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Original Article

A research on flexible ureteroscope lithotripsy versus percutaneous nephrolithotomy for upper urinary tract calculi

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Abstract: Objective: To compare the efficacies of flexible ureteroscope lithotripsy (FURL) and percutaneous nephrolithotomy (PCNL) for the treatment of upper urinary tract calculi (UUTC). Methods: In this retrospective study, 97 patients with UUTC were divided into FURL group (n=49) and PCNL group (n=48) according to the treatment methods. The primary outcomes (operation time, length of hospital stay, and stone clearance rate), and secondary outcomes (incidences of postoperative complications and S.T.O.N.E. nephrolithometry scoring) in the two groups were recorded and compared. Results: The operation time of FURL group was longer than that of PCNL group ($P<0.05$), and the length of hospital stay of FURL group was shorter than that of PCNL group ($P<0.05$). The stone clearance rate of FURL group with stone diameter 3.1-4.0 cm was lower than that of PCNL ($P<0.05$), and the two groups had no difference in the total stone clearance rate ($P>0.05$). The total incidence of postoperative complications of FURL group was lower than that of PCNL group ($P<0.05$). S.T.O.N.E. nephrolithometry scoring showed equal efficacies in the patients with 6-8 scores. The results of multivariate regression analysis showed that size of stones and S.T.O.N.E. nephrolithometry scoring were independent risk factors for stone clearance rate (both $P<0.05$). Conclusion: Compared with PCNL, FURL had an effect on UUTC when the stones were under 3 cm, and the stone clearance rate of patients with 6-8 S.T.O.N.E. nephrolithometry scores could be effectively predicted.

Keywords: Flexible ureteroscope lithotripsy, percutaneous nephrolithotomy, upper urinary tract calculi, efficacy

Introduction

Urolithiasis is a common and frequently occurring disease, and the morbidity worldwide is 1-5% [1]. The number of patients with upper urinary tract calculi (UUTC) is significantly increased, and the incidences of urinary tract infection and obstruction are also rising [2]. Severe obstruction can cause damage to the renal function, and renal insufficiency after injury will have a negative impact on the quality of life of patients [3, 4]. In 2016, the European Association of Urology recommended percutaneous nephrolithotomy (PCNL) for UUTC patients with stones more than 2 cm in the guidelines [5]. However, due to the large surgical scope and amount of blood loss, the stone clearance rate is low with the use of a single channel. Although the use of multiple channels can improve the stone clearance rate, it is likely to cause damage to the renal pelvis and renal parenchyma [6]. Minimally invasive surgery has the characteristics of small trauma, high safety and rapid recovery and it has gradually replaced traditional surgery [7, 8]. Flexible ureteroscope lithotripsy (FURL) has become the preferred approach for urinary tract calculi [9]. Compared with PCNL, FURL has a significantly better efficacy and smaller injury [10, 11]. Studies have confirmed that the stone clearance rate reached 94.7% in the patients with isolated kidney stones below 1 cm, and FURL had no effect on renal function [12]. Another study showed that FURL was more effective than PCNL in treating stones under 2 cm with smaller trauma and faster recovery [13]. However, for patients with renal calculi with an average diameter of 2.5 cm, the single and secondary stone clearance rates could reach 86.6% and 100.0% after FURL treatment [14]. Studies found that with

