The efficacy and safety of miniaturized percutaneous nephrolithotomy versus standard percutaneous nephrolithotomy: A systematic review and meta-analysis of randomized controlled trials

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Purpose: Our aim was to assess the efficacy and safety of miniaturized percutaneous nephrolithotomy (mPCNL) versus standard PCNL (sPCNL) to provide higher-level evidence.

Materials and Methods: Eligible randomized controlled trials were identified from electronic databases. The data analysis was performed by the Cochrane Collaboration's software RevMan 5.3.

Results: A total of 1,219 patients from 9 articles published between 2004 and 2019 were included. Compared with those who received sPCNL, patients who received mPCNL experienced a higher stone-free rate (SFR) (odds ratio [OR], 1.43; 95% confidence interval [CI], 1.03–1.99; p=0.03), lower transfusion rates (OR, 0.33; 95% CI, 0.17–0.63; p=0.0007), and lower drops in hemoglobin (mean difference [MD], -0.72; 95% CI, -1.04 to -0.40; p<0.0001), but the operative time seemed to be significantly longer (MD, 10.98; 95% CI, 3.64–18.32; p=0.003). Of note, there was no significant difference between the two groups regarding the SFR (p=0.09) for renal calculi ≥2 cm. In addition, the meta-analysis results showed no significant differences between the groups regarding urine leakage (p=0.60), postoperative fever (p=0.71), impaired ventilation (p=0.97), or total complications (p=0.29) with no heterogeneity between trials. These results remain unaffected with regard to renal calculi ≥2 cm.

Conclusions: Our findings suggested that mPCNL had a higher SFR than sPCNL and there was no significant difference between the two groups for renal stones ≥2 cm. Besides, mPCNL tended to be associated with significantly less bleeding and a lower transfusion rate, but the duration of the procedure seemed to be significantly longer.

Keywords: Meta-analysis; Minimally invasive surgical procedures; Nephrolithotomy, percutaneous; Randomized controlled trial
INTRODUCTION

At present, the primary treatment modalities for urinary stones include extracorporeal shock wave lithotripsy (ESWL), rigid ureteroscopy (RUS), flexible ureteroscopy (FUS), percutaneous nephrolithotomy (PCNL), and laparoscopic and open surgery. Among these approaches, PCNL is regarded as the first-line treatment for renal stones larger than 2 cm owing its higher stone clearance and cost-effectiveness compared with other treatment alternatives such as ESWL and FUS [1]. However, PCNL has potentially higher rates of blood loss and postoperative pain because of the larger nephrostomy tract [2]. In this scenario, Jackman et al. [3] first proposed the concept and technique of miniaturized PCNL (mPCNL), which is defined as the procedure conducted by forming a ≤22 Fr nephrostomy tract [1]. In recent years, modifications of PCNL have continued with the introduction of micro-PCNL, ultra-mPCNL, and super mPCNL techniques [4].

Currently, whether mPCNL is an equivalent alternative to standard PCNL (sPCNL) remains controversial. A previous meta-analysis [5] concluded that mPCNL results in less bleeding, fewer transfusions, less pain, shorter lengths of hospitalization, and comparable stone-free rates (SFRs) compared with sPCNL. Nevertheless, most of the studies were nonrandomized comparisons and only three randomized controlled trials (RCTs) were available. In addition, heterogeneity among studies was found to be high for several parameters. Thus, we performed this meta-analysis of RCTs to assess the efficacy and safety of mPCNL compared with sPCNL to provide higher-level evidence.

MATERIALS AND METHODS

1. Search results

Electronic databases were searched from inception to October 2019 using PubMed, the Cochrane Library, Embase,
and WANFANG in accordance with the PRISMA guidelines [6] with no limitations as to the language. Related articles were also retrieved by manual searching. All studies reporting the outcomes of interest were included. Informed consent was obtained from all individual participants included in the study. The detailed search strategy is shown in Supplementary material.

2. Data extraction

Studies were considered eligible if they met the following criteria: 1) RCT, 2) comparing mPCNL to sPCNL, 3) reporting at least one outcome of interest mentioned below, and 4) including related data (either reported or could be calculated). Exclusion criteria were as follows: 1) nephrostomy tract size in mPCNL >20 Fr, 2) non-RCT studies or reviews, 3) trials not available, and 4) data not available.

