

Ureteral strictures following ureteroscopic stone treatment

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Abstract

Background and purpose: Ureteral stricture is a rare, but serious complication following ureteroscopy (URS) for stones. The aim of this study was to investigate how many patients ended up with a ureteral stricture after URS at our hospital and how these were treated. We also wanted to identify potential risk factors for post endoscopic stricture formation.

Materials and methods: A retrospective evaluation of 1001 URS for stone treatment at the day-case surgery unit between 2013 - 2018 was performed. Data on pretreatment status, the surgical procedure and follow-up were recorded. Exact χ^2 and independent-samples *t*-tests were used comparing data among those who developed strictures and those who did not. Multiple logistic regression was performed analyzing risk factors for stricture formation.

Results: In total, 1001 URS were performed in 725 patients, 289 women and 436 men. Of these, 995 cases were eligible for analysis. At follow-up with computed tomography after 3 months, 28 (3.0%) strictures were identified. Of these, 20 received endourological treatment with balloon dilatation of which 15 (75%) were successful. Definitive treatment in the 13 patients with failed or unattempted endourological treatment included nephrectomy, reconstructive surgery, permanent nephrostomy or observation with no further treatment. In multiple regression analysis, use of access sheath (UAS) (OR 4.6, $p = 0.011$), ureteral perforation (OR 11.8, $p < 0.0001$) and surgical time > 60 minutes (OR 5.7, $p < 0.005$) were found to be risk factors for stricture formation.

Conclusion: Ureteral stricture is a rare complication of URS. Balloon dilatation should be the first line of treatment. Use of UAS, perforation and excessive operating time were found to be risk factors for post endoscopic ureteral stricture formation. Special attention to these risk factors should be given to reduce the incidence of ureteral strictures.

Introduction

A ureteral stricture is a narrowing of the ureter causing functional obstruction¹. This may cause pain, lead to a deterioration in renal function and hinder ureteral stones from passing spontaneously. It may also act as an obstacle for passage of an endoscope. Ureteroscopy (URS) is a known iatrogenic cause of strictures and risk factors in conjunction with this procedure include perforations and excessive operating time^{1,2}. In addition, URS performed by an inexperienced surgeon has been shown to increase the risk of complications^{3,4}. However, it is still unclear whether surgical experience also affects the risk of developing ureteral strictures.

The introduction of small diameter endoscopes, lasers and auxiliary equipment is thought to have contributed to a reduction in the occurrence of post-endoscopic strictures in recent years, with current rates reported to be 0.3 - 4%^{2,5-7}. However, the role of ureteral access sheaths (UAS) in the development of ureteral strictures is still debated^{8,9}.

The present study was planned with the aim of clarifying questions and identifying factors related to development of ureteral strictures following URS for stone disease. The main objective of this study was to determine how many patients ended up with a ureteral stricture after URS for urolithiasis at our hospital. Furthermore, we wanted to identify possible risk factors for post endoscopic stricture formation.

Secondary aims were to point out possible specific causes for stricture development in each case and see how these strictures were treated.

Materials and methods

Setting, study population and data collection

In October 2013, a new day-case surgery unit opened at Haukeland University Hospital (HUH) in Bergen, Norway. The URS procedures were reorganized from regular in-patient cases to being performed as day-cases in the new unit.

As part of an internal quality evaluation of the endoscopic activity in our department, a retrospective review of all the retrograde ureteroscopic stone treatments performed in the day-case surgery unit since the opening in October 2013 until June 2018, has been done. The indications for URS were the same in the five-year time-frame, and there was no major change in the performance of the procedure or in the equipment used.

In total, 1001 URS for stones were performed in 725 patients, 289 women and 436 men. The mean age at the time of endoscopy was 55 years (range 4 – 95 years). The patients' general condition was assessed using the American Society of Anaesthesiologists Score (ASA-Score), with 2 being the median ASA-Score.

A non-contrast computed tomography (CT) was performed prior to the URS. Stone size was defined as the largest diameter of the calculus. If multiple stones were present, the largest diameter of the biggest stone was registered. Preoperative obstruction was defined as presence of dilatation proximal to the stone seen on preoperative CT, persistent pain or finding of an impacted stone at the time of the URS. Table 1 presents the pre-treatment basic characteristics.

