



Comparison of pre-indwelling double-J stents versus ureteral catheters for artificial hydronephrosis in percutaneous nephrolithotomy: A retrospective cohort study

Tingshuai Yan^{1,*} , Keli Quan^{1,*} , Cong Yan² , Tong Yang¹ , Yingqi Zhao¹ , Jianping Shu¹ , Gaofei He¹

Departments of ¹Urology and ²Oncology, The First People's Hospital of Huaihua, University of South China, Huaihua, Hunan, China

Purpose: To compare the clinical efficacy and safety of pre-indwelling double-J stents versus ureteral catheters for artificial hydronephrosis in percutaneous nephrolithotomy (PCNL).

Materials and Methods: We retrospectively analyzed the data of 1,258 patients who underwent PCNL for kidney stones from August 2017 to July 2020 in our hospital. Among them, 682 patients had double-J stents inserted (DJ group) and 576 patients had ureteral catheters (UC group). We analyzed baseline patient characteristics, perioperative outcomes, and complications in both groups.

Results: The puncture success rate was 97.9% and 97.4% in the DJ and UC groups, respectively ($p > 0.05$). The operation time was 74.5 ± 37.8 minutes in the DJ group compared with 80.8 ± 38.5 minutes in the UC group ($p = 0.004$). The total stone-free rate in the DJ and UC groups was 80.5% and 78.7%, respectively ($p > 0.05$). The incidence of perioperative complications was relatively low in both groups and showed no obvious differences. In the subgroup analysis, the operation time for patients with no obvious or mild hydronephrosis preoperatively was significantly shorter in the DJ group than in the UC group ($p < 0.05$). However, there were no significant differences among patients who had moderate or severe hydronephrosis preoperatively.

Conclusions: It is feasible, safe, and effective to create artificial hydronephrosis by insertion of pre-indwelling double-J stents in PCNL surgery. Furthermore, the operation time was significantly shorter in the DJ group than in the group with pre-indwelling ureteral catheters, especially in patients who had no obvious or mild hydronephrosis preoperatively.

Keywords: Hydronephrosis; Kidney calculi; Percutaneous nephrolithotomy; Ureteral catheters

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INTRODUCTION

China is one of the three areas in the world with a high incidence of urinary calculi, and the incidence has been

increasing in recent years, especially in southern China. According to a nationwide cross-sectional survey, the prevalence of kidney stones in Chinese adults is 5.8% [1]. The incidence and prevalence of kidney stones in Western countries have

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Corresponding Author: Gaofei He <https://orcid.org/0000-0002-3951-5277>

Department of Urology, The First People's Hospital of Huaihua, University of South China, No.144 Jinxi South Road, Huaihua 418000, Hunan, China
TEL: +86-0745-2383807, FAX: +86-0745-2383807, E-mail: hegaofei@zju.edu.cn

*These authors contributed equally to this study and should be considered co-first authors.

also increased in recent decades [2-6]. In the Western world, the prevalence of kidney stones varies from 2% to 20% [1]. Percutaneous nephrolithotomy (PCNL) was first reported in 1976 and has gradually become an important surgical method for the treatment of kidney stones [7]. According to the European Association of Urology (EAU) guidelines, PCNL is the first choice for the treatment of complicated renal pelvis or calyx stones, especially for staghorn kidney stones [8].

Percutaneous renal puncture guided by B-ultrasound to establish a lithotripsy channel is the most critical step in PCNL surgery [9]. It is often necessary to artificially create hydronephrosis during the puncture step, especially in patients with no obvious hydronephrosis preoperatively [10]. Traditional PCNL surgery generally involves pre-placing a ureteral catheter and injecting normal saline into the renal pelvis or initiating a continuous drip of saline to create artificial hydronephrosis. However, many studies have reported the disadvantages of this approach [11,12]. For instance, an anterograde position of the indwelling double-J stents at the end of the surgery has shortcomings and increases the operation time, especially when an emergency happens like massive bleeding and the operation cannot be stopped immediately.