the maturity and improvement of FURL technology, it also showed efficacy on patients with stones above 2 cm [15]. Currently, PCNL has been widely used in the treatment of UUTC, especially in the treatment of renal calculi or renal lithiasis associated with ureterolith, and it has gradually replaced laparotomy [16]. Moreover, PCNL is the first choice for the treatment of stones over 2 cm [5]. Pieras et al. found that for patients with kidney stones at 2-3 cm, FURL and PCNL had similar efficacy, but patients in the FURL group recovered faster and had shorter length of postoperative hospital stay [17]. Another study reported that after FURL treatment for 2-3 cm of renal calculi, the secondary and tertiary stone clearance rates were up to 89.3% and 97.1%, respectively [18]. In the treatment of middle and lower stones, rigid ureteroscopy is commonly used in the clinical treatment [19]. FURL is used in the treatment of not only middle and lower stones, but also upper stones. Some studies have found that the stone clearance rate of FURL can reach 95.7% for renal calculi and upper ureteral calculi at 2-3 cm [14], but another study has suggested that FURL is more suitable for the application of renal calculi and upper ureteral calculi under 2 cm [20]. The above studies have indicated that FURL is still effective in the treatment for stones at 2-3 cm. However, the differences between the two surgical methods in the stone clearance rate for stones at 2-3 cm remain controversial. This study retrospectively analyzed the efficacies of the two surgical methods in order to provide more guidance for clinical application.

Materials and methods

General information

A total of 97 patients admitted to the Department of Urology Surgery of Jiangxi Integrated Chinese and Western Medicine Hospital were retrospectively analyzed, including 54 males and 43 females, aged 19-64 years old, with an average age of 38.34±8.82 years old. These patients were divided into two groups according to surgical methods: FURL group (n=49) and PCNL group (n=48). The two groups were followed up for 3 months. This study was approved by the Ethics Committee of Jiangxi Integrated Chinese and Western Medicine Hospital and all patients signed the informed consent.

Inclusion criteria: patients subjected to surgical treatment due to urinary calculi confirmed under CT scanning; patients aged 18-65 years old; patients with stones 1-4 cm located above the fourth lumbar vertebra; patients without complication of urinary tract infection before operation; patients without obvious stricture on the urethra and ureter.

Exclusion criteria: patients with stones over 4 cm located under the fourth lumbar vertebra; patients without history of PCNL or FURL; patients with serious heart and lung diseases who were not suitable for surgery; patients with severe coagulation disorder; patients who had difficulty or inconvenience for follow-up; other patients who were not suitable for surgery.

Methods

FURL: general anesthesia was performed, and oxygen was supplied through facemask (6-8 L/min). Intravenous injections of midazolam (0.05-0.10 mg/kg; Jiangsu Nhwa Pharmaceutical Co., Ltd., China), propofol (1.0-1.5 mg/kg; Xi'an Libang Pharmaceutical Co., Ltd., China), sufentanil citrate (0.2-0.3 μg/kg; Yichang Humanwell Pharmaceutical Co., Ltd, China) and cisatracurium (0.15-0.20 mg/kg; Jiangsu Hengrui Pharmaceutical Co., Ltd., China) were performed according to the patient's weight. Endotracheal intubation was induced by general anesthesia after 3-min assisted respiration, and an intravenous injection of sufentanil citrate (10-20 μg) was performed 5 min before skin incision. During anesthesia induction and after anesthesia, the monitor was connected to monitor the patient's vital signs. Patients were placed in lithotomy position, and the surgical site was disinfected and covered with surgical towel. Flexible ureteroscope (KARL STORZ SE & Co. KG, Germany) was inserted into the bladder. For patients who had received Double-J stent previously, rigid ureteroscope (Richard Wolf Company, Germany) was used to remove the stent before the above operation. After entering the bladder, Zebra guidewire (American COOK Company, USA) was inserted into the ureter from the ureteral incision. The flexible ureteroscope was able to maximally access the upper portion of the ureter along the entry of the guidewire. The ureteroscope was removed, and F14 flexible ureteral access sheath (Zhuzhou Ruibang Medical Appliance Products

