



# Mini-percutaneous nephrolithotomy for pediatric complex renal calculus disease: one-stage or two-stage?

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## Abstract

**Objectives** To compare two different treatment strategies, one-stage and two-stage multi-tract mini-percutaneous nephrolithotomy (mt-mPCNL), for pediatric complex renal calculus disease.

**Methods** Between the period of July 2016 and July 2018, a total of 36 children aged 15 years and younger, with complex renal calculi disease, who underwent total ultrasound-guided mt-mPCNL by a single experienced urologist were enrolled in our study. All patients were assigned either to Group 1 ( $n = 18$ ) who received one-stage mt-mPCNL or Group 2 ( $n = 18$ ) who received planned two-stage mt-mPCNL.

**Results** The demographic data were comparable between the two groups. There were no serious complications (Modified Clavien Grade  $\geq$  III) observed in either group. The stone-free rate (SFR), operation time, postoperative creatinine increase, and perioperative complication rates were similar in both groups ( $P = 0.603, 0.818, 0.161,$  and  $0.402$ , respectively). The postoperative hospital stay (5.8 days vs. 7.4 days) and cost (17373.3 CNY vs. 23717.1 CNY) were statistically less in Group 1. Group 2 had significantly less total estimated blood loss (70.6 ml vs. 130.0 ml,  $P < 0.001$ ). The operation time of two cases in Group 1 with perioperative sepsis or systemic inflammatory response syndrome (SIRS) was more than two hours.

**Conclusions** Our preliminary results indicated that both one-stage and two-stage mt-mPCNL were safe and effective for pediatric complex renal calculi. Two-stage mt-mPCNL could significantly reduce blood loss; while one-stage mt-mPCNL could significantly decrease the length and costs of hospitalization. We also suggest that the planned two-stage mt-mPCNL should be applied in children with estimated operation time more than two hours.

**Keywords** Multi-tract · Pediatric nephrolithiasis · Percutaneous nephrolithotomy · Staging operation · Ultrasound-guided

## Introduction

Pediatric nephrolithiasis is an important health problem, and some surveys have shown that its incidence rate has been steadily increasing over the past several decades due to the changes of dietary habits, environmental factors, and the prevalence of obesity [1–3]. The pediatric complex renal calculus disease, defined as staghorn stone, multiple caliceal calculi, or those associated with urological anatomical abnormalities, provide the most difficult challenge to urologists. Presently, although extracorporeal shock wave

lithotripsy (ESWL) is considered as the first-line treatment for pediatric urolithiasis, percutaneous nephrolithotomy (PCNL) has been successfully applied in treating pediatric renal stones, especially the large, hard, and complex renal calculus [4, 5]. Furthermore, some previous surveys have shown that mini-PCNL (mPCNL), compared with the standard PCNL, could decrease the injuries to the renal parenchyma and intrarenal vessels by using smaller working sheath (14–20F) [5, 6].

In order to remove staghorn stone or multiple caliceal calculus, multi-tract PCNL (mt-PCNL) with multiple accesses via different calyces is required, since it is very difficult to enter the entire collecting system filled with calculus through any single PCNL tract [7]. However, due to a fragile kidney, small pelvicalyceal system and limited blood volume, urologists are reluctant to perform mt-PCNL in children. Zhao et al. [7] compared one-stage with planned two-stage mt-mPCNL for the treatment of staghorn stones in adult

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patients, but to the best of our knowledge, there is no article referring to the comparison of these two treatment strategies in pediatric patients with complex renal calculus (staghorn stone and complex multiple caliceal calculus). In our present study, we compared the outcomes of one-stage and planned two-stage mt-mPCNL for the treatment of complex stones in children and evaluated which one could achieve better result and less morbidity.