Through literature search, we found that few studies directly explored the role of pre-indwelling double-J stents for creating artificial hydronephrosis in PCNL and only one study with a small sample size was reported [11]. Therefore, we conducted this study with a larger sample size to investigate the clinical efficacy and safety of pre-indwelling double-J stents versus ureteral catheters for creating artificial hydronephrosis in PCNL and achieved good clinical effects.

MATERIALS AND METHODS

1. Patients

The present study was approved by the ethics committee of our hospital and is reported in line with the STROCSS criteria [13]. Informed consent was received from the patients before the operation. From August 2017 to July 2020, our hospital completed a total of 1,536 cases of PCNL and 1,384 patients underwent one-stage PCNL surgery. Patients were randomly assigned before the operation to receive either a double-J stent or a ureteral catheter for artificial hydronephrosis. Because of missing clinical data or loss of follow-up, 94 patients were initially excluded from this study. The inclusion criteria were as follows: patients who (1) were diagnosed with kidney stones with a maximum stone diameter ≥ 2 cm) and (2) underwent one-stage PCNL in our hospital between August 2017 and July 2020. The exclusion criteria

were as follows: 1) abnormal anatomy of the urinary system; 2) urinary tuberculosis or tumor; 3) severe coagulation dysfunction; 4) severe cardiopulmonary insufficiency; and 5) history of previous PCNL. Thirty-two patients were excluded from the study because they did not meet the above inclusion criteria or met one of the exclusion criteria. Finally, a total of 1,258 patients were enrolled in this retrospective cohort study. Among them, 682 patients had double-J stents inserted (DJ group) and 576 patients had ureteral catheters (UC group).

2. Methods

The diagnosis of kidney stones was based on history, physical examination, kidney-ureter-bladder (KUB) X-ray, B-ultrasound, and computed tomography (CT). Baseline patient characteristics, such as age, body mass index (BMI), sex, and comorbidities, were collected preoperatively. The stone location, stone size, and stone density were determined or measured by CT. We then divided the patients into four subgroups according to the degree of hydronephrosis as shown by CT: no obvious hydronephrosis (separation of the renal pelvis < 1.5 cm), mild hydronephrosis (separation of the renal pelvis of 1.5–3 cm), moderate hydronephrosis (separation of the renal pelvis of 3–4 cm), and severe hydronephrosis (separation of the renal pelvis of > 4 cm) [14]. The decrease in hemoglobin and the change in serum creatinine were obtained by comparing the last measured value before the operation with the value on the first postoperative day. The perioperative outcomes and complications of patients in both groups were also collected. In addition, every patient in whom a channel was successfully established during the operation usually underwent a KUB X-ray examination about 3 to 5 days after surgery to assess the position of the double-J stents and any residual stones. Referring to related research, we determined stones with a maximum diameter greater than 4 mm to be incomplete removals [15].

3. Operative procedure

In the present study, all patients underwent routine urinalysis and urine culture before surgery. If a urinary tract infection was confirmed, the patient had to receive effective anti-infective treatment preoperatively. All operations were performed with the patient under general anesthesia and were completed by the same surgeon who is proficient in PCNL. During the operation, we used a high-powered 100-W laser device (Lumenis Medical Systems, Santa Clara, CA, USA) with a 550- μ m fiber to crush the stones by a nephroscope or ureteroscope. In both groups, the inserted double-J stents were generally removed 2 to 4 weeks after surgery

and the nephrostomy tubes were removed about 5 to 7 days (extubation time) after the operation if the patients did not need a second-stage surgery.

