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# Where is it logical to break-up a ureter stone with endoscopic surgery?

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#### **Ethics Committee Approval**

This study was approved by Ethics Committee of Yozgat Bozok University (protocol number: 2017-KAEK-189\_2020.11.11\_02). All procedures in this study involving human participants were performed in accordance with the 1964 Helsinki Declaration and its later amendments.

#### Conflict of Interest

No conflict of interest was declared by the authors.

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#### Abstract

Background/Aim: Today, we have the technology to break up a ureter stone in the ureter, as well as in the renal pelvis, with ureterorenoscopic procedures. In the past, when this option was not available, the surgeons improved several techniques and antiretropulsion devices to let the stone migrate through the renal pelvis. This study was conducted to clarify whether it is more advantageous to dust a stone in the ureter where it is impacted or in a wider area such as the renal pelvis.

Methods: The data of 134 patients who underwent semirigid ureterorenoscopy (srURS) due to single and primary upper ureteral stones were included and analyzed in this retrospective cohort study. The patients were divided into two groups according to the development of spontaneous push-up during surgery (Group 1: The non-push-up group, Group 2: The push-up group).

Results: While hemoglobin levels lowered significantly in both groups after the surgery, creatinine levels increased (P<0.05). However, there was no significant difference between the groups regarding preoperative or postoperative laboratory findings (P>0.05). Operation times were similar in both groups, in contrast with the literature. Stone-free rates were significantly higher in srURS than in intrarenal surgery (RIRS) (P=0.03). Complication rates were also similar in this study.

Conclusion: The application of srURS after fixing an upper ureter stone at its location using a Stone Cone® results in higher stone-free rates than pushing it back to dust it in renal pelvis. We recommend srURS supported by an antiretropulsion method as a treatment for upper ureteral stones.

Keywords: Ureter Stone, Push-up, Stone migration, Antiretropulsion, Flexible ureterorenoscopy, Rigid ureteroscopy

#### Introduction

Urinary stones occupy the agenda of the medical world with both their frequency and high recurrence rates [1]. Over the last 60 years, great strides have been made in urinary stone treatment, and in the previous two decades, endoscopic surgeries have taken the lead in treatment [2, 3].

Ureterorenoscopy (URS) and flexible ureterorenoscopy/retrograde intrarenal surgery (RIRS) are commonly used surgical methods in ureter stone treatment. Although it is not possible to cure kidney stones with URS, since the introduction of RIRS, even kidney stones can be treated endoscopically when accessed through the urethral meatus [2]. One of the most important advantages of RIRS in ureter stone treatment is that the unintended spontaneous stone push-up that could cause the termination of URS in the past does not any longer. Nowadays, if a stone is pushed up, surgeons can stop performing URS and begin using RIRS to treat stones in the kidney, allowing surgeries to be completed successfully [4, 5].

Different techniques and devices have been used to mitigate the push-up problem [6, 7]. However, it is not clear whether these methods are truly necessary with today's technology. To go a step further and dust the stone after pushing it into the kidney instead of dusting it in a narrow area in the ureter might be more advantageous. In this study, our aim is to compare the clinical parameters of semirigid URS (srURS) in the upper ureter with RIRS for upper ureteral stones which are pushed-up during srURS perioperatively.

#### Materials and methods

The data of 134 patients who underwent srURS due to single and primary upper ureteral stones between January 2018-October 2020 were included and analyzed in this retrospective cohort study. The necessary permissions were obtained from Yozgat Bozok University Clinical Research Ethics Committee (protocol number: 2017-KAEK-189\_2020.11.11\_02) for the use and analysis of this data. Seventy-three patients who were treated with srURS successfully were included in Group 1. Sixty-one patients in whom srURS failed due to spontaneous unintended push-up and the surgical technique was changed to RIRS, were included in Group 2 (alpha=0.05; power: 0.89). Surgeries were performed by four surgeons experienced in endourological procedures. Preoperative complete blood count, routine biochemical analysis (glucose, creatinine, electrolytes), complete urinalysis, and urine culture were obtained from all patients. Patients with signs of infection and pyuria were operated on after receiving appropriate oral therapy and obtaining a sterile urinalysis result. Furthermore, the data of patients with stones reported to be enclaved during surgery, a history of a urinary anomaly, nephrectomy, chronic renal failure, and a JJ stent in the preoperative period were excluded.