## Patients and methods

### Study population

Ethical approval of this study protocol was granted by our institutional Ethics and Research committee. Written informed consent was obtained from the parents of all pediatric patients included in our study. Between the period of July 2016 and July 2018, a total of 36 Chinese children (36 renal units), aged 15 years or younger, with staghorn stones or multiple caliceal calculi who underwent one-stage (Group 1,  $n = 18$ ) or intended two-stage (Group 2,  $n = 18$ ) mt-mPCNL were enrolled into our prospective study. We divided the patients into different groups according to their parents' choices of which treatment strategy (one-stage or two-stage mt-mPCNL) they preferred their children to receive after they understood the purpose of our study. Multiple caliceal calculi were defined as stones distributed in at least two calyces which could not be removed through a single percutaneous tract; and the largest diameter or the added diameters of residual stones were approaching or exceeding 2 cm after removing stones from the first tract. The exclusion criteria were patients with moderate to severe anemia (hemoglobin  $< 90$  g/l), ectopic pelvic kidney, or severe scoliosis. All procedures were performed by a single experienced pediatric urologist under general anesthesia. All 36 participants underwent routine preoperative examination including peripheral blood cell count, serum creatinine, urine analysis, urine culture, coagulation tests, and non-contrast computed tomography (CT). We measured the length and width of the stones to calculate the stone surface area (SA); the length of stone was measured by surveying the largest diameter or summing the diameters of multiple stones on CT. The width was defined as the second largest diameter of the stones. We used the formula " $SA = \text{length} * \text{width} * \pi * 0.25$ " ( $\pi = 3.14159$ ) to calculate the stone SA. According to the antibiogram, antibiotics were administered preoperatively to all patients with positive urine culture in both groups until the culture became negative. The other patients with negative urine culture received a single dose of intravenous broad spectrum antibiotic prophylaxis 30 min before their procedures.

### Surgical technique

A 3-Fr or 4-Fr ureteral catheter was inserted into the ureter of the affected side without fluoroscopy to achieve artificial hydronephrosis during renal puncture. The patient was then turned into a prone position and the renal region was elevated after retro-urethral catheterization. In order to reduce or avoid the side effects of ionizing radiation exposure in pediatric patients and doctors intraoperatively, we applied fluoroscopic-free ultrasonography-guided mt-mPCNL procedures. Under ultrasound (GE LOGIQ e; GE Healthcare, Milwaukee, WI) guidance, a gauge coaxial needle was used to puncture the targeted calyx in all cases, after which a guidewire was inserted into the calyx through the needle. Guided by the wire, serial fascial dilators were introduced to accomplish the access until an 18 Fr peelable sheath as the working sheath was placed. The posterior intermediate calyx was the most common first access. A 9.5 Fr semi-rigid ureteroscope (Karl Storz Endoscopes, Germany) was used for endoscopy. The stones within the field of vision were fragmented by pneumatic (Swiss LithoClast; Electro Medical Systems, Nyon, Switzerland) and/or holmium: YAG laser lithotripter (VersaPulse PowerSuite 100 W; Lumenis, Santa Clara, CA), then the fragments were extracted with forceps or irrigated out through the first working sheath. We considered the residual stone(s) with the largest diameter or the added diameters approaching or exceeding 2 cm, or with very hard texture or located in lower renal calyx or in the calyx with narrow infundibula despite the stones' diameter less than 2 cm, which could not be removed through the first percutaneous tract, should be removed in the second-stage mt-mPCNL. In these cases, mt-mPCNL instead of ESWL or RIRS was our prior choice. The additional tracts (16–18 Fr) were then established in the same way to remove the residual stone in the same stage (Group 1) or in a consecutive stage with 4–6 days of interval (Group 2). At no time was bilateral PCNL performed in one session. Finally, a 4.7–6 Fr double-J stent and nephrostomy tube(s) were placed. We removed the ureteric catheter and placed a double-J stent and a nephrostomy tube at the end of the first stage in Group 2; however, we did not replace the double-J stent in the second stage. In Group 2, the nephrostomy tube of the first stage was kept for 4–6 days until the second look in consecutive stage.

