA | Despite longer operation time, mPNL had shorter DHS and higher tubeless rate related to less bleeding. Lower stone burden and size24–26 Fr and hemoglobin (p = 0.042) in PNL group. Otherwise, 16 Fr tube was placed. All PNL had 22 Fr tube. BL reported as percent drop in hematocrit. Analgesic substance included DFA (tramadol): 55.4 mg, 50 mg, 10 mg. AR (piritramide): 73.8 mg, 25 mg, 37 mg. Mean values.

| Miller 2014, case series, UK, 2009–2013, abstract [32] | NA | NA | NA | NA | NA | Despite longer operation time, mPNL had shorter DHS and higher tubeless rate related to less bleeding. Lower stone burden and size24–26 Fr and hemoglobin (p = 0.042) in PNL group. Otherwise, 16 Fr tube was placed. All PNL had 22 Fr tube. BL reported as percent drop in hematocrit. Analgesic substance included DFA (tramadol): 55.4 mg, 50 mg, 10 mg. AR (piritramide): 73.8 mg, 25 mg, 37 mg. Mean values.

| Pence 2001, case series, abstract [23] | NA | NA | NA | NA | NA | Despite longer operation time, mPNL had shorter DHS and higher tubeless rate related to less bleeding. Lower stone burden and size24–26 Fr and hemoglobin (p = 0.042) in PNL group. Otherwise, 16 Fr tube was placed. All PNL had 22 Fr tube. BL reported as percent drop in hematocrit. Analgesic substance included DFA (tramadol): 55.4 mg, 50 mg, 10 mg. AR (piritramide): 73.8 mg, 25 mg, 37 mg. Mean values.

| Pence 2001, case series, abstract [23] | NA | NA | NA | NA | NA | Despite longer operation time, mPNL had shorter DHS and higher tubeless rate related to less bleeding. Lower stone burden and size24–26 Fr and hemoglobin (p = 0.042) in PNL group. Otherwise, 16 Fr tube was placed. All PNL had 22 Fr tube. BL reported as percent drop in hematocrit. Analgesic substance included DFA (tramadol): 55.4 mg, 50 mg, 10 mg. AR (piritramide): 73.8 mg, 25 mg, 37 mg. Mean values.

| Pence 2001, case series, abstract [23] | NA | NA | NA | NA | NA | Despite longer operation time, mPNL had shorter DHS and higher tubeless rate related to less bleeding. Lower stone burden and size24–26 Fr and hemoglobin (p = 0.042) in PNL group. Otherwise, 16 Fr tube was placed. All PNL had 22 Fr tube. BL reported as percent drop in hematocrit. Analgesic substance included DFA (tramadol): 55.4 mg, 50 mg, 10 mg. AR (piritramide): 73.8 mg, 25 mg, 37 mg. Mean values.

| Pence 2001, case series, abstract [23] | NA | NA | NA | NA | NA | Despite longer operation time, mPNL had shorter DHS and higher tubeless rate related to less bleeding. Lower stone burden and size24–26 Fr and hemoglobin (p = 0.042) in PNL group. Otherwise, 16 Fr tube was placed. All PNL had 22 Fr tube. BL reported as percent drop in hematocrit. Analgesic substance included DFA (tramadol): 55.4 mg, 50 mg, 10 mg. AR (piritramide): 73.8 mg, 25 mg, 37 mg. Mean values.