The URS procedures were performed using either a semirigid endoscope (8F/9.8F tapering shaft, Richard Wolf Medical Instruments Corporation, Vernon Hills, IL), a flexible endoscope (URF-V-V3 or P6/P7, Olympus Corporation, Tokyo, Japan), or both. The decision to use a UAS or a safety guide wire (SGW) was entrusted to the surgeon in each case based on their

personal preferences. In these cases, either a 10/12 CH or 12/14 CH UAS (UroPass[®], Olympus Corporation, Tokyo, Japan) was inserted depending on the flexible endoscope used, while a super stiff hydrophilic guide wire with floppy tip (SureGlide[®] 0.035", Olympus Corporation, Tokyo, Japan) was the standard guide wire. It should be noted, however, that a sheath- and wireless procedure is routine at HUH. A holmium laser was utilized for fragmentation of the stone when deemed necessary, and fragments were retrieved with forceps, baskets or left in situ for spontaneous passage depending on the preferences and judgement of the urologist in each case.

To achieve the best possible estimate of post endoscopic strictures, cases in which dilatation of a ureteral stricture was required in order to reach the level of the calculus *prior* to stone treatment, were excluded from further analysis. Characteristics of the URS procedures are presented in table 2.

Follow-up with non-contrast CT was performed after three months. A post endoscopic ureteral stricture was defined as dilatation of the upper urinary tract proximal to a ureteral narrowing verified on CT or verified directly at a second URS. Ureteroscopically, a stricture was noted if the narrowing was not passable for the endoscope in a location where a stenosis or tapering of the ureteral lumen was not registered during the first endoscopy. If dilatation was noted at follow-up, the patient was scheduled for a second URS to verify the presence of a ureteral stricture and continue with endoscopic treatment if considered appropriate.

Initial follow-up imaging was performed 3-6 months after the endoscopic treatment.

Successful treatment was defined as regression of the dilatation seen on CT or ultrasound together with persistent relief of symptoms. Further follow-up was assessed in each case. In cases with persistent dilatation, a subsequent URS with a second attempt of endourological

treatment was performed. If still unsuccessful, an isotope renography was performed whenever there was doubt about renal function before reconstructive surgery, nephrectomy or permanent drainage.

Statistics

Independent-samples t-tests were performed comparing continuous variables, such as stone size and operating time. Categorical variables, such as sex and ASA-scores, were compared using exact chi-squared tests. Multiple regression analysis was performed to determine risk factors for ureteral stricture.

IBM SPSS Statistics 25 (IBM, Armonk, NY) was used for statistical analysis. The p value was considered significant when < 0.05 .

Ethics

The study was approved by The National Committees for Research Ethics in Norway (ID-no: 2018/2545 REK) and The Data Protection Authorities at HUH (ID-no: 1041).

Results

During the study-period, 1001 URS were performed for the treatment of calculi. Six cases were excluded from further analysis because a ureteral stricture was identified and treated during the URS procedure before reaching the level of the stone. Of the remaining, 535 (53.8%) were done for stones located in the renal pelvis, 348 (35.0%) for ureteral stones and 112 (11.3%) for both renal and ureteral stones combined. The preoperative stone status is provided in Table 1.

Follow-up after 3 months with a CT scan was registered in 947 cases (95.2%), and 28 (3.0%) strictures were identified. Figure 1 shows the stricture rate partitioned per year from 2013 to 2018. The stricture rates were stable throughout the study period with a mean rate of 1.8% per year, except 2017 when there was a peak in the number of strictures.

Preoperative, operative and postoperative characteristics were compared for patients who developed a post endoscopic ureteral stricture and those who did not. There was no significant difference in the number of patients having obstruction prior to the URS in the stricture group compared to the non-stricture group, 13 (46.4%) and 305 (33.2%) cases respectively, $p = 0.157$. Preoperative treatment with a JJ-stent was significantly more frequent in the stricture group with 11 cases (39.3%) compared to the non-stricture group with 122 cases (13.3%), $p = 0.001$. This may be related to the trend of more patients in the stricture group having previous URS attempts for the same stone (10 cases, 35.7%) compared to the non-stricture group (211 cases, 23.0%), $p = 0.170$.