The operation time was calculated from the first renal puncture to the placement of nephrostomy tube(s). The removal of nephrostomy tubes and double-J stent was performed in a standardized manner introduced by Xiao et al. [8]. Each child in both groups received non-contrast CT at 4 weeks post-mt-mPCNL; stone free was defined as either no presence of any residual stone or with clinically

insignificant residual fragments  $\leq 4$  mm in diameter on the CT. In Group 2, we defined the operation time and estimated blood loss as sum of those in first- and second-stage, respectively. Modified Clavien classification system [9] was applied to grade the perioperative complications.

We suggested that the mt-mPCNL needed to be aborted when the following conditions presented: firstly, an episode of intraoperative severe sepsis or septic shock; secondly, severe uncontrollable bleeding during surgery; thirdly, patients with infection, obstruction, or renal insufficiency who should be firstly treated in staging operation to improve function and drainage.

### Statistical analysis

The results were expressed as mean  $\pm$  SD or percentage; Student's *t* test, Chi-square test, and Fisher's exact probability test were used for comparison between the two groups. All data were analyzed using the statistical software package SPSS13.0 (SPSS Inc., Chicago, IL). A *P* value  $< 0.05$  was considered statistically significant for all tests.

### Results

All 36 children, who underwent one-stage (Group 1,  $n = 18$ ) or two-stage (Group 2,  $n = 18$ ) total ultrasound-guided mt-mPCNL, were included in the final analysis. No surgical procedure in our study was terminated. The demographic characteristics of the children in both groups are shown in Table 1, including the mean age of the children when they

received mt-mPCNL (9.4 years vs. 9.5 years), the mean surface area of the stone ( $6.06 \text{ cm}^2$  vs.  $5.96 \text{ cm}^2$ ), the percentage of preoperative positive urine culture (22.2% vs. 16.7%), and the percentage of staghorn stone (55.6% vs. 50%). No significant difference was observed between the two groups ( $P = 0.965, 0.929, 1.000$  and  $0.738$ , respectively). There was only one child with previous history of open surgery in each group (5.6% vs. 5.6%,  $P = 1.000$ ).

The intraoperative and postoperative details in both groups are presented in Table 2. Among all 36 patients, only one patient (5.6%) in Group 1 was rendered three nephrostomy tracts; the other 17 children (94.4%) in Group 1 and all cases (100%) in Group 2, required two tracts for mt-mPCNL. The total estimated blood losses were  $130.0 \pm 30.5$  ml in Group 1 and  $70.6 \pm 18.3$  ml in Group 2, respectively, with significant difference across the groups ( $P < 0.001$ ). However, the average hospital stay (5.8 days vs. 7.4 days,  $P = 0.001$ ) and costs (17373.3 CNY vs. 23717.1 CNY,  $P < 0.001$ ) were statistically more in Group 2 than in Group 1. There were no significant differences in mean operation time (81.4 min vs. 80.0 min,  $P = 0.818$ ) and creatinine increase ( $5.22 \mu\text{mol/l}$  vs.  $4.64 \mu\text{mol/l}$ ,  $P = 0.161$ ). The stone-free rate (SFR) in Group 2 (94.4%) was higher than that in Group 1 (83.3%), although there was no significant differences between the groups ( $P = 0.603$ ). Auxiliary procedures for residual stones or fragments were as follows: one patient in each group successfully had retrograde intrarenal surgery (RIRS). In Group 1, one patient had residual stones which were located in the anterior calyces with very narrow infundibula which could not be accessed; another one refused any auxiliary procedures due to economic reasons.