| Pence 2001, case series, abstract [23] | NA | NA | NA | NA | NA | Despite longer operation time, mPNL had shorter DHS and higher tubeless rate related to less bleeding. Lower stone burden and size24–26 Fr and hemoglobin (p = 0.042) in PNL group. Otherwise, 16 Fr tube was placed. All PNL had 22 Fr tube. BL reported as percent drop in hematocrit. Analgesic substance included DFA (tramadol): 55.4 mg, 50 mg, 10 mg. AR (piritramide): 73.8 mg, 25 mg, 37 mg. Mean values.
<table>
<thead>
<tr>
<th>Author(s)</th>
<th>Year</th>
<th>Study Design</th>
<th>Fr.</th>
<th>Stone Size</th>
<th>Benefits</th>
<th>Complications</th>
<th>Duration</th>
<th>Recovery</th>
<th>Conversion to mPNL</th>
</tr>
</thead>
<tbody>
<tr>
<td>Karatag 2014</td>
<td>case series, Turkey, 2013, abstract [31]</td>
<td>4.8 Fr</td>
<td>NA</td>
<td>NA</td>
<td>SFR</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
<td>Desai 2013</td>
<td>case series, India, recruitment period NR, abstract [30]</td>
<td>12 Fr</td>
<td>NA</td>
<td>NA</td>
<td>SFR</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
<td>Abdelhale 2013</td>
<td>case series, Germany, 2007–2011 [18]</td>
<td>18 Fr</td>
<td>NA</td>
<td>Stone size: &lt;2 cm</td>
<td>SFR, ISFR</td>
<td>NA</td>
<td>20 mm</td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
<td>Zimmermann 2012</td>
<td>case series, Germany, recruitment period NR, abstract [31]</td>
<td>18 Fr</td>
<td>All patients, all stone sizes: ≤5 cm</td>
<td>NA</td>
<td>SFR</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
</tr>
</tbody>
</table>

mPNL is alternative to standard PNL for medium renal stones, with better morbidity profile. However, there is no comparison group. Tubeless mPNL associated with better morbidity profile.
<table>
<thead>
<tr>
<th>Study, Country, Recruitment Period</th>
<th>Intervention</th>
<th>Comparator</th>
<th>16 Fr</th>
<th>14 Fr</th>
<th>7.7 mm</th>
<th>p Values</th>
<th>Conclusion</th>
</tr>
</thead>
<tbody>
<tr>
<td>China, 2009–2010 [23]</td>
<td>mPNL</td>
<td>ISFR</td>
<td>0.26</td>
<td>0.44</td>
<td>0.48</td>
<td>0.02</td>
<td>TB mPNL has the advantages of shorter hospital stay and fewer complications.</td>
</tr>
<tr>
<td>Korea, 1999–2002 [25]</td>
<td>Tubeless mPNL</td>
<td>ISFR</td>
<td>0.62</td>
<td>0.62</td>
<td>0.62</td>
<td>0.01</td>
<td>ISFR: 14 (87.5%) compared to 13 (81.3%) with 16 Fr.</td>
</tr>
<tr>
<td>Japan, 2000–2002 [32]</td>
<td>Standard PNL</td>
<td>ISFR</td>
<td>0.43</td>
<td>0.51</td>
<td>0.51</td>
<td>0.003</td>
<td>Conversion to mPNL occurred in approximately 3% of the procedures.</td>
</tr>
</tbody>
</table>