The following outcomes were extracted. Demographic data and stone characteristics: age, sex, body mass index (BMI), stone size, hydronephrosis, and operation side; operative data: operative time; complications and postoperative outcomes: SFR, hospitalization time, hemoglobin drop, blood transfusion rate, fever, impaired ventilation, urine leakage, and total complication rate.

The primary outcomes were SFR, hemoglobin drop, and blood transfusion rate. The secondary outcomes were operative time, hospitalization time, fever, impaired ventilation, urine leakage, and total complication rate.

3. Quality assessment

Two independent reviewers (DCF, XH) evaluated the study quality (Fig. 1) according to the Cochrane Collaboration’s Risk of Bias tool in the Review Manager software (https://community.cochrane.org/help/tools-and-software/revman-5) [4,7-14]. This tool primarily evaluates seven domains: random sequence generation (selection bias), allocation concealment (selection bias), blinding of participants and personnel (performance bias), blinding of outcome assessment (detection bias), incomplete outcome data (attrition bias), selective reporting (reporting bias), and other bias (such as funding sources). Three independent investigators (DCF, XH, and YT) screened the study based on titles and abstracts. Studies that satisfied the inclusion criteria were retrieved for full-text assessment. Data were independently extracted by two reviewers (DCF, XH). Disagreements were resolved by another researcher (XW). The manuscript was revised by the reviewer (PH).

4. Statistical analysis

Data are presented as means and standard deviations (SDs). Median and range were used to estimate mean and SD.
Table 1. The baseline characteristics of the included studies

| Study ID          | Sample size | Country | Duration       | Population                      | Access sheath size | Dilator          | Lithotripsy            |
|-------------------|-------------|---------|----------------|---------------------------------|--------------------|-------------------|------------------------|
| Cheng et al. [11] | 187         | China   | 2004–2007      | NA                              | M: 16 Fr, S: 24 Fr | M: TMD            | M: pneumatic          |
| Zhong et al. [9]  | 54          | China   | 2008–2009      | Staghorn calculi                 | M: 16 Fr, S: 26 Fr | M: FD             | N: ultrasound+pneumatic |
| Song et al. [8]   | 60          | China   | 2008–2009      | Renal stones ≥2.0 cm             | M: 16 Fr, S: 24 Fr | M: FD, S: FD      | M: pneumatic, N: pneumatic |
| Haghighi et al.   | 70          | Iran    | 2016–2017      | Renal or upper ureteric stones: 10–20 mm | M: 16 Fr, S: 30 Fr | M: FD, S: “one shot” dilatation | M: pneumatic, N: pneumatic |
| Güler et al. [4]  | 97          | Turkey  | 2016–2017      | Renal stones ≥2.0 cm             | M: 16.5 Fr or 20 Fr, S: 30 Fr | M: AD, S: balloon dilator or AD | M: laser, N: ultrasound+pneumatic |
| Kandemir et al.   | 148         | Turkey  | 2016–2018      | Renal stones ≥2.0 cm             | M: 16.5 Fr or 20 Fr, S: 31 Fr | M: balloon dilator or AD, S: balloon dilator or AD | Laser, ultrasound or pneumatic |
| Wang et al. [13]  | 168         | China   | 2006–2010      | NA                              | M: 18 Fr, S: 24 Fr | NA                | NA                     |
| Tian et al. [10]  | 96          | China   | 2008–2010      | Renal stones >2.5 cm             | M: 18 Fr, S: 24 Fr | M: FD, S: FD      | M: pneumatic, N: pneumatic |
| Zhou [14]         | 71          | China   | 2013.1–2013.12 | Renal stones: 1.3–5.9 cm         | M: 18 Fr, S: 24 Fr | M: FD, S: FD      | M: pneumatic, N: pneumatic |

NA, not available; M, minimally invasive percutaneous nephrolithotomy; TMD, telescoping metal dilators; S (or N), standard percutaneous nephrolithotomy; FD, fascial dilators; AD, Amplatz dilators.
The percentiles, 25th and 75th percentiles as well as 5th and 95th percentiles, were transformed to SD by use of the following formula: SD≈Norm IQR=(P75-P25)×0.7413 (where IQR is interquartile range, P75 is 75th percentile, and P25 is 25th percentile) [16]. Continuous and dichotomous variables were described as means±SD and proportions, respectively.

