Effect of Preoperative Hydronephrosis on Ureteral Stenosis after Flexible Ureteroscopy: A Propensity Scores Matching Analysis

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Research Article

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Effect of preoperative hydronephrosis on ureteral stenosis after flexible ureteroscopy: A propensity scores matching analysis

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Abstract

OBJECTIVES: Ureteral stenosis is a serious complication after flexible ureteroscopy. Other studies have confirmed that stone impaction and intraoperative ureteral injury are important factors causing stricture, and how to predict the occurrence of stricture before surgery may be an important topic. This study retrospectively studied the influence of preoperative hydronephrosis degree on ureteral stenosis after flexible ureteroscopy to explore whether preoperative hydronephrosis degree could predict postoperative ureteral stenosis.

METHODS: A retrospective study was conducted on patients who received flexible ureteroscopy in our hospital for upper ureteral calculi from January 2015 to June 2018. The postoperative follow-up was performed for 36 months, and intraoperative and postoperative complications were recorded. According to the degree of hydronephrosis, the patients were divided into mild hydronephrosis group and moderate and severe hydronephrosis group. Preoperative clinical baseline data of the patients were adjusted by propensity matching score, and differences in intraoperative mucosal injury, operative time, incidence of postoperative ureteral stricture, and SFR 1 month after surgery were statistically analyzed. Kaplan-Meier method and Log-rank test were used to compare the differences in the cumulative incidence of ureteral stenosis between the two groups. Cox regression analysis was used to compare the hazard ratio of ureteral stenosis between the two groups.

RESULTS: A total of 447 patients with 469 sides surgery were included, including
349 sides in the mild hydronephrosis group and 120 sides in the moderate and severe hydronephrosis group. 30 sides in 29 patients developed ureteral stenosis. The stenosis rate before propensity matching analysis was 6.4%, and 8% after propensity matching analysis. However, the SFR and operation time were not statistically consistent. Kaplan-Meier showed a significant difference in the cumulative incidence of ureteral stenosis between the two groups.

CONCLUSIONS: Preoperative patients with moderate to severe hydronephrosis are more likely to have intraoperative mucosal injury, and the incidence of ureteral stricture is higher after flexible ureteroscopy. Preoperative hydronephrosis is an important predictor of ureteral stricture. Preoperative hydronephrosis is an important predictor of ureteral stricture.

Keywords: ureteral stenosis, flexible ureteroscopy, upper ureteral stones, hydronephrosis, propensity scores matching analysis

Background

With the development of flexible ureteroscope technology in recent years, the treatment of upper ureteral calculi with flexible ureteroscope is gradually increasing. Guideline of EAU [1] suggests that "percutaneous nephrolithotomy is considered for ureteral stone larger than 15mm with stone impaction". However, in practical work, the indications for flexible ureteroscope are gradually broadened. Some doctors prefer flexible ureteroscope because it is more minimally invasive and have a lower risk of bleeding. Compared with percutaneous nephrolithotomy, flexible ureteroscope causes less postoperative pain and are more acceptable to
patients. But more minimally invasive does not mean better, and what we find in surgery is that as the flexible ureteroscope is used more often, the number of postoperative complications increases. The incidence of ureteral stenosis, a rare complication after ureteroscopy, is now increasing, and stenosis often requires reoperation, causing more pain to the patient and increasing the financial burden. Ureteral stenosis is commonly reported in hard and semi-hard endoscopic surgery, and the reported incidence is (0.30%-23.81%)[2]. Some scholars have studied the risk factors of ureteral stenosis, and believe that stone burden, stone impaction and operation time are important factors causing Ureteral stenosis[3]. "Stone impaction" has been mentioned in the EAU guideline and many literatures[1, 4, 5]. It has been shown that renal parenchyma thickness and thickness of the ureteral wall on CT is related to stone impaction[6, 7]. In addition, few other studies have been conducted on how to determine "stone impaction". In clinical diagnosis and treatment, we found that regardless of the size of stones, the degree of hydronephrosis is closely related to the occurrence of intraoperative mucosal injury and ureteral stricture. The degree of hydronephrosis may represent the severity of stone incarceration, which is another indicator for preoperative prediction of ureteral stricture. We conducted a retrospective study to confirm this conclusion.