#### **Surgical procedures**

Before srURS, cystourethroscopy was performed on the patients. A Stone Cone® was placed in the ipsilateral ureter under fluoroscopy during cystoscopy. Ureteral access was gained with a 9.5F semi-rigid ureterorenoscope (Karl Storz, Tuttlingen, Germany) with a guidewire. After the stone was reached by the ureterorenoscope, it was dusted with a 272 µm holmium: YAG

(Ho YAG Laser; Dornier MedTech; Munich, laser Germany/Dornier Med-Tech GmbH, Medilas H20 and HSolvo, Wessling, Germany) at a frequency of 8-12 Hz and an energy level of 0.8-1.5 J. When a spontaneous unintended push-up occurred during ureteral access or Stone Cone® placement before starting to dust the stone, the surgeon altered the instruments and continued to RIRS. A ureteral accessory sheath (UAS) (Elite Flex, Ankara, Turkey) was placed over the guidewire into the ureter. Following this, the stones were reached by advancing the flexible ureteroscope (Flex-X2, Karl Storz, Tuttlingen, Germany/Karl Storz, Flex X2, GmbH, Tuttlingen, Germany). The stones were dusted with a 272 µm laser. In both procedures, no stone fragment was extracted, and a JJ stent was placed in the ureter. The time from the entrance to the urethral meatus to the end of JJ stent placement after starting to RIRS was recorded as the operative time.

#### Patient follow-up

On the first postoperative day, patients received a direct urinary system radiography to check for the presence of opaque stones and ultrasonography to check for the presence of non-opaque stones. JJ stents were removed at the third postoperative week in all patients. All patients underwent non-contrast computed tomography in the first month postoperatively to evaluate residual fragments and stone free status. The procedure was considered successful for patients with a residual stone fragment of 2 mm or less. Follow-up or medical expulsive therapy was administered to patients with residual stone fragments larger than 2mm. A summary of Clavien-Dindo classification for complications is given in Table 2 [8].

#### Statistical analysis

All statistical analyses were performed with the IBM® SPSS® Statistics version 25 data analysis program (IBM Corp. Released 2017. IBM® SPSS® Statistics version 25.0. Armonk, NY: IBM Corp). The distributions were determined according to the skewness and kurtosis values. Normally distributed data were given as mean (standard deviation), while median (minimum-maximum) values were presented when no normal distribution was observed. Student t-test and Mann-Whitney U test were used for numerical data to compare the two groups. A chi-squared test was used for categorical data. The significance level for the *P*-value was 0.05.

#### **Results**

The demographic and clinical data of the cases are summarized in Table 1. We observed no statistically significant differences between the two groups in terms of age, gender, body mass index (BMI), laboratory data, presence of hydronephrosis, stone size, stone density, operation time, and complication rates (P>0.05 for all). However, stone-free rates were significantly higher in srURS compared to intrarenal surgery (RIRS) (P=0.03).

The hemoglobin (Hb) and creatinine (Cre) levels of the patients before and after surgery were compared separately, and a significant change was observed (Table 1). The Hb values before and after surgery were 14.50 g/dL and 13.05 g/dL, respectively, in Group 1, and 14.30 g/dL and 13.30 g/dL, respectively, in Group 2. In group 1, the mean creatinine value was 0.94 mg/dL preoperatively and 0.87 mg/dL afterwards. The

mean creatinine levels in Group 2 were 0.89 mg/dL and 0.83 mg/dL before and after the surgery, respectively. The rate of the patients with grade 3 and higher hydronephrosis were below 7% in both groups.

Complication rates were similar in both groups (*P*=0.87) (Table 1). After the operation, 1 patient from group 1 and 3 patients from group 2 developed renal colic. The patient in Group 1 had steinstrasse. Additional interventions were performed in these 4 patients in the second session (Stage 3). Urosepsis developed secondary to ureteral perforation in one patient from Group 1 (Stage 4). The patient recovered following appropriate parenteral antibiotherapy and intensive care support. Urinary infection developed in one patient in Group 2 (stage 2) which improved following oral antibiotherapy given in accordance with the urine culture results. One patient had a fever of >38.5°C, which recurred with antipyretic therapy. Macroscopic hematuria was observed in one patient. He improved with bed rest and standard hydration practices (Table 2).