We calculated pooled estimates of the mean difference (MD) or standard MD (SMD) and odds ratios (ORs) for continuous and dichotomous variables, respectively. We used the Cochran Q test to evaluate between-study heterogeneity [17]. We also did I² testing to assess the magnitude of the heterogeneity with values ≤50% regarded as being of acceptable heterogeneity [18]. The random effects model was used when the trials yielded heterogeneous (p<0.1) results. Otherwise, the fixed effects model was used. Significance was set at p<0.05.

We thought that the relatively small stone size in this study may have been the cause. The patients in this study had renal or upper ureteric stones of 10 to 20 mm in diameter.

### RESULTS

#### 1. Search results

The initial search yielded 1,219 potential studies and 9 RCTs [4,7-14], including 470 mPCNL cases and 481 sPCNL cases that were included in the final meta-analysis after duplicates were removed, titles and abstracts screened, and full-text articles assessed. The study selection process is shown in Fig. 2 [19].

Only 2 [4,7] of the 9 RCTs [4,7-14] described pelvic stones and multiple calyx stones. Five RCTs [4,7-10] compared mPCNL with sPCNL for patients with renal calculi ≥2 cm. Table 1 details the baseline characteristics of the included studies [4,7-14].

#### 2. Demographic data and stone characteristics

There were no significant differences with regard to age, proportion of males, BMI, stone size, hydronephrosis, or operation side, with no statistically significant p-values and no significant between-study heterogeneity. These results are shown in Table 2.

#### 3. Primary outcomes

Patients receiving mPCNL experienced a higher SFR (OR, 1.43; 95% CI, 1.03–1.99; p=0.03) and lower transfusion rates (OR, 0.33; 95% CI, 0.17–0.63; p=0.0007) compared with their counterparts in the sPCNL group. In addition, the hemoglobin drop was lower in the mPCNL group (MD, -0.72; 95% CI, -1.04 to -0.40; p<0.00001) with moderate heterogeneity between the trials (I²=68%). The trial of Haghighi et al. [12] seemed to be the source of the heterogeneity. The hemoglobin drop was still lower in the mPCNL group (MD, -0.53; 95% CI, -0.71 to -0.36; p<0.00001) after the exclusion of this study, which resulted in no heterogeneity between trials (I²=0%).

#### 4. Secondary outcomes

Compared with sPCNL, operative time was longer in the mPCNL group (MD, 10.98; 95% CI, 3.64–18.32; p=0.003) and there was no significant difference between mPCNL and sPCNL with regard to hospitalization time (SMD, -0.24; 95% CI, -0.75 to 0.27; p=0.35).

However, both results showed high heterogeneity. Surgeon experience and hospital regulations for hospitalization may have been the cause of the heterogeneity in operative time and hospitalization time, respectively.

The results of the meta-analysis showed no significant differences between the groups regarding urine leakage (OR,
The primary outcomes

A Stone-free rate

| Study or subgroup | mPCNL Events Total | sPCNL Events Total | Weight | Odds ratio M–H, fixed, 95% CI | Odds ratio M–H, fixed, 95% CI |
|------------------|---------------------|---------------------|--------|-----------------------------|-----------------------------|
| Cheng et al. [11] (2010) | 61 72 | 92 115 | 18.2% | 1.39 [0.63, 3.05] | 
| Güer et al. [4] (2019) | 39 51 | 33 46 | 13.7% | 1.28 [0.51, 3.18] | 
| Haghghi et al. [12] (2017) | 33 35 | 33 35 | 3.2% | 1.00 [0.13, 7.53] | 
| Kandemir et al. [7] (2020) | 57 76 | 52 72 | 22.5% | 1.15 [0.56, 2.40] | 
| Song et al. [8] (2011) | 27 30 | 22 30 | 3.7% | 3.27 [0.77, 13.83] | 
| Tian et al. [10] (2011) | 40 56 | 29 40 | 16.3% | 0.95 [0.38, 2.34] | 
| Wang et al. [13] (2011) | 76 86 | 67 82 | 13.4% | 1.70 [0.72, 4.04] | 
| Zhong et al. [9] (2011) | 24 29 | 14 25 | 4.4% | 3.77 [1.09, 13.11] | 
| Zhou [14] (2014) | 32 35 | 33 36 | 4.7% | 0.97 [0.18, 5.16] | 
| Total (95% CI) | 470 481 | 100.0% | 1.43 [1.03, 1.99] | 
| Total events | 389 375 | | | |