In the DJ group, the patient was first placed in the lithotomy position and a 6-F double-J stent was inserted under the guidance of a zebra guidewire. Surgeons then placed an 18-F or 20-F three-way Foley catheter and temporarily clamped the drainage cavity. Subsequently, a 3,000-mL bag of normal saline was connected to the flushing cavity of the catheter. The hanging height of the normal saline was about 60 to 80 cm above the plane of the bladder. When patients were switched to the prone position, normal saline was infused accordingly. Because of the reflux effect of the double-J stents, the normal saline injected into the bladder drains into the renal pelvis. After an ideal and stable artificial hydronephrosis was established, we used a disposable fascial dilator to expand the percutaneous passage gradually from 8 F to 18 F or 20 F guided by the zebra guidewire under the surveillance of B-ultrasound. After completing the puncture and successfully establishing a channel, the drainage cavity of the three-way Foley catheter was opened again. At the end of the surgery, a 16-F nephrostomy tube was routinely indwelled.

In the UC group, however, we inserted a 6-F ureteral catheter on the affected side when the patient was in the lithotomy position. After the patient was switched to the prone position, normal saline was injected into the renal pelvis through this ureteral catheter to form artificial hydronephrosis. When the lithotripsy was complete, the pre-indwelled ureteral catheter was removed and a 6 F double-J stent was inserted into the bladder antegrade. The remaining steps were the same as in the DJ group.

4. Statistical analysis

In this study, the measurement data are reported as means±standard deviations and categorical variables as numbers with percentages. Continuous variables, like age, stone size, stone density, operation time, decrease in hemoglobin, and hospital stay, were assessed by Student's t-test. Categorical variables, like sex, stone side, stone location, and degree of hydronephrosis, were assessed by the Pearson chi-squared test or Fisher exact test. SPSS software version 25.0 was used to complete these statistical tasks and p-values <0.05 were considered statistically significant.

Table 1. Baseline patient characteristics in the DJ and UC groups

Parameter	DJ group (n=682)	UC group (n=576)	p-value
Age (y)	49.5±13.4	48.8±13.6	0.359
BMI (kg/m ²)	22.2±2.5	22.1±2.3	0.464
Sex			0.683
Male	423 (62.0)	364 (63.2)	
Female	259 (38.0)	212 (36.8)	
Stone side			0.778
Right	337 (49.4)	280 (48.6)	
Left	345 (50.6)	296 (51.4)	
Stone location			0.757
Upper calyx	157 (23.0)	124 (21.5)	
Middle calyx	156 (22.9)	136 (23.6)	
Lower calyx	192 (28.2)	173 (30.0)	
Renal pelvis	187 (27.4)	157 (27.3)	
Staghorn stone	71 (10.4)	62 (10.8)	
Stone size (mm)	31.7±3.4	31.8±3.6	0.613
Stone density (HU)	816.7±216.4	820.5±208.3	0.752
Degree of hydronephrosis			0.711
No	119 (17.4)	109 (18.9)	
Mild	221 (32.4)	188 (32.6)	
Moderate	205 (30.1)	163 (28.3)	
Severe	137 (20.1)	116 (20.1)	

Values are presented as mean±standard deviation or number (%). DJ, double-J stents; UC, ureteral catheters; BMI, body mass index.

RESULTS

1. Baseline patient characteristics in the DJ and UC groups

Table 1 shows the baseline patient characteristics of both groups, such as mean age, BMI, sex, stone side, stone location, stone size, stone density, and degree of hydronephrosis. There were no significant differences in baseline characteristics between the groups (p>0.05).

2. Perioperative outcomes of patients in the DJ and UC groups

As shown in Table 2, in 29 patients, the puncture procedure was not successfully completed for various reasons, such as pneumothorax or massive bleeding that occurred during puncture. The mean time to establish a channel in the two groups did not differ significantly (p>0.05). However, the overall operative time was shorter in the DJ group than in the UC group (p=0.004). The total stone-free rate of the DJ group was 80.5%, which was higher than the 78.7% in the UC group. However, this difference was not statistically significant (p>0.05).