Table 1: Demographic and clinical parameters of two groups

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Parameters		Group 1 (n=73)	Group 2 (n=61)	P-value
Age		46.25 (12.87)	45.51 (14.36)	0.75
Gender (n, %)	Female	18 (24.7)	20 (32.8)	0.39
	Male	55 (75.3)	41 (67.2)	
BMI		28.38 (21.51-37.89)	27.34 (20.20-47.56)	0.36
Preoperative Hb (g/dL)		14.50 (9.1-17.9)	14.30 (10.6-17)	0.72
Postoperative Hb (g/dL)		13.05 (7.9-17.0)	13.05 (7.9-17.0)	0.98
Preoperative Cre (mg/dL)		0.94 (0.6-2.63)	0.89 (0.47-2.24)	0.22
Postoperative Cre (mg/dL)		0.87 (0.51-1.75)	0.87 (0.51-1.75)	0.33
Preop vs Postop Hb**		-6.6	-5.7	< 0.001
Preop vs Postop Cre**		-3.2	-3.7	< 0.001
Hydronephrosis	Absent	14 (19.2)	15 (24.6)	0.67
(n, %)	Grade 1	21 (28.8)	21 (34.4)	
	Grade 2	33 (45.2)	22 (36.1)	
	Grade 3	4 (5.5)	3 (4.9)	
	Grade 4	1 (1.4)	0 (0)	
Stone size (mm)		9 (5-16)	10 (5-24)	0.54
Stone density (HU)		986 (480-1428)	900 (254-1632)	0.06
Operation time (dk)		46.97 (20.51)	48.54 (27.98)	0.70
Stone-free	Residual +	3 (4.2)	9 (15.0)	0.03
(n, %)	Residual -	69 (95.8)	51 (85.0)	
Complication	Absent	56 (77.8)	46 (76.7)	0.87
(n, %)	Present	16 (22.2)	14 (23.3)	

Data were given as mean (SD) in cases with normal distribution, and as median (min-max) in data that did not show normal distribution. For categorical data, it was shown as n (%). BMI: Body mass index; HU: Hounsfield unit; mm: millimeters. \* P < 0.05 \*\* It is shown as "Z value" for Wilcoxon test.

Table 2: The numerical distributions of complications between the groups due to Clavian-Dindo classification

Complication Grade	Group 1 (n=16)	Group 2 (n=14)
Grade 1	14	9
Grade 2	0	1
Grade 3	1	3
Grade 4	1	0

Data were given as frequency (n) in all cases.

#### **Discussion**

The development of stone push-up during URS was a significant problem that resulted in the termination of urinary stone surgeries in the past. Sun et al. reported this rate as 10% for all ureteral stones [9], while Knispel et al. [10] reported it as 40% for upper ureteral stones. To address this problem, various manipulations and antiretropulsion devices or techniques were developed. In an experimental study, Patel et al. [11] showed that the inclination of the patient on the operating table can preclude the development of push-ups during ureteroscopy. Zehri et al. [12] reported that gel instillation to the proximal part of the stone increased stone-free rates. Dretler [13] demonstrated that a ureteral balloon advanced over a guidewire to the proximal part of the stone is useful in averting a push-up. A year later, Dretler [14] reported the successful results of a device called a Stone

Cone<sup>®</sup>. Wang et al. [15] reported that an N-trap occlusion device is effective in preventing stone migration. Heat-sensitive polymers, Lithovac, Lithocatch, Parachute and PercSys devices were developed and put into use [16–18]. As can be seen, stone push-up directly affected the stone-free rates and unsuccessful surgery. However, with the introduction of laser lithotripsy and RIRS, stone push-up is no longer such an impediment to successful surgical completion. Even if a ureter stone migrates retrograde to the kidney during URS, the surgeon can continue the surgery by altering the surgical instrument and successfully complete the operation.

It is known that intrarenal pressure increases during both URS and RIRS. The use of UAS during RIRS significantly reduces intrarenal pressure [19, 20]. This can be considered an advantage of RIRS over URS. However, whether this creates a clinical result in terms of renal functions is controversial. In a study conducted on patients who underwent RIRS, Yang et al. did not detect a significant increase in creatinine on the first postoperative day and in the 1st month postoperatively in stones smaller than 3 cm, while they reported that there was a significant increase in creatinine on the first postoperative day in stones larger than 3 cm and that this regressed in the first postoperative month [21]. Based on these findings, a temporary deterioration of renal function can be expected, especially in cases where surgery time is prolonged. Öztekin et al. reported that they did not detect a significant creatinine change either preoperatively or postoperatively between the two groups who underwent RIRS and URS [22]. In this study, although our operative times were not long in both groups, we did not observe a significant difference between pre-and postoperative creatinine levels.

