

## Risk Factors for Failure of Endoscopic Management of Stone-related Ureteral Strictures

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**Purpose:** To investigate factors determining the outcomes of endoscopic management for stone-related ureteral stricture.

**Materials and Methods:** Data of patients who underwent endoscopic surgery for ureteral stricture due to stones from January 2016 to April 2020 were retrospectively analyzed. We compared cases successfully treated with endoscopic surgery with cases that resulted in failure. We focused on factors associated with treatment success, including cause and length of stricture, methods of stricture treatment, surgical time, and duration of hydronephrosis before the treatment. Treatment success was defined as improvement in hydronephrosis status.

**Results:** Nineteen patients were treated for stone-related ureteral stricture. Hydronephrosis was successfully improved in 12 patients (63.2%). Seven patients with failed endoscopic management had ureteroscopic lithotripsy-related stricture, whereas 3/12 (25.0%) patients with ureteroscopic lithotripsy-related stricture and 7/12 (58.3%) patients with impacted stone-related stricture were successfully treated by endoscopic management ( $P = .004$ ). The prevalence of stricture length  $> 15$  mm was significantly higher in the patients with failed management than in the patients with successful management (71.4 vs 16.6%,  $P = .046$ ). Intraoperative endoscopic observation demonstrated that the mucosa of the ureteroscopic lithotripsy-related stricture had ischemic appearance with relatively long stricture length ( $P = 0.13$ ) compared to the impacted stone-related stricture. No association was observed between treatment outcome and method of endoscopic management, including laser incision, balloon dilation, or both.

**Conclusion:** Ureteroscopic lithotripsy as a cause and stricture length  $> 15$  mm could affect the success rate of endoscopic management of ureteral stricture. In such cases, reconstructive management should probably be considered in the early stages.

**Keywords:** hydronephrosis; impacted stones; ureteral stricture; ureteroscopy

## INTRODUCTION

In recent years, the prevalence of ureteral stones has been consistently increasing in the world due to the effects of the increasing incidence of obesity and changes in dietary habits.<sup>(1,2)</sup> Ureteroscopic lithotripsy (URSL) has become a common treatment for middle and lower ureteral stones.<sup>(3,4)</sup> Although it is effective and minimally invasive, it could cause significant complications such as intraoperative ureteral injury, bleeding, infection, and postoperative ureteral strictures (US).<sup>(5)</sup> US is reported to occur in 1–4% of patients after ordinary URSL; however, it occurs in 7.8–24% of patients when URSL is performed for impacted stones.<sup>(6–8)</sup> Moreover, there are non-iatrogenic ureteric strictures such as those associated with impacted stones or chronic inflammatory disorders.<sup>(9,10)</sup>

The main purpose of the management of US is to improve hydronephrosis and protect renal function.<sup>(11)</sup> Recently, a wide variety of therapeutic options have become available to urologists, such as endoscopic management and open/laparoscopic/robot-assisted reconstruction. Laser incision (LI) and balloon dilation

(BD) as endoscopic management techniques for benign US have been described in previous reports; Razdan et al. reported that these techniques had a success rate of 74% in 50 patients.<sup>(9)</sup> Further, May et al. reported that 27.5% of 40 patients were successfully managed with endoscopic techniques.<sup>(12)</sup> The factors that influence the success rate of the endoscopic management of US (e.g., the cause and length of the stricture, the duration of hydronephrosis, the surgical management technique, and the number of placed ureteral stents) are controversial. To identify the factors associated with successful endoscopic management of US, we retrospectively investigated patients who underwent endoscopic management for benign US related to ureteral stones and/or their treatments.

## MATERIALS AND METHODS

### Study population

The present cross-sectional study was approved by the Institutional Review Board of the Nagoya City University Hospital. All patients provided informed consent for the use of their data.