**Methods**

*The patient information*

From January 2015 to June 2018, 688 patients with upper ureteral stone
underwent flexible ureteroscopy in our hospital. Most of them were patients who had not discharged calculi after extracorporeal lithotripsy and were not suitable for extracorporeal lithotripsy due to large stone burden. The patient data were extracted from the hospital database, and the unstored data were obtained by referring to the medical records. Inclusion criteria: 1. Patients with upper ureteral calculi above the level of iliac vessels, including calculi at the ureteropelvic junction; 2. Double J tubes were reserved 1 to 2 weeks before surgery. Exclusion criteria: 1. Previous history of ipsilateral upper ureteral calculi surgery[8], including ureteroscopy, percutaneous nephrolithotomy, laparoscopy or open surgery; 2. Preoperative ureteral stricture; 3. Patients with too much missing important data; 4 urinary malformation; 5 neurogenic bladder; 6 orthotopic neobladder surgery history.

We selected patients with mild hydronephrosis as the case group, and patients with moderate and severe hydronephrosis as the control group. The main observed outcome was ureteral stenosis, and the secondary outcomes included operative time, intraoperative mucosal injury and stone clearance rate 1 month after surgery.

Definition of terms in this paper

Onset time: the time from the onset of symptoms or the detection of stones by examination to the date of surgery.

Calculi size and hydronephrosis: refer to the CT measurement of urinary system. The width of renal pelvis less than 2cm was considered mild hydronephrosis, while
that larger than 2cm was considered moderate and severe hydronephrosis.

Stone burden calculation: maximum length× maximum width×π×0.25(π=3.14)

Stone removal: KUB indicates residual stone ≤4mm.

Postoperative and perioperative management

Preoperative CTU examination excluded ureteral stenosis. Double J tubes were placed preoperatively for 1 to 2 weeks to dilate the ureter. All patients received general anesthesia. The ureteroscope (Wolf 6/7.5 or 8/9.8) was used to remove the stent, and then the ureteral orifice was found. The middle and lower sections of the ureter were explored by ureteroscope, and the guide wire was placed through the working channel. After the endoscope was removed, the sheath of F12 (Cook Company) was placed through the guide wire, and the flexible ureteroscope (Olympus8F) was placed through the sheath to the middle and upper sections of the ureter. The stone was crushed by 200μm Holmium laser with power of 0.8-1.2J and frequency of 15-25Hz, and then a double J tube was indwelled. During the perioperative period, antibiotics was used to prevent infection for 24 to 48 hours and double J tubes were removed 15-60 days after surgery according to the situation.

Postoperative follow-up

All patients were followed up in the outpatient department, KUB was reexamined 1 month after surgery, and B-ultrasound of urinary system was reexamined 3 months, 6 months, 1 year, 2 years and 3 years after extubation. If there was no aggravation of hydronephrosis, no follow-up was performed.
**Postoperative complications**

Postoperative complications were graded according to the Clavien - Dindo grading system. The system is divided into 5 grades according to the severity of complications, different treatment measures and prognosis[9].

**Statistical analysis**

Excel 16 was used for data record and IBM SPSS 25 was used for data statistical analysis. Continuous variables was expressed as mean plus or minus the standard deviation, and clinical features were compared between the two groups using the independent sample t-test (continuous variable) or the independent sample chi-square test (categorical variable). The clinical baseline characteristics of patients were adjusted by 1:1 propensity scores matching analysis. After propensity scores matching analysis, paired sample T test (continuous variable) or McNEMA test (categorical variable) was used to compare the clinical characteristics of the two groups. The Kaplan–Meier method was used to estimate the rate of cumulative events, and log-rank test was used to compare the differences between the two groups. A Cox proportional-hazards model was used to evaluate the hazard ratio for each event in both groups.
Results

Among 688 patients with upper ureteral calculi who underwent flexible ureteroscope in our hospital, 659 patients did not have stenosis, 29 patients had stenosis on 30 sides, 61 patients had missing operation time data, 32 patients had missing other important data, and the patients excluded for other reasons were shown in Figure 1. 469 sides surgical procedures for 447 patients are included in our retrospective analysis, 349 in the mild hydronephrosis group and 120 in the moderate and severe hydronephrosis group. The mean age of patients is 50.43±12.14 years, the mean time of onset is 46.80±55.34 days, the mean BMI is 24.05±3.65, and the mean stone burden is 86.66±46.76 mm². Before propensity scores matching analysis, there are significant differences in age, onset time, renal colic and stone burden between the two groups. A total of 75 pairs of patients are
obtained after 1:1 propensity scores matching analysis, and the baseline clinical characteristics of patients reaches a balance between the two groups (Table 1).