**Table 2 (Continued)**

### 3.5. Case series

Ten case series were included, five of which were full-text articles [8,18,20,23,25] and five congress abstracts [29–33]. The smallest tract size studied was 4.8 Fr (µPNL) in a case series of 68 patients (70 renal units) [31]. SFR was high (98.5%), while blood loss, complication rates, procedure duration, and hospital stay were low (Table 2). Three studies [8,20,30] involved case series in which patients (n = 74, 62, and 26, respectively) were treated using tract sizes of 11–13 Fr. SFRs were high (92.4%, 86.7%, and 97.2%, respectively), while blood loss, complication rates, procedure duration, and hospital stay were low (Table 2). Conversion to mPNL occurred in approximately 3% of the procedures. One study of 72 patients treated with 14 Fr mPNL [25] had SFR of 87.5% and an extended hospital stay of 7.7 ± 3.2 d (range 4–22). Two studies reported on a tract size of 18 Fr. Lu et al [23] compared procedures with and without placement of a final nephrostomy tube (both n = 16) [23], and Abdelhafez et al [18] compared stones measuring in <20 mm (n = 98) to stones measuring ≥20 mm (n = 93) in maximal diameter. Lu et al [23] found that ISFRs were comparable, but that tubeless procedures were associated with fewer patients reporting back pain (p = 0.003) and shorter hospital stay (3 vs 4 d; p = 0.032; Table 2). Abdelhafez et al [18] found that the ISFR was higher for patients with smaller stones (90.8% vs 76.7%; p = 0.007), while the SFRs at 1 mo after auxiliary procedures were comparable (98.9% vs 94.6%; p = 0.1). Complication rates were comparable (p = 0.2), while blood loss was lower (p = 0.015) and the procedure duration (p < 0.001) and hospital stay were shorter (p = 0.002) in patients with smaller stones. One abstract reported on 301 procedures utilizing tracts <20 Fr (the smallest tract size used was not stated) [29]. The SFR was high at 99%, while blood loss, analgesic requirements, and complication rates were low, and procedure duration and hospital stay short. Two abstracts reporting on mPNL did not explicitly state the size of the sheaths used [32,33], so this information was obtained via e-mail correspondence with the authors: Miller et al [32] used 16.5 Fr and Zimmermanns et al [33] used 18 Fr. Using data from the CREOS PNL Global Study, Miller et al [32] reported a comparatively low ISFR (46.5%) with a fair rate for immediate clinically insignificant residual fragments (79.4%). Complication rates were comparatively high (eg, urosepsis in 12.9% of patients) and the procedure duration was 174 min (Table 2). Zimmermanns et al [33] presented results for two groups: the complete cohort of 652 patients (all stone sizes) and a subgroup of 183 patients with stones measuring ≥500 mm² in area. No p values were reported, although the ISFR was comparable in both groups (93.6% vs 91.8%).

### 3.6. RoB and confounding assessment

Figure 2 summarizes the key RoB and confounding assessments. Only two studies were RCTs; the remaining 16 were either NRCSs or case series resulting in high RoB associated with no randomization, incomplete outcome data (attrition bias), and selective outcome data reporting.
Most studies reported stone sizes but did not report stone location. Fewer than half of the studies contained information on obesity (or body mass index). The risk of confounding was moderate to high for previous open surgery, access site, and access location, since only one or two studies reported on these factors (Fig. 2). The tract size used and the stone types and locations (when reported) were heterogeneous.

3.7. Discussion

3.7.1. Principal findings

SFRs were comparable in patients with renal stones treated with mPNL and standard PNL (Fig. 3). Smaller tracts tended to be associated with significantly lower blood loss (Fig. 4) or need for blood transfusion [11,19,21,24,26–28] at the cost of a significantly longer procedure [11,19,24,28] (Fig. 5). Hospital stay length was mostly shorter for mPNL [11,22,24,34] (Fig. 6). The studies were heterogeneous with respect to tract and stone sizes, and the RoB and confounding risk were generally high.

The terms used to describe tract sizes, such as “mini-PNL”, “ultra-mini-PNL”, and “micro-PNL”, have not been well defined and partly overlap. In general, tracts sized ≤18 Fr are used for miniaturized techniques [28,35]. Urologists need to be aware that such terms describe not only the size of the access sheath but also of specific instruments, dilators, and operative concepts [36–40]. This systematic review indicates that mPNL is a safe and effective evolution of the PNL technique, and thus warrants further investigation. RCTs are necessary to better assess the benefits and harms in relation to both disease-related parameters (stone size, quantity and location) and interventional parameters (tract size, puncture locations, and intrapelvic pressure).

![Fig. 3](https://example.com/fig3.png) Forest plot showing the stone-free rates reported in the randomized controlled trial (RCTs) and nonrandomized comparative studies (NRCSs). Reference numbers for studies are given in Table 1. PCNL = percutaneous nephrolithotomy; M-H = Mantel-Haenszel; CI = confidence interval.