Co., Ltd., China) was entered into the upper segment of the ureter along the guidewire. Then the inner core of the sheath was removed and the flexible ureteroscope was inserted into the renal pelvis under the direct vision of the sheath. After locating the stones, the Zebra guidewire was removed. After that, holmium laser fiber (Lumenis, USA) was inserted, and the stones were pulverized by holmium laser lithotripsy machine. Intraoperative irrigation was performed to ensure a clear field of vision. For patients with greater difficulty in direct lithotripsy, basket manipulation (American COOK Company, USA) was used to remove the stones to the renal pelvis before lithotripsy. After lithotripsy, repeated careful examinations of residual calculi, bleeding and other conditions were conducted. The guidewire was inserted into the renal pelvis along the sheath, and then the flexible ureteroscope and sheath were removed. Double-J stent was placed along the guidewire, and the catheter was remained. The operation was completed. Three days after the operation, KUB was reviewed to observe Double-J stent and the excretion of residual calculi. Removal of Double-J stent was considered after 4 weeks.

PCNL: the anesthesia, disinfection and surgical position of PCNL group were the same as those of FURL group. Rigid ureteroscope was used to access to the upper ureter, and the ureter catheter was inserted into the renal pelvis. During this process, rigid ureteroscopic lithotripsy could be performed if there were stones, or the stones could be pushed into the renal pelvis. Then the rigid ureteroscope was removed, and the ureter catheter was retained and fixed to the upper portion of the ureter. The patients were changed to place in uninjured side and the waist was raised. The surgical site was disinfected and covered with surgical towel. Hydronephrosis was formed after 0.9%Nacl infusion in the ureteral catheter. The puncture point was measured on B-ultrasound images. The needle direction was slightly tilted towards skull and spine for 5°. The inclination angle depended on the position of the puncture point. When the needle core was pulled out at the hydronephrosis site after puncture, the outflow of yellowish liquid indicated that the puncture was successful. Then the guidewire was inserted, and the puncture needle was pulled out. A 1-cm skin incision was made by the scalpel. The fascia dilators (Create Medic Co., Ltd., Japan) were inserted along the guidewire, expanding from size F8 to F24. The peel-away sheath (Shenyang Shenda Endoscope Co., Ltd., China) was retained in the skin to establish a single channel. Percutaneous nephroscope (Shenyang Shenda Endoscope Co., Ltd., China) was put through the single channel into the kidney to find stones. After that, the holmium laser fiber was inserted, and the stones were pulverized by holmium laser lithotripsy machine. Intraoperative irrigation was conducted to ensure a clear field of vision. The larger stones were removed by lithotomy forceps (American COOK Company, USA). After lithotripsy, repeated careful examinations of residual calculi, bleeding and other conditions were conducted. The percutaneous nephroscope was removed. Double-J stent was placed along the guidewire, and the catheter and nephrostomy tube were remained. The operation was completed. The postoperative review was the same as the FURL group.

Outcome measures

Main outcome measures were as follows. First, the operation time was recorded from the entering of ureteroscope to the end of the operation. Second, the length of hospital stay was recorded as the number of days spent in the ward after surgery until discharge. Third, stone clearance was defined according to *the Chinese guidelines for the diagnosis and therapy of urological diseases in 2014*: there was no clinical symptom, and the reexamination of KUB 4 weeks after surgery revealed that the high-density shadow or spotted shadow was less than 0.4 cm [21]. The stone clearance rate was recorded.

Fourthl, the S.T.O.N.E. nephrolithometry scoring was calculated and recorded [22]. 1) Size of stone was measured as maximum width × maximum length (mm^2). The scores of ≤399 mm^2, 400-799 mm^2, 800-1,599 mm^2, and ≥1,600 mm^2 are 1, 2, 3 and 4 respectively. 2) Distance from skin to puncture channel: ≤100 mm, 1 score; >100 mm, 2 scores. 3) Obstruction: no obstruction or mild hydronephrosis, 1 score; moderate or severe hydronephrosis, 2 scores. 4) The number of stones and renal calyces: 1-2 stones and renal calyces, 1 score; ≥3 stones and renal calyces, 2 scores; staghorn calculi, 3 scores. 5) Density of stones was judged by the results of CT examination: CT value ≤950, 1 score; CT value >950, 2 scores. Because the