**Table 1** Characteristics of pediatric patients in both groups

Parameters	Group 1 (one-stage)	Group 2 (two-stage)	<i>P</i> value
Renal units (patients) ( <i>n</i> )	18 (18)	18 (18)	–
Age, years, mean $\pm$ SD (range)	$9.4 \pm 3.1$ (4–15)	$9.5 \pm 3.1$ (3–15)	0.965
Gender, male/female ( <i>n</i> )	10/8	7/11	0.317
Stone laterality, right/left ( <i>n</i> )	9/9	8/10	0.738
Stone size, $\text{cm}^2$ , mean $\pm$ SD (range)	$6.06 \pm 2.91$ (1.60–11.07)	$5.96 \pm 2.70$ (1.76–10.30)	0.929
Positive urine culture, <i>n</i> (%)	4 (22.2)	3 (16.7)	1.000
Previous open surgery, <i>n</i> (%)	1 (5.6)	1 (5.6)	1.000
Preoperative creatinine ( $\mu\text{mol/l}$ ), mean $\pm$ SD (range)	$49.68 \pm 6.98$ (39.7–62.5)	$48.70 \pm 4.77$ (42.1–59.2)	0.598
Impaired preoperative creatinine, <i>n</i> (%)	0 (0)	0 (0)	–
Type of stone			0.738
Staghorn stone, <i>n</i> (%)	10 (55.6)	9 (50.0)	
Multiple calyces, <i>n</i> (%)	8 (44.4)	9 (50.0)	
Two calyces, <i>n</i> (%) <sup>a</sup>	5 (27.8)	7 (38.9)	
More than two calyces, <i>n</i> (%) <sup>b</sup>	3 (16.7)	2 (11.1)	

A statistically significant *P* value was defined as  $< 0.05$

<sup>a</sup>The residual stones located in a single calyx after removing stones from the first tract

<sup>b</sup>The residual stones distributed in more than one calyx after removing stones from the first tract

**Table 2** Intraoperative and postoperative details in both groups

Parameters	Group 1 (one-stage)	Group 2 (two-stage)	<i>P</i> value
Renal units (patients) ( <i>n</i> )	18 (18)	18 (18)	–
Operation time, min, mean ± SD (range)	81.4 ± 25.3 (50–140)	80.0 ± 11.8 (60–100)	0.818
Total tracts in one renal unit, <i>n</i> (%)			1.000
Two	17 (94.4)	18 (100)	
Three	1 (5.6)	0 (0)	
Supracostal puncture, <i>n</i> (%)	5 (27.8)	4 (22.2)	1.000
Lithotripsy technology			1.000
Pneumatic lithotripsy, <i>n</i> (%)	3 (16.7)	2 (11.1)	
Laser lithotripsy, <i>n</i> (%)	14 (77.8)	15 (83.3)	
Pneumatic + laser, <i>n</i> (%)	1 (5.6)	1 (5.6)	
Total estimated blood loss, ml, mean ± SD (range)	130.0 ± 30.5 (80–170)	70.6 ± 18.3 (50–100)	<0.001
Postoperative creatinine (μmol/l), mean ± SD (range)	55.46 ± 7.72 (43.2–68.7)	53.34 ± 5.08 (44.9–65.3)	0.272
Impaired postoperative creatinine, <i>n</i> (%)	0 (0)	0 (0)	–
Creatinine change (μmol/l), mean ± SD (range)	5.22 ± 1.11 (3.5–7.5)	4.64 ± 1.44 (2.7–7.0)	0.161
Postoperative hospital stay, days, mean ± SD (range) <sup>a</sup>	5.8 ± 1.2 (4–8)	7.4 ± 1.2 (6–10)	0.001
Hospitalization cost, CNY, mean ± SD (range) <sup>a</sup>	17,373.3 ± 2408.9 (15,239–23,262)	23,717.1 ± 2280.8 (18,220–26,850)	<0.001
Stone-free rate, <i>n</i> (%)	15 (83.3)	17 (94.4)	0.603
Stone-free entirely, <i>n</i> (%)	14 (77.8)	15 (83.3)	
Insignificant residual (≤4 mm), <i>n</i> (%)	1 (5.6)	2 (11.1)	
Complications rate, <i>n</i> (%)	5 (27.8)	2 (11.1)	0.402
Modified Clavien Grade I, <i>n</i> (%)	3 (16.7)	2 (11.1)	
Modified Clavien Grade II, <i>n</i> (%)	2 (11.1)	0 (0)	
Modified Clavien Grade ≥ III, <i>n</i> (%)	0 (0)	0 (0)	

A statistically significant *P* value was defined as <0.05

<sup>a</sup>Calculated from the operative day in Group 1 or from the operative day of the first-stage in Group 2