![Fig. 4](https://example.com/fig4.png) Forest plot showing the postoperative hemoglobin decrease in (A) g/dl and (B) percent reported in randomized controlled trials (RCTs) and nonrandomized comparative studies (NRCSs). Reference numbers for studies are given in Table 1. PCNL = percutaneous nephrolithotomy; SD = standard deviation; CI = confidence interval; IV = inverse variance.
3.7.2 Implications for practice

Our systematic review demonstrates that the use of miniaturized PNL systems is effective. This was demonstrated in most studies, including the first series published by Jackman et al [6]. The authors reported SFR of 85% in children and 85% in adults for stones sized 12–15 mm. One of the few studies showing inferiority for smaller instruments was the series described by Giusti et al [11]. However, this study demonstrates the confusion caused by non-standardized terminology, as the instruments used were not dedicated for PNL but rigid ureteroscopes of small diameters. The major disadvantage of small instruments is that it is necessary to fragment stones into smaller pieces that fit through the narrower sheaths, leading to longer operating times compared to standard PNL, which allows removal of large stone fragments with forceps and baskets. Conversely, extraction of stone fragments seems to be facilitated by modified Amplatz sheaths, as fragments can be removed via vacuum suction, an effect that works best for tracts sized 13–18 Fr [41–43].

The idea behind downsizing PNL is based on the assumption of lower morbidity than for conventional PNL. However, there is still controversy regarding whether miniaturized tracts have only been confirmed in a few studies. Mishra et al [24] reported a slight but clinically significant advantage for 18 Fr compared to 26 Fr access. However, others could not confirm such a benefit [22]. The observation in many series that the rate of tubeless procedures is much higher than in conventional PNL series may support the idea of lower intraoperative bleeding, if it is assumed that a tubeless procedure is performed after uncomplicated access and stone removal [22,24]. In addition, a meta-analysis of tubeless versus standard PNL procedures [46] indicated that tubeless procedures led to shorter hospital stays, less postoperative pain, and possible quicker recovery, and may therefore contribute to lower morbidity in miniaturized PNL. However, most patients with so-called tubeless procedures received a double-J stent instead of a nephrostomy tube. As stent-related discomfort is common, this has to be taken into account and evaluated in future studies. Sealants are used in tubeless procedures, but their potential benefit remains controversial [47,48]. Complication rates for mPNL according to the Clavien-Dindo classification range from 11.9% to 37.7% [49,50]. Most complications in published series of were of low grade, with
higher rates of blood transfusion and arterial embolization in complex stone situations [51].

Identifying the right indications remains key in establishing the optimal use of miniaturized systems, but published outcomes are heterogeneous in terms of SFR and complication rates reported. Miniaturized PNL seems to be more effective for smaller rather than larger renal stones >20 mm [18,52]. The question arises whether miniaturized PNL may compete more with SWL and ureteroscopy (URS) than with conventional PNL. While most published series so far reported an advantage for percutaneous techniques over URS [53,54], De et al. recently published a meta-analysis comparing percutaneous stone removal with URS [51]. Although the overall SFR was in favor of PNL, subgroup analysis indicated that URS provided a significantly higher SFR rate than miniaturized systems. However, the same limitations as for the present analysis apply to their systematic review, with one of the major weaknesses being the inclusion of different tract sizes. De et al. concluded that URS should be recommended over minimally invasive PNL for stones sized <20 mm because of the generally lower morbidity of retrograde access. When compared to SWL, miniaturized PNL demonstrates higher SFR and a lower rate of auxiliary measures, although most data come from pediatric series that were not included in this systematic review [55–58]. On the basis of the current literature and experiences, downsized instruments may be used for stones in all locations accessible for standard PNL. The best indications seem to be medium stones of up to 20 mm, although there are no data to support an upper limit. In general, instruments should be adapted to the anatomy. Patients with tiny collecting systems may especially benefit from the use of smaller systems. Another potential indication might be stones located within calyceal diverticula. Future research should evaluate such issues.