Table 2. Perioperative outcomes of patients in the DJ and UC groups

Outcome	DJ group (n=682)	UC group (n=576)	p-value
Successfully established channel	668 (97.9)	561 (97.4)	0.574
Channel establishment time (min)	7.9±3.0	8.1±3.1	0.246
Operation time (min)	74.5±37.8	80.8±38.5	0.004*
Decrease in hemoglobin (g/L)	12.9±3.8	13.2±4.0	0.174
Creatinine change (μmol/L)	6.6±15.3	6.5±14.8	0.907
Extubation time (d)	6.4±1.6	6.5±1.7	0.283
Postoperative hospitalization (d)	6.5±2.3	6.4±2.6	0.469
Stone-free rate (%)	80.5	78.7	0.399

Values are presented as number (%) or mean±standard deviation.

DJ, double-J stents; UC, ureteral catheters.

*p-values <0.05 were considered statistically significant.

3. Perioperative complications of patients in the DJ and UC groups

As shown in Table 3, one patient developed a pneumothorax during the puncture process in the DJ and UC group, respectively. No colon injury occurred in either group. In addition, there were 15 patients with massive hemorrhage in the DJ group and 6 cases required a blood transfusion, whereas in the UC group 16 patients had massive hemorrhage and 4 cases required a blood transfusion, respectively. The other postoperative complications did not differ significantly between the groups ($p>0.05$). Nevertheless, abnormal positions of the DJ stents were found in eight cases in the UC group after the operation, whereas only one such case was found in the DJ group. The difference between groups was statistically significant ($p=0.014$).

4. Perioperative outcomes of patients with no obvious or mild hydronephrosis preoperatively in the DJ and UC groups

As shown in Table 4, in the subgroup with no obvious hydronephrosis, the operative time in the DJ group was less than in the UC group ($p=0.039$). However, time to establish a channel, decrease in hemoglobin, and creatinine change did not differ significantly between groups ($p>0.05$). The stone-free rate was 82.4% in the DJ group compared with 79.8% in the UC group ($p>0.05$).

In the subgroup with mild hydronephrosis, the operative time of the DJ group was less than that of the UC group and the difference was statistically significant ($p=0.012$). The time to establish a channel, decrease in hemoglobin, and creatinine change did not differ significantly between groups ($p>0.05$). The stone-free rate of the DJ group was 81.4%, which was higher than the 78.2% of the UC group ($p>0.05$).

Table 3. Perioperative complications of patients in the DJ and UC groups

Complication	Grade	DJ group (n=682)	UC group (n=576)	p-value
Pneumothorax	3	1 (0.15)	1 (0.17)	>0.999
Colon injury	3	0 (0.0)	0 (0.0)	-
Massive hemorrhage	3	15 (2.2)	16 (2.8)	0.585
Blood transfusion	2	6 (0.9)	4 (0.7)	0.762
Angioembolization	3	4 (0.6)	4 (0.7)	>0.999
ARF needing dialysis	4	0 (0.0)	0 (0.0)	-
Postoperative fever	1	26 (3.8)	20 (3.5)	0.766
Sepsis	2	15 (2.2)	11 (1.9)	0.843
Septic shock ICU manage	4	7 (1.0)	5 (0.9)	>0.999
Abnormal position of DJ stents	1	1 (0.1)	8 (1.4)	0.014*

Values are presented as number (%).

DJ, double-J stents; UC, ureteral catheters; ARF, acute renal failure; ICU, intensive care unit.

*p-values <0.05 were considered statistically significant.

5. Perioperative outcomes of patients with moderate and severe hydronephrosis preoperatively in the DJ and UC groups

As shown in Table 5, in the subgroup with moderate hydronephrosis, the operative time was 74.8±45.3 minutes in the DJ group compared with 79.7±45.8 minutes in the UC group, respectively ($p>0.05$). These perioperative outcomes, including the decrease in hemoglobin and creatinine change in the two groups were not significantly different between groups ($p>0.05$). The stone-free rate of the DJ group was slightly higher than that of the UC group, but not significantly so ($p>0.05$).