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**Table 1.** Patient characteristics, surgical data, and treatment classifications (success or failure)

Factor	Overall (n = 19)	Failure (n = 7)	Success (n = 12)	P value <sup>b</sup>
Age (years) <sup>a</sup>	69 [58, 73]	71.5 [58.0, 75.3]	60.0 [58.0, 66.0]	0.253
Sex				
Male	12 (63.2%)	3 (42.9%)	9 (75.0%)	0.326
Female	7 (36.8%)	4 (57.1%)	3 (25.0%)	
BMI (kg/m <sup>2</sup> ) <sup>a</sup>	24 [21, 26.9]	25.0 [24.0, 26.9]	23.5 [20.8, 26.5]	0.611
Preoperative hydronephrosis				
Grade 1	3 (15.8%)	0 (0.0%)	3 (25.0%)	0.61
Grade 2	5 (26.3%)	2 (28.6%)	3 (25.0%)	
Grade 3	5 (26.3%)	2 (28.6%)	3 (25.0%)	
Grade 4	6 (31.6%)	3 (42.9%)	3 (25.0%)	
Duration of hydronephrosis before surgery (months) <sup>a</sup>	4.0 [2.5, 5.5]	5.0 [3.5, 5.0]	4.0 [2.0, 7.5]	0.898
Laterality				
Right	11 (57.9%)	3 (42.9%)	8 (66.7%)	0.38
Left	8 (42.1%)	4 (57.1%)	4 (33.3%)	
Location				
Proximal	7 (36.8%)	2 (28.6%)	6 (50.0%)	0.63
Distal	12 (63.2%)	5 (71.4%)	6 (50.0%)	
Cause of stricture				
URSL	10 (52.6%)	7 (100%)	3 (25.0%)	0.004
Impacted stone	7 (36.8%)	0 (0.0%)	7 (58.3%)	
Other	2 (10.6%)	0 (0.0%)	2 (16.7%)	
Length of stricture (> 15 mm)	7 (36.8%)	5 (71.4%)	2 (16.6%)	0.045
Prestenting	5 (26.3%)	0 (0.0%)	5 (41.7%)	0.106
Surgical time (min) <sup>a</sup>	71.0 [64.5, 93.5]	69.0 [64.5, 83.5]	76.0 [63.8, 95.0]	0.554
Endoscopic management				
Laser incision (LI) and balloon dilation (BD)	8 (42.1%)	4 (57.1%)	4 (33.3%)	0.481
LI	2 (10.6%)	0 (0.0%)	2 (16.6%)	
BD	3 (15.8%)	0 (0.0%)	3 (25.0%)	
Drainage				
Single stent	8 (42.1%)	1 (14.3%)	7 (58.3%)	0.12
Double stents	9 (47.3%)	5 (71.4%)	5 (41.7%)	
Nephrostomy tube	1 (5.3%)	1 (14.3%)	0 (0.0%)	
Duration of the post-surgery follow-up (days) <sup>a</sup>	654[546, 1134.5]	618[516.5, 652]	563[877.5, 1304]	0.384

**Abbreviations:** BMI, body mass index; URSL, ureteroscopy lithotripsy; LI, laser incision; BD, balloon dilation

<sup>a</sup>Median [25%, 75% interquartile range].