After surgery, 17 patients were lost to follow-up, including 13 patients with stenosis, 4 patients did not return to the outpatient department, and 9 patients went to other hospitals for diagnosis and treatment. Four patients with non-stenosis were lost to follow-up. The differences of observed outcomes before and after propensity scores matching analysis are shown in Table 2. A total of 29 patients had ureteral stenosis on 30 sides after operation. The stenosis rate before the propensity scores matching analysis is 6.4%, while that after the propensity scores matching analysis is 8%. The SFR and operation time tend to be significantly different in the moderate and severe hydronephrosis group before propensity scores matching analysis but is similar in both groups after propensity scores matching analysis.

Table 1. Patients' baseline clinical characteristics

|                     | Before propensity matching | After propensity matching |
|---------------------|---------------------------|---------------------------|
|                     | Mild hydronephrosis       | Moderate and severe       | P-value | Mild hydronephrosis | Moderate and severe | P-value |
|                     | N=349                     | N=120                     | 0.01    | N=75               | N=75               | 0.48     |
| Age (year)          | 49.58±12.03               | 52.91±12.18               | 0.47    | 52.00±10.54        | 53.29±11.94        | 0.77     |
| Male (%)            | 69.1%                     | 69.2%                     | 0.98    | 68.0%              | 66.7%              | 1.00     |
| BMI                 | 23.97±3.53                | 24.27±4.00                | 0.47    | 24.43±3.21         | 24.26±3.95         | 0.77     |
| Disease time (d)    | 41.95±45.41               | 60.88±75.81               | 0.01    | 46.63±42.26        | 43.00±41.59        | 0.59     |
| Renal colic (%)     | 65.6%                     | 31.7%                     | 0.00    | 34.7%              | 37.3%              | 0.80     |
| Fever (%)           | 4.6%                      | 7.5%                      | 0.22    | 8.0%               | 8.0%               | 1.00     |
The median follow-up time of both groups was 36 months, and the mean follow-up time of mild hydronephrosis group and moderate and severe hydronephrosis group was 35.26 months and 30.88 months. Figure 2 shows that the Kaplan–Meier cumulative incidence of ureteral stenosis is higher in the moderate and severe hydronephrosis group before propensity scores matching analysis [hazard ratio (HR) 8.72; 95% confidence interval (95% CI), 3.88–19.60; P = 0.000] when both clinical backgrounds are adjusted, moderate and severe hydronephrosis group is associated with a significantly higher risk of ureteral stenosis compared with mild hydronephrosis group (HR 69.86; 95% CI 0.67–7279.84; P = 0.073). (Figure 2).

According to the statistics of postoperative complications, there were 2 cases
of low fever (Clavien1), 12 cases of high fever (body temperature > 38.5) with urinary tract infection (Clavien2), 71 cases of residual stones (Clavien3a), 29 cases of ureteral stricture requiring reoperation (Clavien3b), and 1 case of postoperative sepsis requiring intensive care (Clavien 4). Long-term follow-up revealed 2 cases of nonfunctional hydronephrosis (Clavien3b).

![Figure 2](image1.png)

**Figure 2.** Kaplan–Meier cumulative event curves of ureteral stenosis before and after propensity score-matching. Adjusted risks of mild hydronephrosis relative to moderate and severe hydronephrosis.
Moderate and severe hydronephrosis are shown

Among the patients with postoperative stenosis, 21 were reoperated in our hospital, among which 2 patients underwent nephrectomy due to non-functional hydronephrosis, 11 patients were cured after resection and anastomosis of ureteral stenosis, and 1 person was cured after ureteral balloon dilation. Four patients underwent endoscopic holmium laser resection of ureteral stenosis, and after failure, they went to other hospitals for further treatment. Three patients were indwelling ureteral stents, and one of them was recanalized after extubation, while the remaining two patients did not get better after extubation, so they went to other hospitals for further treatment.

Discussion

The main results of our research are as follows. First, the incidence of stenosis in moderate and severe hydronephrosis group is higher than that in mild hydronephrosis group. Second, in the moderate and severe hydronephrosis group, the incidence of intraoperative mucosal injury is higher, the duration of operation is longer, and the postoperative SFR is lower. However, there is no difference in the SFR and operation time between the two groups after the adjustment of baseline characteristics. Third, the Kaplan–Meier curve shows that the cumulative incidence of ureteral stricture was higher in the moderate and severe hydronephrosis group.