Heterogeneity: Chi²=5.26, df=8 (p=0.73); I²=0%
Test for overall effect: Z=2.14 (p=0.03)

B Hemoglobin drop

| Study or subgroup | mPCNL Mean SD Total | sPCNL Mean SD Total | Weight | Mean difference IV, random, 95% CI | Mean difference IV, random, 95% CI |
|------------------|---------------------|---------------------|--------|------------------------------------|------------------------------------|
| Cheng et al. [11] (2010) | 0.53 0.79 72 0.97 1.42 115 | 23.6% | −0.44 [−0.76, −0.12] | 
| Güer et al. [4] (2019) | 1.35 1.11 51 2.07 1.59 46 | 15.9% | −0.72 [−1.27, −0.17] | 
| Haghghi et al. [12] (2017) | 1.65 1.2 35 3.13 1.06 35 | 16.5% | −1.48 [−2.01, −0.95] | 
| Kandemir et al. [7] (2020) | 0.7 1.3 76 1.4 1.5 72 | 18.9% | −0.70 [−1.15, −0.25] | 
| Zhong et al. [9] (2011) | 3.2 0.45 29 3.7 0.55 25 | 25.2% | −0.50 [−0.77, −0.23] | 
| Total (95% CI) | 263 293 | 100.0% | −0.72 [−1.04, −0.40] | 
| Total events | 415 293 | | | |

Heterogeneity: Tau²=0.08; Chi²=12.32, df=4 (p=0.02); I²=68%
Test for overall effect: Z=4.48 (p<0.0001)

C Blood transfusion rate

| Study or subgroup | mPCNL Events Total | sPCNL Events Total | Weight | Odds ratio M–H, fixed, 95% CI | Odds ratio M–H, fixed, 95% CI |
|------------------|---------------------|---------------------|--------|-----------------------------|-----------------------------|
| Cheng et al. [11] (2010) | 1 72 | 12 115 | 25.0% | 0.12 [0.02, 0.95] | 
| Güer et al. [4] (2019) | 1 51 | 7 46 | 19.8% | 0.11 [0.01, 0.94] | 
| Haghghi et al. [12] (2017) | 2 35 | 4 35 | 10.4% | 0.47 [0.08, 2.75] | 
| Kandemir et al. [7] (2020) | 2 76 | 4 72 | 11.0% | 0.46 [0.08, 2.59] | 
| Tian et al. [10] (2011) | 5 56 | 3 40 | 8.8% | 1.21 [0.27, 5.38] | 
| Wang et al. [13] (2011) | 2 86 | 6 82 | 16.5% | 0.30 [0.06, 1.54] | 
| Zhong et al. [9] (2011) | 1 29 | 3 25 | 8.5% | 0.26 [0.03, 2.69] | 
| Total (95% CI) | 405 415 | 100.0% | 0.33 [0.17, 0.63] | 
| Total events | 14 39 | | | |

Heterogeneity: Chi²=5.16, df=6 (p=0.52); I²=0%
Test for overall effect: Z=3.39 (p=0.0007)

Fig. 3. (A–I) The pooled results of the primary and secondary outcomes. mPCNL, miniaturized percutaneous nephrolithotomy; sPCNL, standard percutaneous nephrolithotomy; M–H, Mantel–Haenszel; CI, confidence interval; IV, inverse variance.

0.69; 95% CI, 0.17–2.75; p=0.60), postoperative fever (OR, 1.10; 95% CI, 0.68–1.78; p=0.71), impaired ventilation (OR, 1.03; 95% CI, 0.28–3.78; p=0.097), or total complication rate (OR, 0.74; 95% CI, 0.43–1.29; p=0.29) with no heterogeneity between trials. The pooled results of the primary and secondary outcomes are summarized in Fig. 3 [4,7-14].