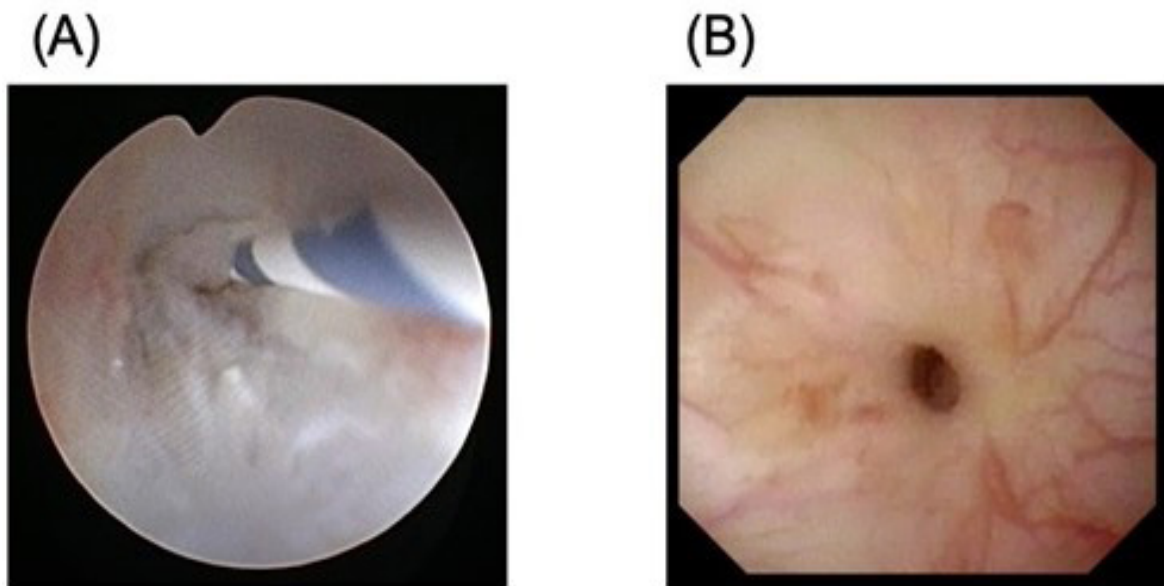
<sup>b</sup>Comparison between the failure and success groups

Patients who underwent endoscopic management for US between January 2016 and April 2020 were analyzed. These patients were referred to our hospital for endoscopic management of ureteral stricture due to impacted stones or postoperative complications after laser ureteric lithotripsy. They underwent LI and/or BD management and one or two ureteral stents or a nephrostomy catheter were placed at the end of the surgery. Patients with a solitary kidney, urinary diversion, poorly controlled diabetes, and those who were pregnant were excluded from this study. We obtained patients' demographics, such as sex, age, and body mass index (BMI), from the medical records. Additionally, the laterality, location, cause, and length of the US, as well as the status of hydronephrosis were also captured. The US related to URSL was defined as follows: US with damage caused by either the laser or access sheath during URSL, which was not detected during previous surgery. In contrast, the US related to an impacted stone was defined as follows: US following stone impaction without damage caused by either the laser or access sheath during URSL, which was detected during previous surgery. Regarding hydronephrosis, Grade 0 hydronephrosis was defined as no swelling of the renal pelvis or calyx, Grade 1 as swelling of the renal pelvis, Grade 2 as swelling of the renal calyx, Grade 3 as swelling of the renal pelvis and calyx, and Grade 4 as swelling of the renal pelvis and calyx with bending of the ureter. Surgical parameters, including surgical time, and success or failure of treatment were analyzed. Success of treatment was defined as improvement in the status of

hydronephrosis examined by either ultrasonography or computed tomography conducted 3 months after removing the ureteral stents. The urine flow through the treated ureter was confirmed by retrograde pyelography when the ureteral stents were removed.

#### Surgical techniques

All patients were placed under general anesthesia, and the operation was performed in the lithotomy position. Before treatment, the status of the stricture was confirmed using retrograde ureteropyelography. A 6.0 Fr semi-rigid ureteroscope (Olympus, Tokyo, Japan) was inserted and used to observe the stricture site. Then, we inserted a 0.035-inch hydrophilic guide wire through the stricture site. BD was conducted when the diameter of the stricture allowed the insertion of the URO MAX Ultra™ before inflation; otherwise, LI was performed instead. In contrast, both procedures were conducted with mucosal findings of rigid appearance. As for the LI procedure, we cut the mucosa and muscular layer of the stricture site (including 5 mm before and after) using a 272 μm fiber (Cyber Ho, Quanta system, Milan, Italy) until we could visualize the fat tissue outside of the ureter. The energy setting was 6.0 W (1.0 J × 6 Hz) and the incision was conducted using the 'Soft Tissues' mode. For the BD, we dilated the ureteral lumen up to 15 Fr using a balloon catheter (URO MAX Ultra™; Boston Scientific Japan, Tokyo, Japan). One or two double-J ureteral stents (4.7 or 6.0 Fr, INLAY OPTIMA™, BD, Franklin Lakes, NJ and 4.8 Fr, Tria™, Boston Scientific, Marlborough, MA), chosen by the main operator, were placed into the ureter at the end of procedures.