Table 2 compares characteristics from the surgical procedures between patients who did not develop ureteral strictures and those who did. Two high volume endourologists performed more than half the number of procedures in addition to assisting residents in most of their URS. The remaining procedures were performed by another six urologists.

UAS was used almost exclusively when treating renal stones. Only two cases of ureteral stones required UAS. The opposite was found regarding SGW, which was used in three cases of renal stones and 16 cases with ureteral stone.

In 21 cases (75.0%) the strictures occurred on the left side. Distal ureter was the predominant location for stricture formation followed by proximal and middle ureter in 12 cases (42.9%), 11 cases (39.3%) and 5 cases (17.8%), respectively. Twenty-two strictures (78.6%) were less than < 2 cm long.

Table 3 presents possible risk factors for development of ureteral strictures determined by multiple regression analysis. Use of UAS, intraoperative ureteral perforation and operating time above 60 minutes all increased the risk for post endoscopic stricture significantly.

In most cases, more than one cause associated with stricture formation could be identified.

In 20 cases (71.4%), events related to the URS procedure were registered as a possible cause of stricture development and impacted stones in 18 cases (64.3%). Previous radiation therapy as a contributing factor to stricture formation was registered in three cases (10.7%).

Of the 28 patients who ended up with a ureteral stricture, endourological treatment was attempted in 21. Of these, 20 were treated with balloon dilatation. Fifteen patients (75.0%) were treated successfully with this procedure. Ten patients required a single treatment and five patients needed two consecutive URS procedures with balloon dilatation before persistent success. One patient had laser incision of the ureteral stricture as the only endourological treatment, which was unsuccessful. Endourological treatment was not successful in any of the patients with previous radiation therapy.

Mean follow-up time was 14 months (range 1 - 42 months) in patients receiving endourological stricture treatment with a mean number of 3 follow-up consultations (range 1 - 6). Mean follow-up time for the 15 patients with successful treatment with balloon

dilatation was 17 months (range 2 - 42 months), with 3 consultations (range 1 - 6). In the six patients with unsuccessful endourological treatment, the mean time from failed balloon dilatation or laser incision until final surgery was 8 months (range 1 - 15).

Location of the stricture in the ureter was not related to successful management with balloon dilatation. On the other hand, strictures < 2 cm had significantly higher success rate after endourological treatment compared to strictures > 2 cm, 14 cases (87.5%) and 1 case (20.0%), respectively, $p = 0.011$.

Definitive treatment in the 13 patients with failed or unattempted endourological treatment, include nephrectomy in four, reconstructive surgery in another five, permanent drainage with a nephrostomy tube in one and observation with no further treatment in the last three patients who all had severe comorbidities or were asymptomatic secondary to a non-functioning kidney.

Discussion

By reviewing all the retrograde URS procedures performed for stones in the day-case surgery unit at HUH since the opening in October 2013, we have determined the incidence of post endoscopic ureteral strictures, identified risk factors for stricture formation and mapped out how the strictures were treated.

At follow-up after 3 months, 28 strictures (3.0%) were identified. This is in accordance with other studies^{5,6,8,10}. The stricture rates were stable throughout the study period except a peak in the number of incidences in 2017. We could not point out any specific reason for this increase as the indications for URS, the performance of the endoscopy and the equipment used were unchanged during the study-period.

The mechanisms of stricture formation following ureteroscopic stone treatment may be multifactorial and are not fully understood. Intraoperative ureteral injury and a long-term inflammation caused by impacted stones may be contributing factors¹¹. The inflammatory process following injury produces a fibrinous exudate that precipitates on traumatized areas, promoting adherence and ultimately stricture formation. In addition, periureteral fibrosis may also develop when urine is extravasated from the ureter, especially in the presence of infection¹². This means that any factor or event leading to ureteral wall injury is a potential risk factor for the development of ureteral stricture.