5. Pelvic stones and multiple calyx stones

Only two RCTs [4,7] were available for meta-analysis regarding pelvic stones and multiple calyx stones. There was no significant difference between the groups with regard to operative time (p=0.06) or SFR (p=0.57) for pelvic stones. For multiple calyx stones, the mPCNL group seemed to have a longer operative time (MD, 3318; 95% CI, 4.41–21.95; p=0.003) compared with the sPCNL group and there was no significant difference between mPCNL and sPCNL regarding the SFR (OR, 1.48; 95% CI, 0.69–3.18; p=0.32). The pooled results for pelvic stones and multiple calyx stones are also shown in
6. Renal calculi $\geq 2$ cm

Five RCTs [47-50] were available for meta-analysis with regard to renal calculi $\geq 2$ cm. The mPCNL group had a longer operative time (MD, 12.26; 95% CI, 1.39–23.13; p=0.03), lower transfusion rate (OR, 0.42; 95% CI, 0.18–0.97; p=0.04), and lower hemoglobin drop (MD, 0.58; 95% CI, 0.79 to 0.36; p=0.00001) compared with the sPCNL group. There were no significant differences between the groups regarding the SFR (OR, 1.45; 95% CI, 0.95–2.20; p=0.09), hospitalization time, postoperative fever, impaired ventilation, or total complication rate. The meta-analysis results of renal calculi $\geq 2$ cm are shown in Fig. 4 [47-50].

DISCUSSION

Urolithiasis is one of the most common diseases in urol-
The prevalence rates for urinary stones vary from 1% to 20% depending on geographic, climatic, ethnic, dietary, and genetic factors [1]. Traditional open or laparoscopic stone surgery is gradually being replaced by minimally invasive techniques owing to the greater trauma and complications of the former surgical methods. Currently, PCNL is recommended as the standard procedure for large renal calculi [1]. The first PCNL was completed in 1976 by Fernström and Johansson (requoted from reference [21]). However, because the nephrostomy tract reached 30 Fr at that time, it was traumatic and dangerous, and complications such as severe bleeding often occurred. For these reasons, mPCNL came into being [3].

At present, there is no accurate definition of the access tracts for mPCNL and sPCNL. There is a consensus that standard access tracts are 24 to 30 Fr and miniaturized access tracts are smaller than 22 Fr [1]. Recently, smaller renal access sheaths including micro-PNL (4.5 Fr outer sheath), ultra-mPNL (7.5 Fr nephroscope and 11–13 Fr outer sheath), and super-mPNL (7.5 Fr nephroscope and modified 10–14 Fr outer sheath) techniques have been introduced as alternative procedures to decrease the operation-related morbidities [4]. However, whether mPCNL is a comparable alternative to sPCNL remains controversial. A previous meta-analysis [5] included only 3 RCTs and the results were not very stable or reliable. Thus, our meta-analysis of RCTs was warranted to confirm and update the conclusions.

Unlike the previous study [5], the results of our study suggested that the mPCNL group had a higher SFR than the sPCNL group. However, the SFR was not significantly different between groups with regard to renal calculi ≥2 cm. As for pelvic stones and multiple calyx stones, we cannot reach a conclusion owing to the limited number of RCTs. We believe that mPCNL can be carefully manipulated by...
tiny operating instruments, such as RUS, the pneumatic lithotripter, and holmium laser lithotripsy [22], and mPCNL is more prone to bleeding, which affects the surgical field and increases the operative risk. Therefore, mPCNL may be more suitable than sPCNL for kidney stones <2 cm.

Tract size is one of the crucial factors determining bleed-

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**Fig. 4.** (A–H) Results of the meta-analysis of renal calculi ≥2 cm. Complications were stratified by the Clavien–Dindo system into minor (grade 1–2) and major (grade 3–5) complications [20]. mPCNL, miniaturized percutaneous nephrolithotomy; sPCNL, standard percutaneous nephrolithotomy; M–H, Mantel–Haenszel; CI, confidence interval; IV, inverse variance.
ing during PCNL [2]. It is easy to understand that mPCNL results in less blood loss and a lower transfusion rate than sPCNL owing to less renal parenchymal and renal vasculature damage [23]. On the other hand, mPCNL has the disadvantage of a more restricted visual field with the miniature endoscopes and the need to break the stones into smaller fragments for their removal through the smaller tract [5]. Thus, operative time was longer in the mPCNL group than in the sPCNL group. Despite these significant differences, our pooled analysis showed no significant differences between the groups regarding hospitalization time.