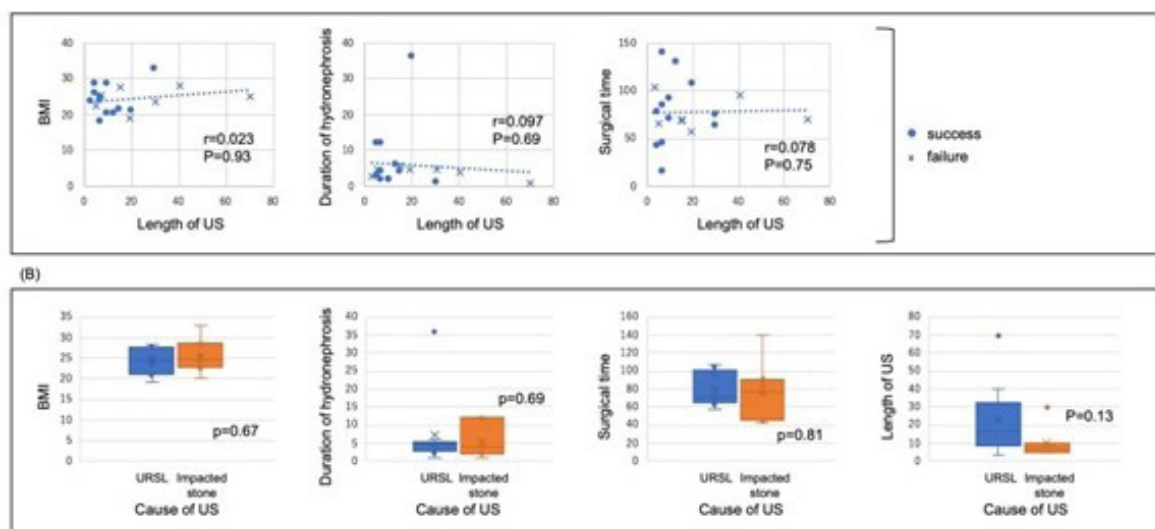
**Figure 1.** (A) Findings from ureteroscopy of URSL-related US. The ureteral mucosa appeared white and poor blood vessels were observed. (B) Findings from ureteroscopy of impacted stone-related US. Relatively normal blood vessels were observed on the mucosa. URSL, ureteroscopic lithotripsy; US, ureteral stricture

### Statistical analysis

Non-normally distributed variables are expressed as medians (25%, 75% interquartile range). Categorical variables are presented as frequencies (percentages). Data were analyzed using EZR for R (R project 3.6.3, R Foundation for Statistical Computing, Vienna, Austria) (13). To compare the patients with failed or successful management and the factors associated with the cause of US, the Fisher's exact test and Mann-Whitney *U* tests were used. The correlation coefficient between the length of US and perioperative parameters was computed using Spearman's rank correlation coefficient.

### RESULTS

A total of 19 patients were identified as having undergone endoscopic treatment for US after laser lithotripsy for ureteral stones. The characteristics of the patients and surgical data are summarized in **Table 1**. Preoperative hydronephrosis was Grade 1 in 3 patients (15.8%), Grade 2 in 5 (26.3%), Grade 3 in 5 (26.3%), and Grade 4 in 6 (31.6%). The median duration of hydronephrosis before surgery was 4.0 months. The stricture cause was identified as URSL in 10 patients (52.6%), impacted stone in 7 (36.8%), and chronic inflammatory disorders in 2 (10.5%). Seven patients had a US longer