According to the modified Clavien classification system [9], no Grade ≥ III complication was observed in either group (Table 2). There was no statistical significance in the incidence rate of total perioperative complication between the two groups (27.8% vs. 11.1%, *P* = 0.402). There were three patients in Group 1 (16.7%) and two patients in Group 2 (11.1%) with postoperative pain or fever without antibiotic therapy, Grade I complications. There were only two children in Group 1 (11.1%), who had operation time of more than two hours. These were the only patients in our study with this length of operation time and required antibiotic therapy owing to sepsis or systemic inflammatory response syndrome (SIRS) [10], Grade II complications. One of them was a 12-year old boy with complete staghorn stone (SA = 9.54 cm<sup>2</sup>), and he had a preoperative negative urine culture. We took a long time on lithotripsy because of the very hard texture of the stone. Another patient was a 14-year girl with multiple caliceal stones (SA = 8.42 cm<sup>2</sup>) which was distributed in almost all calyces with very narrow infundibula, and she had a preoperative positive urine culture. During the operation of this patient, most of the operative time was spent on finding (endoscopic) and accessing (endoscopic or percutaneous) the renal calyces. As a result,

she was the only patient in our study who was rendered three nephrostomy tracts.

## Discussion

With an approximate annual growth rate of 6–10% [3], pediatric renal stone disease is considered as a significant public health problem all over the world. In China specifically, there has been great emphasis on this subject by the government and pediatric urologists owing to the discovery of the relationship between melamine-contaminated powdered formula and pediatric nephrolithiasis since 2008 [11]. Although ESWL is recommended as the first option for the treatment of pediatric kidney stones, many researchers have found that there are still some deficiencies such as decreased success rates with increasing hydronephrosis and stone burden, the need for multiple sessions, and unknown long-term effects on the pediatric kidney [4, 12, 13]. ElSheemy et al. [14] compared the efficacy and safety of mPCNL and ESWL for single renal pelvic or lower calyceal calculi (10–25 mm) in preschool children (aged 6 years or less). They reported that the SFR in mPCNL group was significantly higher

than in ESWL group after both the first (88.9% vs. 43.8%,  $P < 0.001$ ) and last sessions (94.4% vs. 81.2%,  $P = 0.032$ ). They also found that the retreatment rate in mPCNL group was significantly lower when compared with the ESWL group (7.4% vs. 50%,  $P < 0.001$ ). However, analysis of the incidence rate of complications showed that there were no significant differences between the two groups (16.7% vs. 12.5%,  $P = 0.521$ ).

In 1985, Woodside et al. [15] first reported the application of PCNL in pediatric urolithiasis. Since then, an increasing number of urologists have reached a consensus that PCNL, as a minimal invasive surgical method, can be performed safely and effectively by experienced urological surgeons to remove kidney stones, especially the large, hard, and complex renal calculi, in children of all ages; even though there are still some complications of PCNL such as bleeding, urosepsis, and renal parenchymal damage [4–6, 16, 17]. In our present study, with no significant differences, the SFR in both groups (83.3% and 94.4%) were consistent with those previously reported results of 71.4–94% [4–6, 16, 17].

Ganpule et al. [18] found that the SFR was suboptimal by using single-tract PCNL with flexible endoscope for staghorn calculi, although the hospital stay and blood loss was less. Aron et al. [19] further pointed out that excessive torque of the rigid endoscope in trying to remove the hard-to-get calculi during PCNL was the main reason for serious perioperative bleeding. As a result, in order to achieve satisfactory results, mt-PCNL with multiple percutaneous tracts via different renal calyces is often required for staghorn stone or multiple caliceal calculus treatments, which are difficult to manage with a single tract in either adult or pediatric patients. In the present study, only one patient required three nephrostomy tracts, and the remaining 35 children in both groups needed two tracts for mt-mPCNL. Furthermore, it is reported that mPCNL with smaller diameter working sheaths (14–20F) and smaller sized endoscopes, comparing to the standard PCNL with 24–30F access sheaths and adult instruments, could reduce the perioperative complications and mortality rates in children, especially the incidence rates of severe bleeding [5, 20]. In our study, by using 9.5 Fr semi-rigid ureteroscope and 16–18 Fr working-tracts, no patient in neither groups needed blood transfusion (Grade II complication), but the total blood loss in Group 1 (130.0 ml) was significantly more than that in Group 2 (70.6 ml) ( $P < 0.001$ ).