Table 1. General information

	FURL group (n=49)	PCNL group (n=48)	χ^2/t	P
Gender (male/female)	28/21	26/22	0.087	0.768
Age (year)	38.53±7.60	38.15±10.00	0.214	0.831
Size of stones (cm)	2.24±0.74	2.28±0.70	-0.316	0.753
Number of stones	2.63±0.84	2.96±1.12	-1.662	0.100
CT value	931.50±271.60	977.29±294.41	-0.796	0.428
Type of stones (n)			0.147	0.929
Type I	20	19		
Type II	24	25		
Type III	5	4		

Note: FURL, flexible ureteroscope lithotripsy; PCNL, percutaneous nephrolithotomy; type I, unilateral ureteral calculi combined with renal pelvis and calyceal calculi; type II, multiple renal pelvis and calyceal calculi; type III, staghorn calculi.

Table 2. Operation time and length of hospital stay

	FURL group (n=49)	PCNL group (n=48)	t	P
Operation time (min)	88.71±27.24	77.00±25.82	2.173	0.032
Length of hospital stay (d)	3.25±1.30	6.82±1.89	-10.818	<0.001

Note: FURL, flexible ureteroscope lithotripsy; PCNL, percutaneous nephrolithotomy.

scoring system was specific to the renal pelvis and calyceal calculi, the patients complicated with ureteral calculi in this study were excluded. The scores of five items were added: ≤5 scores, mildly complex; 6-8 scores, generally complex; ≥9 extremely complex.

Secondary outcome measure: postoperative complications were recorded, including fever, pain, hematuresis, etc.

Statistical analysis

Statistical analysis was conducted using SPSS 17.0. Continuous variables were expressed by mean ± standard deviation ($\bar{x}$ ±sd). Data with normal distribution and homogeneity of variances were compared by t-test, conversely, by rank sum test. Count data were expressed as rate and were analyzed by Pearson chi-square test or Fisher exact test. The relevant factors were analyzed by multiple logistic regression analysis. P<0.05 is considered statistically significant.

Results

No significant difference in general information between the two groups

FURL group included 28 males and 21 females, with an average age of 38.53±7.60 years old, including 20 cases of unilateral ureteral calculi combined with renal pelvis and calyceal calculi, 24 of multiple renal pelvis and calyceal calculi, and 5 of staghorn calculi. PCNL group recruited 26 males and 22 females, with an average age of 38.15±10.00 years old, including 19 cases of unilateral ureteral calculi combined with renal pelvis and calyceal calculi, 25 of multiple renal pelvis and calyceal calculi, and 4 of staghorn calculi. There was no statistical difference in the general information between the groups, including gender, age, size of stones, number of stones, CT value, type of stones (all P>0.05). See **Table 1**.

Longer operation time and shorter length of hospital stay in FURL

The operation time of FURL group was longer than that of PCNL group (88.71±27.24 vs. 77.00±25.82 min; P<0.05) and the length of hospital stay of FURL group was shorter than that of PCNL group (3.25±1.30 vs. 6.82±1.89 day; P<0.05). See **Table 2**.

No significant difference in stone clearance rate of stones at 1.0-3.0 cm between the two groups

There was no statistical difference in the stone clearance rate of the patients with stones at 1.0-2.0 and 2.0-3.1 cm between the two groups (both P>0.05). The stone clearance rate of patients with stones at 3.1-4.0 cm in the FURL group was lower than that in the PCNL group (28.57% vs. 83.33%; P<0.05). See **Table 3**.

Less postoperative complications in PURL group than that in PCNL group

In both the FURL and PCNL groups, 2 patients had a fever (temperature more than 38), and the body temperature dropped to normal after the antibiotics were administered under the examinations of hematological parameters.