**Figure 2.** (A) Correlation between length of US and BMI, duration of hydronephrosis and surgical time. The correlation coefficient (*r*) was computed using Spearman's rank correlation coefficient. (B) Comparison of perioperative parameters between URSL-related and impact stone-related US. BMI, body mass index; URSL, ureteroscopic lithotripsy; US, ureteral stricture

than 15 mm. Prestenting 3 months before surgery was performed in 5 patients (26.3%). Eight patients (42.1%) underwent both LI and BD. Two patients (10.6%) underwent LI alone, while 3 (15.8%) underwent BD alone. A single stent was placed in 8 patients (42.1%) and double stents were placed in 9 (47.3%). We were unable to perform LI or BD in 3 patients (15.8%) as the stricture was too severe. Specifically, although we were able to insert the guidewire in 1 patient, imaging of the direction of incision was not possible and we placed a ureteral stent. In the other 2 patients, we were not able to insert the guidewire at all and we placed a nephrostomy tube in 1 patient. The median duration of the post-surgery follow-up was 654 days.

**Table 1** also classifies the data as treatment success or failure. The success rate of the treatment was 63.2% (12/19). URSL-related US occurred in 7 and 3 patients in the failure and success groups, respectively ( $P = .004$ ). The ureteral mucosa appeared to become white in color and poor blood vessels were observed in URSL-related US (**Figure 1A**). Contrarily, all 7 patients with impacted stone-related US were successfully treated with endoscopic management. Relatively normal blood vessels were observed on the mucosa in the impacted stone-related US (**Figure 1B**). Five patients in the failure group (71.4%) had a US longer than 15 mm, whereas only 2 patients in the success group (16.6%) had a US longer than 15 mm ( $P = .045$ ). Based on the post-surgery follow-up, 2 patients in the success group (16.6%) underwent re-treatment. Specifically, 1 patient had the ureteral stent replaced and the other had LI at 1257 and 1735 days, respectively, from the first endoscopic surgery. Furthermore, 3 patients in the failure group (42.9%) underwent open surgeries and 1 patient (14.3%) underwent BD again.

The correlation between length of US and other perioperative parameters, as well as the comparison of perioperative parameters between URSL-related and impacted-stone related US are shown in **Figure 2A and 2B**. The correlation coefficients between length of US and BMI, duration of hydronephrosis, and surgical time were 0.023, 0.097, and 0.078, respectively ( $P = .93, .69, \text{ and } .75$ ). The median BMI, duration of hydronephrosis, surgical time, and length of US in the patients with URSL-related and impacted stone-related US were 24.4 and 26.6 kg/m<sup>2</sup>, 4.5 and 4.0 months, 70.5 and 77.5 minutes, and 17.0 and 7.0 mm, respectively ( $P = .67, .69, .81, \text{ and } .13$ ).

## DISCUSSION

The development and innovation of endourologic tools has enabled urologists to choose endoscopic management techniques, such as endoureterotomy and endoscopic dilation, for patients with US.<sup>(14)</sup> These techniques are safer and less invasive than open surgical repair; however, success rates vary widely between reports.<sup>(9,15)</sup> We would investigate the factors that influence the success rate of the management for stone-related US.

Intraoperative ureteral damage during URSL is one of the causes of US.<sup>(6)</sup> US caused by ureteral damage is associated with ischemic changes, which results in lower success rates following treatment for US.<sup>(7)</sup> On the other hand, it is reported that stones embedded in the ureteral mucosa stimulate inflammation, which might result in US.<sup>(16)</sup> US caused by stones embedded in the ureteral

wall does not always involve ischemic changes; therefore, relatively normal blood vessels may be observed on the mucosa (**Figure 1B**) and it is likely to be curable with additional treatment.<sup>(11)</sup> Netto et al. reported that the success rates of BD for non-ischemic and ischemic US were 89 and 29%, respectively.<sup>(17)</sup> In the current study, 52.6% of the USs were related to URSL; the success rate of the management for URSL-related US was significantly lower compared to that of the management for impacted stone-related US. The mucosal change in URSL-related US indicated ischemic change, which could result in a poor success rate. There were no significant differences in perioperative parameters, including the length of US, between the patients with URSL-related and impacted stone-related US. These data suggest that treating URSL-related US with endoscopic management is challenging.