Table 5 also shows that in the subgroup of patients with severe hydronephrosis, the time to establish a channel was shorter in the DJ group than in the UC group. In addition, the operative time was also shorter in the UC group than in the DJ group. However, these differences, including the decrease in hemoglobin and creatinine change, were not statistically significant ($p>0.05$). For this subgroup, the stone-free rate was 78.1% in the DJ group and 77.6% in the UC group ($p>0.05$).

DISCUSSION

On the whole, the puncture success rate and one-stage stone-free rate were high in both groups. This finding shows that the two methods of establishing artificial hydronephrosis in PCNL are feasible and effective. However, we found a significant difference between the two groups in the total operation time, which was shorter in the DJ group. We suggest several reasons for the shorter overall operation time in

Table 4. Perioperative outcomes of patients with no or mild hydronephrosis preoperatively in the DJ and UC groups

Parameter	No hydronephrosis (n=228)		p-value	Mild hydronephrosis (n=409)		p-value
	DJ (n=119)	UC (n=109)		DJ (n=221)	UC (n=188)	
Age (y)	48.8±12.7	48.5±13.0	0.860	47.9±10.6	47.6±11.3	0.782
BMI (kg/m ²)	22.1±2.0	22.2±2.4	0.732	21.9±2.6	22.0±2.1	0.673
Sex			>0.999			0.467
Male	76 (63.9)	69 (63.3)		140 (63.3)	126 (67.0)	
Female	43 (36.1)	40 (36.7)		81 (36.7)	62 (33.0)	
Stone side			0.894			>0.999
Right	65 (54.6)	58 (53.2)		105 (47.5)	90 (47.9)	
Left	54 (45.4)	51 (46.8)		116 (52.5)	98 (52.1)	
Stone location			0.827			0.490
Upper calyx	24 (20.2)	19 (17.4)		46 (20.8)	37 (19.7)	
Middle calyx	33 (27.7)	29 (26.6)		40 (18.1)	38 (20.2)	
Lower calyx	49 (41.2)	40 (36.7)		65 (29.4)	56 (29.8)	
Renal pelvis	25 (21.0)	28 (25.7)		56 (25.3)	47 (25.0)	
Staghorn stone	7 (5.9)	5 (4.6)		14 (6.3)	10 (5.3)	
Stone size (mm)	30.5±3.0	30.7±2.9	0.610	31.6±3.6	31.5±3.2	0.769
Stone density (HU)	812.3±201.5	813.3±199.5	0.970	818.2±231.6	820.4±228.0	0.923
Successfully established channel	110 (92.4)	102 (93.6)	0.800	218 (98.6)	184 (97.9)	0.708
Channel establishment time (min)	9.4±3.4	9.0±4.5	0.464	8.4±2.8	8.1±3.7	0.356
Operation time (min)	70.5±36.2	81.6±41.4	0.039*	72.5±40.1	83.2±44.5	0.012*
Decrease in hemoglobin (g/L)	13.4±4.5	13.7±5.2	0.641	12.4±4.1	13.1±5.0	0.121
Creatinine change (µmol/L)	6.1±11.4	5.8±10.2	0.835	5.6±13.5	6.7±14.6	0.429
Stone-free rate (%)	82.4	79.8	0.735	81.4	78.2	0.458

Values are presented as mean±standard deviation or number (%).

DJ, double-J stents; UC, ureteral catheters; BMI, body mass index.