Table 3. Stone clearance rate

Size of stones	FURL group (n=49)	PCNL group (n=48)	χ^2	P
1.0-2.0 cm	85.00% (17/20)	93.33% (14/15)	0.588	0.443
2.1-3.0 cm	77.27% (17/22)	80.95% (17/21)	0.088	0.767
3.1-4.0 cm	28.57% (2/7)	83.33% (10/12)	5.698	0.017
Total stone clearance rate	73.47% (36/49)	85.42% (41/48)	2.115	0.146

Note: FURL, flexible ureteroscope lithotripsy; PCNL, percutaneous nephrolithotomy.

Table 4. Postoperative complications (n, %)

Item	FURL group (n=49)	PCNL group (n=48)	χ^2	P
Fever	2 (4.08)	2 (4.17)		
Pain	1 (2.04)	8 (16.67)		
Hematuresis	0	2 (4.17)		
Total	3 (6.12)	12 (25.00)	6.610	0.010

Note: FURL, flexible ureteroscope lithotripsy; PCNL, percutaneous nephrolithotomy.

Table 5. S.T.O.N.E. nephrolithometry scoring (6-8 scores)

Item	FURL group (n=17)	PCNL group (n=23)	χ^2	P
6 scores (n)	5 (29.41)	6 (26.09)		
7 scores (n)	9 (52.94)	12 (52.17)	0.122	0.941
8 scores (n)	3 (17.65)	5 (21.74)		
Total stone clearance rate (n, %)	13 (76.47)	20 (85.96)	0.744	0.388

One patient in the FURL group had intolerant pain, 8 patients in the PCNL had obvious pain, and they were relieved after the use of analgesics. In the PCNL group, 2 patients had hematuresis and were relieved after the use of hemostatic drugs. See **Table 4**.

No significant difference in total stone clearance rate between the two groups

In the FURL group, 6 cases were with scores ≤5 (mildly complex), 17 cases with scores 6-8 (generally complex) and 6 cases with scores ≥9 (extremely complex). The stone clearance rates in the FURL group were 100.00%, 76.47% and 33.00% (mildly, generally, and extremely complex, respectively). In the PCNL group, none of the patients was with scores ≤5 (mildly complex), 23 cases with scores 6-8 (generally complex) and 6 cases with scores ≥9 (extremely complex). The stone clearance rates in the FURL group were 0, 85.95%, and 33.33% respectively. This study compared the efficacies of patients with 6-8 scores between the two group, because there was no patient with scores ≤5 in the PCNL group and the number of patients with scores ≥9 was very low (only 12 patients in the two groups). Patients with 6-8 scores were statistically comparable (P>0.05), and there was no significant difference in the total stone clearance rate between the two groups. See **Table 5**.

Multivariate regression analysis for stone clearance rate

The results of multivariate regression analysis showed that size of stones and S.T.O.N.E. nephrolithometry scoring were independent risk factors for stone clearance rate (both P<0.05). See **Table 6**.

Discussion

Comparing the efficacies of extracorporeal shockwave lithotripsy (ESWL), rigid ureterscopy lithotripsy and FURL, Eisenmenger et al. found that the first fragmentation success rate was only 67.4%, while that of FURL was up to 96.4% [23]. It also found that 16.7% of patients failed to the treatment because the stones had returned to the kidney after the treatment of rigid ureterscopy lithotripsy. And 10.7% of patients had stones returning to the kidney after the treatment of flexible ureterscopy, but all of stones were successfully removed by basket manipulation. FURL can also be used for special types of stones. In this study, it was found that compared with PCNL, FURL had longer operation time and shorter length of postoperative hospitalization stay. This indicated that FURL was with smaller trauma and faster recovery, which was consistent with the above studies. The longer operation time of FURL may be related to the prolonged operation time caused by the change of stone position in the process of lithotripsy.