Impacted stones are considered to be one of the main predictors of stricture formation^{13,14}. Detailed information regarding stone impaction was not available in the database. This data was retrieved from the patient charts for all patients who developed strictures. Preoperative obstruction may be an indication of the stone being impacted. However, dilatation may also be seen in stones that are unimpacted. This may explain why there was no significant

difference in the number of strictures at follow-up in patients with preoperative obstruction compared to those with no preoperative obstruction.

Surprisingly, pretreatment with a JJ-stent was more frequent in patients who developed strictures. Pre-stenting has been demonstrated to reduce the risk of ureteral lesions during URS¹⁵⁻¹⁷. Nevertheless, the protective properties of the stent might not fully have abolished the deleterious effects of an impacted stone in the present study, and may explain why more strictures occurred in the pre-stented patients. In addition, there was a trend towards more patients in the stricture group having had a previous procedure for the same stone compared to the non-stricture group. This may also explain the higher incidence of pre-stenting. Another trend that may have contributed to the higher pre-stenting rate in the stricture group was larger stone size and more stones located in the ureter in these patients. Three-quarters of the strictures were located in the left ureter. May et al. have suggested that the left ureter might have an anatomical or functional predisposition to obstruction as more strictures seem to occur on this side². This finding could not be confirmed in the present study. Nor could we identify a predilection site for strictures with regards to the level of the ureter. Castro and coworkers were also unable to demonstrate such an association¹⁸. In most cases, the level of the strictures coincided with the location of the stones.

Even though most strictures developed after treating stones in the ureter, we found no significant association between stricture formation and stone location. It is noteworthy that more than 35% of the strictures in our material were seen after URS for stones in the renal pelvis. This suggests that surgical technique is a major contributor to stricture formation.

A SGW was used in 19 (2.0%) cases only, with no difference between patients who developed strictures and those who did not. The use of a SGW has not been considered

mandatory at HUH since URS was introduced in the early 1980s. In a previous study comparing URS for ureteral stones with and without a SGW, we could not demonstrate any difference in the number of intraoperative complications⁷. However, the post endoscopic stricture rate was significantly higher when a SGW was used compared to when it was omitted⁷.

The use of UAS during URS is debated. Advocates for its use claim superior stone free rates (SFR), shorter operating time and lower intrarenal pressure^{19,20}. However, other studies have shown that insertion of UAS may lead to ureteral lesions¹⁵. In addition, large cohort studies have shown no difference in the SFRs whether a UAS has been used or not²¹. Due to these controversies, the EAU Guidelines on Urolithiasis state that the decision to use a UAS is up to the surgeon based on his or her preference¹⁰. UAS was rarely used in the present study, and conclusions should therefore be drawn with caution. Nevertheless, significantly more strictures were found when a UAS was used compared to when it was omitted. The use of UAS was also found to be a significant risk factor for development of stricture in multiple regression analysis with an OR of 4.6, $p = 0.011$. In a randomized trial, Lallas et al. demonstrated a transient decrease in ureteral blood flow when a UAS was inserted²². Even though blood flow returned to normal after a short period of time, the transiently impaired blood supply to the ureter may explain the higher rate of strictures when a UAS was used. Intraoperative perforation and excessive operating time were found to be significant risk factors for stricture formation. These findings are in accordance with other reports^{1,2}. The inflammatory response following a perforation may explain stricture formation. Excessive operating time might reflect a more complicated stone situation. In addition, an extended operating time undeniably causes reduced blood flow to the ureter either when dilated by the endoscope, or even worse, by insertion of the bigger UAS.

On the other hand, surgical experience was not found to increase the risk of stricture formation. This finding is in contrast to the increased risk of complications in URS performed by inexperienced surgeons reported by others^{3,4}. An explanation may be that more complicated cases were operated by experienced surgeons in our series.

In total, 20 of the 28 patients who developed strictures were treated with balloon dilatation, 15 (75%) successfully. The success rate was higher when the strictures were < 2 cm compared to longer strictures. Both findings are in accordance with other studies^{2,5}.