There are several retrospective studies on the risk factors of ureteral stricture.
In a prospective study, Amr E. Darwish et al. included variables such as stone burden, stone impaction, operative time, and double J tube indwention time into logistic regression analysis, and found that "stone impaction is associated with ureteral stricture". There were only 4 cases of Ureteral stricture in the article[3]. Xeng Inn Fam et al. studied the risk factors for the formation of ureteral stricture after ureteroscopic treatment of impaction calculi. The variables included ureteral perforation, mucosal injury, stone impaction, impaction time, stone size, impaction location, etc., but they failed to find any predictive factors for the formation of ureteral stricture. However, there were only 5 cases of Ureteral stricture[10]. Both of the above two studies adjusted for other factors through Logistic regression analysis, but the overall sample size and the number of stenosis cases were small, which may affect the statistical accuracy. In our study, 29 patients with ureteral stenosis are included. Patients are grouped according to hydronephrosis, and baseline characteristics of patients are adjusted through propensity scores matching analysis. On the basis of homogenization of patients in the two groups, sample size is ensured as far as possible to improve the accuracy of statistical results.

There are many speculations about the mechanism of ureteral stenosis after Ureteroscopic surgery, such as stone impaction, soft sheath compression injury, large stone burden, intraoperative ureteral perforation and the surgeon's experience[2, 11]. Daniel A Wollin et al. designed an in vitro model to study the water temperature at different perfusion rates during holmium laser lithotripsy.
The authors found that, even with high laser power, adequate irrigation could still maintain a relatively stable temperature. With the decrease of the perfusion velocity, the maximum temperature of the laser can be significantly increased even with the use of lower laser power, which may cause damage to the ureteral tissue[12]. Shiulian Chen et al. included 1555 patients in 8 studies in a meta-analysis, and the results showed that the incidence of ureteral stenosis after holmium laser lithotripsy was higher than pneumatic lithotripsy. The authors believe that further studies should be conducted to evaluate this problem[13]. In our actual work, we find that if the calculi can not be pushed during the operation, the possibility of ureteral stricture after the operation is higher. If the ureteral stone loosens or is pushed into the renal pelvis after brief intraoperative holmium laser lithotripsy, there is almost no postoperative ureteral stenosis, which is consistent with Daniel A Wollin's model. The above studies suggest that stone impaction and mucosal injury may be causal, and the key is how to predict the likelihood of these events before surgery. Stone impaction is a vague concept, which is difficult to judge only by preoperative findings. The thickening of ureteral wall on CT may indicate that the ureteral wall is thickened and the stones are surrounded by polyps, which can predict postoperative stenosis[6]. In our practice, we found that the degree of hydronephrosis was associated with postoperative stenosis, which might be another indicator for predicting postoperative stenosis after flexible ureteroscope surgery. Therefore, we grouped according to the degree of hydronephrosis and confirmed this conclusion through retrospective
The present study has several limitations. First, this is a single-center retrospective study with a limited sample size. Surgical equipment and techniques are restricted by the level of the research center. Randomized controlled studies will be ideal, but studies of postoperative complications may be difficult to achieve. Retrospective studies combined with propensity scores matching analysis can reduce baseline differences. Second, after propensity scores matching analysis, there is no statistical difference of the operative time and SFR, possibly because the patients with ipsilateral ureteral calculi complicated with large renal stones accounts for a large proportion, which prolongs the operative time and reduces SFR. However, the addition of exclusion criteria may significantly reduce the number of included patients, affecting the statistical accuracy of ureteral stenosis events. Third, the author did not participate in all the operations and could only evaluate the patient’s condition according to the medical records and imaging, so intraoperative details may be omitted. Fourth, Patients are lost to follow-up and the presence of missing data may affect the true outcome.

Conclusions

Moderate and severe hydronephrosis increases the incidence of mucosal injury during flexible ureteroscopy and postoperative ureteral stenosis, and the prevalence of ureteral stenosis increases with time. The degree of hydronephrosis may be related to stone impaction. Preoperative CT diagnosis of moderate and severe hydronephrosis is an important factor in predicting postoperative ureteral
stenosis, which suggests clinicians to change the surgical method and adopt ureterolithotomy or percutaneous nephrolithotomy.

**List of abbreviations**

FURS = flexible ureteroscopy

SWL = extracorporeal shock wave lithotripsy

BMI = body mass index

CTU = computed tomography urography

KUB = kidneys-ureters-bladder

SFR = stone-free rate

**Declarations**

*Ethics approval and consent to participate*

All included patients gave their oral and written informed consent. The study was approved by the Ethics Committee (full name: Medical Research and Ethics Committee of the First People's Hospital of Huzhou) to the Department of urology, the First People's Hospital of Huzhou, China.

*Consent for publication*

Not applicable

*Availability of data and material*

The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request.

*Competing interests*

The authors declare that they have no competing interests
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Authors’ contributions

Sihi Shao contributed to the conception of the study;

Anping Xiang collected information and followed up patients,

Yuefan Shen performed the data analyses and wrote the manuscript.

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