*p-values <0.05 were considered statistically significant.

the DJ group. First, during the lithotripsy process, the pre-inserted double-J stents can effectively prevent larger stones from escaping to the ureter and can drain mini stones into the bladder, which may reduce the operation time. Second, the continuous intraoperative perfusion not only reduces the formation of clots but also provides a clearer vision for the operation and increases the safety of the operation. Continuous intraoperative perfusion can also assist in rushing the gravel out of the peel-away sheath and improves the efficiency of the lithotripsy. Third, the original ureteral catheter needs to be removed and a new double-J stent should be indwelled when the lithotripsy process is over. We know that there are some disadvantages to placing double-J stents anterogradely, and it also increases the length of the operation, especially when an emergency such as massive bleeding occurs.

To further explore the safety of pre-indwelling double-J stents versus ureteral catheters to make artificial hydronephrosis in PCNL, we recorded and graded the perioperative complications experienced by the patients in both groups [16,17]. Consistent with many studies in the past, most com-

plications were minor [10,18]. In our study, the two most common perioperative complications of PCNL were infection and bleeding, which is similar to the results of previous studies [19,20]. One patient in each of the two groups developed pneumothorax, which improved after thoracentesis and drainage. In the DJ group, six patients with massive hemorrhage received a blood transfusion, and four of them also underwent super-selective renal angiography and embolization. Patients in the UC group who had massive hemorrhages also recovered and were discharged after active blood transfusion therapy or super-selective renal arteriography embolization. Some patients in both groups developed fever or even sepsis after surgery, and some of them progressed to septic shock and required intensive care unit treatment, but none of the patients died as a result. More patients in the UC group than in the DJ group had an abnormal position of the double-J stents after the operation, which indirectly shows that there is a certain failure rate of indwelling double-J stents when they are anterograde. These patients require repositioning of the tubes through a cystoscope after the operation.

Table 5. Perioperative outcomes of patients with moderate or severe hydronephrosis preoperatively in the DJ and UC groups

Parameter	Moderate hydronephrosis (n=368)		p-value	Severe hydronephrosis (n=253)		p-value
	DJ (n=205)	UC (n=163)		DJ (n=137)	UC (n=116)	
Age (y)	49.6±14.2	49.9±15.3	0.846	51.7±13.1	49.2±13.9	0.143
BMI (kg/m ²)	22.5±2.1	22.6±2.2	0.657	21.3±2.3	21.4±2.8	0.755
Sex			0.570			0.380
Male	145 (70.7)	110 (67.5)		62 (45.3)	59 (50.9)	
Female	60 (29.3)	53 (32.5)		75 (54.7)	57 (49.1)	
Stone side			>0.999			0.529
Right	95 (46.3)	76 (46.6)		72 (52.6)	56 (48.3)	
Left	110 (53.7)	87 (53.4)		65 (47.4)	60 (51.7)	
Stone location			0.545			2.536
Upper calyx	58 (28.3)	47 (28.8)		29 (21.2)	21 (18.1)	
Middle calyx	48 (23.4)	40 (24.5)		35 (25.5)	31 (26.7)	
Lower calyx	46 (22.4)	37 (22.7)		32 (23.4)	40 (34.5)	
Renal pelvis	65 (31.7)	45 (27.6)		41 (29.9)	37 (31.9)	
Staghorn stone	24 (11.7)	18 (11.0)		31 (22.6)	26 (22.4)	
Stone size (mm)	32.0±3.8	32.2±3.5	0.604	33.7±4.6	32.8±4.7	0.126
Stone density (HU)	815.5±232.6	817.6±225.8	0.931	820.8±215.5	830.7±210.0	0.713
Successfully established channel	203 (99.0)	159 (97.5)	0.412	137 (100.0)	116 (100.0)	-
Channel establishment time (min)	6.6±3.5	7.3±3.6	0.063	6.5±3.1	7.2±3.8	0.108
Operation time (min)	74.8±45.3	79.7±45.8	0.306	80.4±37.8	78.6±35.1	0.697
Decrease in hemoglobin (g/L)	11.4±3.7	11.0±3.9	0.315	14.5±4.7	14.8±5.0	0.624
Creatinine change (μmol/L)	6.8±16.8	5.8±14.5	0.547	8.0±12.7	7.6±11.5	0.795
Stone-free rate (%)	80.0	79.1	0.897	78.1	77.6	>0.999

Values are presented as mean±standard deviation or number (%).