Zhao et al. [7] emphasized that the demand for high SFR during mt-mPCNL should equilibrate with controlling operation time and protecting renal function. With no significant differences between groups ( $P = 0.818$  and  $0.161$ , respectively), the mean operation time and perioperative creatinine changes in both groups (81.4 min vs. 80.0 min,  $5.22 \mu\text{mol/l}$  vs.  $4.64 \mu\text{mol/l}$ ) were in accordance with those previously reported results [4–6, 16, 17]. However, in order to improve the SFR, we prolonged the

operation time of more than 2 h (130 and 140 min) in two patients in Group 1, and one of them was rendered with three nephrostomy tracts.

Post-PCNL infection complication, including urinary tract infection, postoperative fever, SIRS, and sepsis, is a common and inherent problem that may lead to longer hospitalization, additional antibiotic therapy, and even surgical intervention. Sepsis, especially severe sepsis and septic shock [10], is considered as one of the leading cause of death following PCNL; many investigators have proven that it is associated with bacteria in the urine, infection in stone, stone burden, and operation time of PCNL, etc. [21–23]. In our present study, there were two cases in Group 1 with perioperative sepsis or SIRS, one of whom with preoperative positive urine culture received intravenous ceftazidime therapy according to the antibiogram and the other without antibiotic treatment because of the negative urine culture. Many studies, either retrospective or prospective, indicated that positive urine culture had a positive correlation with infection related complications including SIRS and sepsis [23, 24]. Considering the protective effects of renal stones for bacterial pathogens against antibiotics, Mariappan et al. [22] introduced stone and pelvic urine culture as better predictors of potential post-PCNL urosepsis than bladder urine culture. We think this is the reason for perioperative sepsis or SIRS in the child without preoperative positive bladder urine culture. Additionally, some investigators also found that the occurrence of SIRS, sepsis, and septic shock was in direct proportion to the overall duration of PCNL procedure [25, 26]. In our present study, we were surprised to find that there were only two patients in Group 1 with total operation time more than two hours, and both of them suffered SIRS or sepsis perioperatively; these data seemed to suggest that the operation time of one-stage mt-mPCNL should be limited within two hours, or the planned two-stage mt-mPCNL should be applied in children with estimated operation time of more than two hours instead of one-stage mt-mPCNL.

Limitations of our study deserve mention. Firstly, our results may be potentially limited by the insufficient cases of pediatric patients with complex renal stones who received mt-mPCNL. We also realized that the low sample size would compromise the reliability of our conclusion for this study, including non-significance of the difference of SFR and perioperative complication rates between the two groups. Although it is not a rare disease, this special group of pediatric patients with complex renal stones who need mt-mPCNL is still few. So, a further large clinical multicenter trial with larger cohorts is necessary and expected in the near future. Secondly, the surgeon's experience and preference might influence the final accuracy.

## Conclusions

Our preliminary results suggest that both one- and two-stage mt-mPCNL are safe and effective treatment strategies for pediatric complex renal stones. Two-stage mt-mPCNL can significantly reduce total blood loss; while one-stage mt-mPCNL can significantly decrease the length and costs of hospitalization. Additionally, we suggest that the operation time of one-stage mt-mPCNL should be controlled within two hours to eliminate or reduce the incidence rate of peri-operative SIRS, sepsis, and septic shock. Or the planned two-stage mt-mPCNL should be applied in the children with estimated operation time more than two hours instead of one-stage mt-mPCNL.

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## Compliance with ethical standards

**Conflict of interest** The authors have no conflict of interest.

**Ethical approval** All procedures performed in studies involving human participants were in accordance with the ethical standards of our institutional research committee and with the 1964 Helsinki declaration and its later amendments.

**Informed consent** Informed consent was obtained from the parents of all individual participants included in the study.

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