We conducted a meta-analysis of postoperative complications, including fever, impaired ventilation, and urine leakage. The results suggested that there were no significant differences between mPCNL and sPCNL. A systematic review including almost 12,000 patients disclosed the following incidences of complications in PCNL: fever, 10.8% transfusion, 7% thoracic complications, 15% and sepsis, 0.5% [1,24]. Among these complications, perioperative fever can occur, even with a sterile preoperative urinary culture and perioperative antibiotic prophylaxis, because the kidney stones themselves may be a source of infection [1].

The present study did have the following limitations. First, the sample size of the studies included was relatively small and might not have achieved sufficient power to make a definitive conclusion. Second, heterogeneity between trials was high for several outcomes. This may have been caused by the broad heterogeneity in study populations, designs, and definitions of outcome measures. Finally, we were unable to assess the impact of surgical history, stone location, type, and number of tracts on surgical outcomes. In addition, we also were unable to decide on the optimal tract size.

| Study or subgroup | mPCNL | sPCNL | Weight |
|------------------|-------|-------|--------|
| Güler et al. [4] (2019) | 48 | 26.3 | 51 | 68.8 | 43.2 | 46 | 33.9% | ~0.53 [-0.93, -0.12] |
| Kandemir et al. [7] (2020) | 64.3 | 36.5 | 76 | 75.5 | 34 | 72 | 35.0% | -0.32 [-0.64, 0.01] |
| Zhong et al. [9] (2011) | 9.8 | 1.75 | 29 | 8.05 | 1.5 | 25 | 31.1% | 1.05 [0.48, 1.63] |
| Total (95% CI) | 156 | 143 | 100.0% | 0.04 [-0.76, 0.83] |

Test for overall effect: Z=0.09 (p=0.92)

| Study or subgroup | mPCNL | sPCNL | Weight |
|------------------|-------|-------|--------|
| Güler et al. [4] (2019) | 1 | 51 | 0 | 46 | 4.2% | 2.76 [0.11, 69.50] |
| Kandemir et al. [7] (2020) | 0 | 76 | 2 | 72 | 21.1% | 0.18 [0.01, 3.91] |
| Song et al. [8] (2011) | 3 | 30 | 4 | 30 | 29.7% | 0.72 [0.15, 3.54] |
| Tian et al. [10] (2011) | 15 | 56 | 3 | 40 | 21.2% | 4.51 [1.21, 16.64] |
| Zhong et al. [9] (2011) | 3 | 29 | 3 | 25 | 23.9% | 0.85 [0.15, 4.62] |
| Total (95% CI) | 242 | 213 | 100.0% | 1.53 [0.74, 3.15] |

Test for overall effect: Z=1.14 (p=0.25)

| Study or subgroup | mPCNL | sPCNL | Weight |
|------------------|-------|-------|--------|
| Güler et al. [4] (2019) | 0 | 51 | 1 | 46 | 38.1% | 0.29 [0.01, 7.41] |
| Kandemir et al. [7] (2020) | 1 | 76 | 2 | 72 | 49.5% | 0.47 [0.04, 5.26] |
| Zhong et al. [9] (2011) | 1 | 29 | 0 | 25 | 12.4% | 2.68 [0.10, 68.87] |
| Total (95% CI) | 156 | 143 | 100.0% | 0.68 [0.15, 3.09] |

Test for overall effect: Z=0.50 (p=0.61)
CONCLUSIONS

Our findings suggested that mPCNL had a higher SFR than sPCNL and there was no significant difference between the two groups regarding renal stones ≥2 cm. Besides, mPCNL tended to be associated with significantly less bleeding and a lower transfusion rate, but the duration of the procedure seemed to be significantly longer. There were no significant differences in other complications, such as postoperative fever, urine leakage, or impaired ventilation. Further research is needed to assess the impact of surgical history, stone location, type, and number of tracts on surgical outcomes and to determine the optimal tract size.

CONFLICTS OF INTEREST

The authors have nothing to disclose.

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AUTHORS’ CONTRIBUTIONS

Research conception and design: Dechao Feng. Data analysis and interpretation: Dechao Feng, Xiao Hu, and Yin Tang. Drafting of the manuscript: Dechao Feng. Critical revision of the manuscript: Xin Wei. Obtaining funding: Ping Han and Yin Tang. Administrative, technical, or material support: Ping Han. Supervision: Ping Han. Approval of the final manuscript: Xin Wei.

SUPPLEMENTARY MATERIAL

Scan this QR code to see the supplementary material, or visit https://www.icurology.org/src/sm/icurology-61-115-s001.pdf.

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