US length is thought to be an important predictor of the outcome after endoscopic management for US in several reports. Netto et al. reported a lower success rate for the management of USs longer than 10 mm.<sup>(17)</sup> Thomas et al. reported a poorer outcome of BD for USs longer than 15 mm.<sup>(18)</sup> Meretyk et al. reported that the 20 mm length was the most reliable predictor of success rate of LI.<sup>(15)</sup> The current study demonstrated that more than 70% of patients in whom endoscopic treatment failed had a US longer than 15 mm. Moreover, the length of US poorly correlated with other perioperative parameters. According to these data, which are consistent with previous reports, our study revealed that a length of 15 mm was likely to be an important factor to affect success rate of endoscopic treatment.

Prior studies report that the duration of the US is associated with the success rate for endoscopic management. Byun et al. reported that the duration of US (shorter or longer than 3 months) was an important factor that affected the success rate.<sup>(19)</sup> In contrast, Wolf et al. reported that the duration of the US did not significantly affect the success rate of US treatment.<sup>(20)</sup> In the current study, the median duration of hydronephrosis before surgery was not significantly different between the patients with endoscopic treatment failure and success.

The success rate of LI using a holmium YAG laser was reported to be 67-68.4%.<sup>(21,22)</sup> Moreover, previous reports demonstrated that the success rate of BD for US was 50-76%.<sup>(23,24)</sup> A Holmium YAG laser with both cutting and coagulating functions provides precise incision to a depth of the fat tissue outside of the ureter with effective hemostatic effect.<sup>(25)</sup> We assumed that the combination of LI and BD enabled the equally centered expansion of the lumen on the incision line, which prevented restenosis. However, the current study showed that there were no significant differences in the management between the patients with success or failure; 57% patients underwent both LI and BD in the failure group, whereas 33.3% patients underwent both procedures in the success group.

Ureteral stents are preoperatively used for avoiding infection and kidney failure before the management of urolithiasis. They dilate the ureteral lumen and straighten the ureter, which makes it easy to insert a ureteroscope or ureteral access sheath.<sup>(26)</sup> For these reasons, prestenting would also elevate the success rate of endoscopic management for US. In our study, all 5 patients with prestenting had successful endoscopic management; therefore, we believe prestenting could contribute

to improved treatment success rates.

The placement of two ureteral stents was first reported in cases of malignant obstruction.<sup>(27)</sup> The authors suggested that two stents have more power to stand up to the comprehensive force of the tumor than one thick stent. The use of two ureteral stents has been applied for the management of benign US.<sup>(9,28,29)</sup> Some urologists prefer to insert as large of a ureteral stent as possible; however, larger stents cause ischemia of the ureter, which tend to develop restenosis.<sup>(29)</sup> It is reported that two stents slide against each other via peristalsis of the ureter, which maintain the expanded lumen.<sup>(30)</sup> This motion may prevent ischemia or pressure necrosis of the ureter, which is believed to result in a better success rate; however, our study showed no statistical difference in treatment success rates between the patients with single and double stents.

Our study is limited by its relatively small number of patients. Due to the nature of the disease, it was difficult to collect a large number of cases, even in this multicenter study. Therefore, we could not perform the multivariate logistic regression and interaction analysis of risk factors for unsuccessful treatment and care should be taken when interpreting the results. However, the significance of this study lies in the fact that it focused on the stricture associated with urinary stones and identified a lower success rate of US endoscopic management following damage during URSL. Moreover, given that identifying the beginning of US development was difficult without close monitoring, we may not have been able to provide an accurate estimate of the US duration. Furthermore, although improvement of hydronephrosis was defined as successful in this study, other factors, e.g., change in split renal function, should have been assessed as well. Despite these limitations, we believe that our study findings will be helpful for choosing endoscopic management or other options, such as open/laparoscopic/robot-assisted reconstruction, as treatment for stone-related US.

## CONCLUSIONS

URSL as the cause of US and US with a length of > 15 mm could affect the success rate of the endoscopic management of US. In such cases, reconstructive management for US should probably be considered in the early stages.

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Not applicable

## CONFLICT OF INTEREST

The authors declare no competing interests.

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