DJ, double-J stents; UC, ureteral catheters; BMI, body mass index.

To determine the role of pre-indwelling double-J stents versus ureteral catheters for creating artificial hydronephrosis for patients with various degrees of hydronephrosis, we divided the two groups of patients into four subgroups for analysis. We found that the operation time of the DJ group was significantly shorter than in the UC group in patients who had no obvious or mild hydronephrosis preoperatively. This indicated that the use of pre-indwelling double-J stents for creating artificial hydronephrosis in PCNL is superior for patients with low hydronephrosis, which may be related to the fact that pre-indwelling double-J stents can create a more stable and continuous artificial hydronephrosis. On the other hand, there were no significant differences between the groups in patients who had moderate and severe hydronephrosis preoperatively. This may be because the preoperative hydronephrosis in these cases is obvious, and it is relatively easy to perform percutaneous renal puncture. Nevertheless, we noticed that the time to establish a channel did not differ significantly in the four subgroups.

In the current study, we found that when the suspension height of normal saline was 60 to 80 cm higher than the bladder plane, stable artificial hydronephrosis could be

formed in the target renal pelvis. We know that there is an important special structure between the ureter and the bladder named the Waldeyer's sheath. This structure prevents the backflow of urine from the bladder to the renal pelvis. But this physiological mechanism is destroyed after we place a double-J stent into the ureter. Therefore, normal saline should be continuously infused into the target renal collection system through the pre-indwelling double-J stents under the internal pressure of the bladder wall.

Our method still has certain limitations. First, we cannot directly inject a contrast agent into the renal pelvis to find the exit position of the renal pelvis or determine whether the puncture is successful. Second, a double-J stent placed retrogradely may not be able to reach the renal pelvis smoothly in patients whose upper ureter is blocked by huge stones. Third, the double-J stent may be accidentally injured in the subsequent laser lithotripsy process, resulting in the formation of mural stones and affecting drainage after surgery. Therefore, the surgeon should always pay attention to avoid the double-J stent or use a peeling sheath to separate it during the lithotripsy process. In addition, we can insert a safety guidewire first under the direct view of the uretero-

scope, and then place the double-J stent under the guidance of the guidewire after it has passed the stone and entered the renal pelvis.

Our work has some limitations. First, this was a retrospective comparative study. Second, the grading method we used to determine the degree of hydronephrosis was not sufficient. Third, the randomization method in both groups was relatively simple and not rigorous, which will introduce a certain selection bias. Last, the present study reports the experience of our single medical center. Therefore, more multicenter, prospective, and high-quality studies are needed to further confirm our conclusions.

CONCLUSIONS

In summary, our study demonstrated that it is feasible, safe, and effective to create artificial hydronephrosis by use of pre-indwelling double-J stents in PCNL surgery. Furthermore, the total operation time for patients with pre-indwelling double-J stents was significantly shorter than that for patients with pre-indwelling ureteral catheters, especially in patients who had no obvious or mild hydronephrosis preoperatively.

CONFLICTS OF INTEREST

The authors have nothing to disclose.

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AUTHORS' CONTRIBUTIONS

Research conception and design: Gaofei He. Data acquisition: Tong Yang and Yingqi Zhao. Statistical analysis: Cong Yan. Data analysis and interpretation: Cong Yan and Gaofei He. Drafting of the manuscript: Tingshuai Yan and Keli Quan. Critical revision of the manuscript: Tingshuai Yan, Keli Quan, and Gaofei He. Obtaining funding: none. Administrative, technical, or material support: Tingshuai Yan, Keli Quan, and Jianping Shu. Supervision: Gaofei He and Jianping Shu. Approval of the final manuscript: all authors.

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