Hemodynamic, electrolyte, and metabolic changes have been prospectively evaluated when comparing miniaturized with standard PNL [26]. Interestingly, a trend towards metabolic acidosis was observed in the mPNL group, possibly associated with prolonged operating time and higher intrarenal irrigation pressure. Tepeler et al. [28] measured intrarenal pelvic pressure during PNL procedures using 4.8 Fr nephroscopes in comparison to conventional PNL. Intrarenal pressure was significantly lower in the conventional group during all steps of the procedure. Even though there was no difference in outcome in their series, surgeons should be aware of higher pressure for downsized systems [36]. Placement of a ureteral catheter may be helpful for irrigation outflow to allow intermittent flushing [59].

It is sobering that even the simplest parameter, SFR, is generally difficult to compare because of different definitions of SFR with regard to the time until stone-free status is achieved and whether or not residual fragments are accepted, as well as the maximum fragment size allowable to justify classification as “clinically insignificant”. Furthermore, the imaging modality used to assess stone-free status varies, with most series using ultrasound or kidney/ureter/bladder X-ray (KUB), although CT is more sensitive for small residual fragments [60,61].

3.7.3. Implications for research
The concept of reducing the morbidity of PNL by downsizing the access tract seems convincing. The findings that success rates are high with miniaturized instruments demonstrate that the concept does not negatively impact the outcome. However, well-designed studies are missing and no conclusion can be drawn in terms of potentially lower morbidity.

3.7.4. Limitations
This review has several limitations. Many of the studies included may be affected by selection bias, outcome-reporting bias, and the use of different tract sizes. More than half of the studies were single-arm case series. For five of the studies, only abstracts were published, severely limiting the information available and its quality. Furthermore, the studies were heterogeneous in design, with differences in the size of tracts used in both the interventional and control arms (when available) and in the size and location of stones treated.

Many of the studies included also suffered from other important methodological limitations. Importantly, most of the studies on mPNL used single-step dilation, whereas conventional PNL procedures were performed with step or balloon dilatation, entailing different complication rates for bleeding, for example [62]. Moreover, most mPNL procedures were performed with low intrapelvic pressure, while standard PNL operations were much more frequently performed at high pressure, with implications for postoperative fever and sepsis, for example [63,64]. In addition, assessment of the postoperative SFR was obfuscated by the use of both less sensitive standard radiology (KUB) and significantly more sensitive CT [65]. Finally, many studies did not report statistical calculations of differences between interventional groups for the main outcome measures.

4. Conclusions
The available evidence indicates that mPNL is at least as efficacious and safe as standard PNL for the removal of renal calculi, with a limited risk of significant (Clavien grade ≥2) complications. However, the quality of the evidence was poor and drawn mainly from small studies, the majority of which were single-arm case series and NRCSs, and only two of which were RCTs. Hence, the risks of bias and confounding were high. Furthermore, the tract sizes used and the types of stones treated were heterogeneous. Thus, more reliable data from well-designed and adequately sampled and powered RCTs are warranted.

Author contributions: Thomas Knoll had full access to all the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

Study concept and design: Knoll, Türk, Ruhayel, Tepeler.
Acquisition of data: Knoll, Ruhayel, Tepeler, Yuan.
Analysis and interpretation of data: Knoll, Türk, Ruhayel, Tepeler.
Drafting of the manuscript: Knoll, Ruhayel, Tepeler, MacLennan, Yuan.
Critical revision of the manuscript for important intellectual content: Knoll, Türk, Ruhayel, Tepeler, Dabestani, MacLennan, Petfik, Skolarikos, Seitz, Straub, Yuan.
Statistical analysis: None.
Obtaining funding: None.
Administrative, technical, or material support: None.
Supervision: Knoll, Türk, Ruhayel, Dabestani.
Other: None.

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References