Studies reported that with the treatment of FURL, the stone clearance rate was up to 96.5% (stone ≤2 cm), while that was significantly

Table 6. Multivariate regression analysis for stone clearance rate

Variable	Wald	P	Regression coefficient	Standard error	OR	95% CI
Size of stones	4.626	0.009	1.578	0.798	3.002	1.689-15.246
Stone location	1.656	0.236	1.125	0.456	1.336	1.689-7.633
S.T.O.N.E. nephrolithometry score	4.369	0.013	1.642	0.869	4.365	2.987-11.328
Number of stones	1.589	0.365	1.098	0.523	1.265	1.592-8.265

reduced to 58.3% (stone >2 cm) [24]. For patients with stones above 3 cm, a meta-analysis showed that FURL was safe and effective, but the stone clearance rate of PCNL was significantly higher than that of FURL [25]. Haghighi et al. found that the stone clearance rate of PCNL for renal calculi was up to 94.9% [26]. In this study, the total stone clearance rates of FURL and PCNL were 79.59% and 85.42% respectively, with no statistical difference. For patients with stones 1-3 cm, there was no difference in the stone clearance rate between the two surgical methods. However, for patients with stones over 3 cm, the stone clearance rate of PCNL group was higher than that of FURL group, which was consistent with the above studies.

Bleeding is the most common postoperative complication. In the PCNL, because the single channel often cannot meet the needs of the operation, it is necessary to establish multiple channels, thus increasing the risk of bleeding [27]. However, for the FURL, the intraoperative retaining of Double-J stent can cause local mucosal hyperplasia, thus reducing the risk of bleeding [28]. This study found that 2 patients and 0 patient had hematuria in the PCNL and FURL groups respectively, which was consistent with the above studies. Postoperative fever may be related to immune disorder caused by the surgery-induced body stress response, or the systemic inflammatory reaction caused by poor postoperative drainage [29, 30]. In a single-center study, preoperative antibiotics were used to prevent infection in the 403 patients who underwent FURL, and there were still 31 cases of infection after surgery, with an incidence of 7.7% [31]. In this study, the infection rate of FURL group was 4.08%, which was similar to the above study. Since the trauma in the PCNL group was larger than that in the FURL group, the incidence of pain in the FURL group was higher, which was consistent with previous studies [6].

S.T.O.N.E. nephrolithometry scoring system is often used to evaluate the situation of patients with stones and the complexity of surgery before the operation, but the application of the evaluation system is limited due to the interference of some factors, such as stone location, CT value and stone burden [32]. With the improvement of CT imaging technology, the evaluation of stones with S.T.O.N.E. nephrolithometry scoring based on CT scan was clinically certified [33]. According to the risk grades of S.T.O.N.E. nephrolithometry scoring, the stone clearance rate of the mildly, generally and extremely complex groups should have reached 94-100%, 83-92% and 27-64%, respectively [34]. Studies on different risk grades have found that the higher the risk level is, the more difficult the operation will be and the lower the stone clearance rate will be [35]. In this study, the stone clearance rates of FURL in the mildly, generally and extremely complex groups were 100.00%, 76.47% and 16.67%, respectively. However, no mildly complex case was included in the PCNL group, and the stone clearance rates in the generally and extremely complex groups were 85.95% and 33.33% respectively. This was basically consistent with the above stone clearance rates of risk grades. This study found that the stone clearance rates with 6-8 scores of the two groups were similar. For patients in the extremely complex group, FURL was not used as the first choice, and the number of such cases in this study was small, thus failing to conduct a comparative study between the two groups [36].

This study has some limitations. First, this study was a single-center study. Second, the sample size of this study was small. Thus, the sample size can be further expanded in the future. Moreover, the comparative study of the two surgical methods for patients with extremely complex score can be added.

In conclusion, FURL is safe and effective in the treatment of UUTC under 3 cm, and the stone

clearance rate of patients with 6-8 S.T.O.N.E. nephrolithometry scores can be effectively predicted with the treatment of FURL.

Disclosure of conflict of interest

None.

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