Considering the larger number of manipulations of RIRS, operation time is expected to be longer in RIRS than srURS. In a study where they compared RIRS with srURS in the treatment of upper ureteral stones, Kartal et al. [4] reported that operation times where RIRS was performed were significantly longer. Similar findings were also reported by Karadag et al [23]. Although Özkaya et al. [24] reported that the use of UAS in patients who underwent RIRS shortened the operative time compared to those in whom UAS was not used, Galal's study [5] comparing RIRS with URS showed that operation times where srURS was carried out were significantly shorter. In our study, although the average length of operations using srURS were shorter than those using RIRS, these differences were not statistically significant.

It is evident that the development of push-up in ureter stones during surgery will make a significant difference between RIRS and srURS in terms of stone-free rates and surgery success. Researchers developed antiretropulsion devices to prevent stone push-up [18, 25]. In addition, methods such as putting patients in the Trendelenburg position or applying gel to the proximal part of the stone were employed to increase stone-free rates [6, 12, 26]. As the surgical technology and technique of RIRS improves, it seems likely that push-up developing during srURS will be treated more easily, and there will no longer be a need for antiretropulsion techniques or devices. However, there are scarcely any studies in the literature comparing the stone-free rates of srURS with antiretropulsion and RIRS. In their study, in

which they did not use an antiretropulsion device, Karadag et al. [23] reported that stone-free rates were superior when RIRS was used compared to srURS both directly after the surgery and in the following months. Similarly, Kartal et al. [4] reported a significant stone-free rate in RIRS procedures compared to srURS without antiretropulsion. Galal et al. [5] found RIRS superior in terms of stone-free rates as a result of their studies comparing rigid URS and RIRS, which they performed without using an antiretropulsion device. However, they added the comment that if they had used a Stone Cone® or N-Trap basket, a higher rate would probably have been achieved using rigid URS. In our study, stone-free rates were significantly higher when srURS was performed compared to RIRS. This may be because we used a Stone Cone® as a standard part of the srURS procedure. In addition, leaving the stone fragments and dust particles in the natural flow path of urine may have given this result. During URS, the surgeon works in a narrow space and may cause iatrogenic damage to the fragile tissue of the ureter, especially in impacted stones. Furthermore, complication rates are lower when RIRS is used [5, 27]. Özkaya et al. [24] reported that complications such as fever, infection, and unsuccessful surgery are less common when using UAS in RIRS. Therefore, RIRS seems to be a more advantageous method. However, not all the data in the literature supports this point of view. Kartal et al. [4] reported that they could not find a significant difference in intraoperative complication rates between RIRS and srURS in upper ureteral stones. Karadag et al. [23] also reported that there was no difference in intraoperative complications. Finally, Galal et al. [5] reported no significant difference between both intraoperative and postoperative complications. In our study, the complication rates were similar between the two groups.

In the light of all this information, it seems that preferring RIRS over srURS in an upper ureteral stone will not make a difference in terms of renal functions; indeed, the possibility of using UAS during RIRS may even provide other benefits [24]. Although the shorter operation time of srURS in the literature suggests that dusting such stones at the location of impaction in the ureter will give faster results, no significant difference was shown in terms of operation times in this study. While it has been reported in the literature that srURS without using antiretropulsion will obtain a lower score than RIRS in terms of stone-free rates, we showed that srURS using antiretropulsion can be superior to RIRS in terms of stone-free rates. Moreover, there is no significant difference between these two surgical options regarding complication rates in upper ureteral stones.

#### Limitations

The limitations of our study include its retrospective design, a small sample size, and a short follow-up period. Prospective studies should be conducted with larger patient groups. The advantage of our study is that there are few studies comparing URS or srURS with RIRS in upper ureteral stones. In addition, it is a unique study in the literature comparing stone dusting after stone push-up with stone dusting performed in the ureter.

#### Conclusion

While choosing between RIRS or srURS in patients with an upper ureteral stone, the idea of pushing a stone that can

easily be treated with srURS to the kidney and, instead, treating it with RIRS is not supported by the findings of this study. The application of srURS after fixing an upper ureter stone at its location using a Stone Cone® results in higher stone-free rates. For these stones, RIRS and srURS yield similar results in terms of laboratory values, complication rates and operation time. Surgeons should use antiretropulsion devices and break the stone in the proximal ureter rather than breaking it in the kidney. Further prospective randomized controlled studies are needed.

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