The retrospective design of this study is a limitation. This may have contributed to rough registration of data and underestimation of complications that could have affected the outcome. Incomplete renographic data makes it difficult to assess the renal function after endoscopic treatment. However, regression of dilatation and remission of symptoms may still indicate successful treatment. Furthermore, in cases of persistent dilatation or pain, patients were investigated with a subsequent URS or an isotope renography. The added diagnostic value of controlling *all* stricture patients with an isotope renography may therefore be questioned in the present study.

Detailed data on stone impaction was only available for patients who developed strictures. This limitation has prevented us from including stone impaction as an independent risk factor in the multiple logistic regression analysis. Another limitation is the relatively low number of strictures. This may have caused important risk factors to falsely turn out as nonsignificant in the analyses. In addition, the low number of adverse events make adjusted analyses of the background characteristics difficult. Despite the relatively low number of strictures, the present study is still one of the largest of its kind.

Conclusion

Ureteral stricture is a rare, but serious complication following URS. Our study suggests that endourological balloon dilatation should be the first line treatment, with an expected success rate of about 75%. Risk factors for post endoscopic ureteral stricture formation were found to be use of UAS, perforation and excessive operating time. Special attention to these risk factors should be given in order to reduce the incidence of ureteral strictures.

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Disclosure Statement

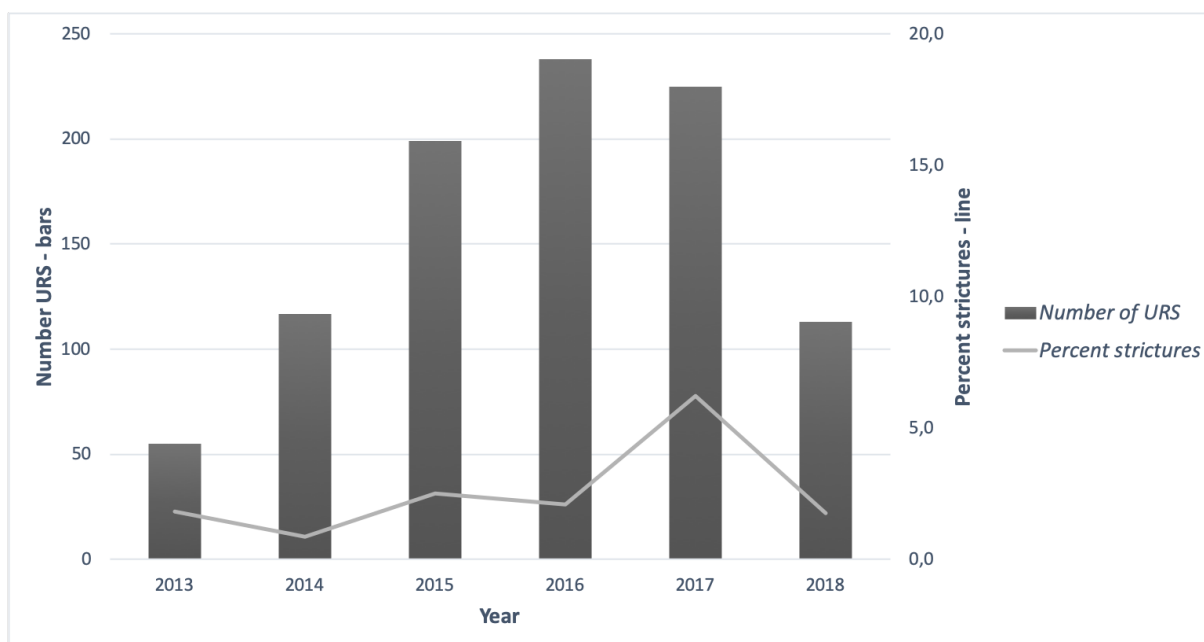
Øyvind Ulvik is a consultant for Olympus, who was not involved in the design, collection, analyses, interpretation or reporting of the data. The two other authors have nothing to disclose.

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Figure 1 Ureteral stricture rates per year throughout the study period

In 2013, only procedures performed between October and December were included. In 2018, only procedures performed before July were included.

Table 1 Preoperative characteristics

Characteristics		
<i>Side of treatment</i>		
	Right	427 (42.9%)
	Left	568 (57.1%)
<i>Stone status</i>		
<i>Renal pelvis</i> (n=647)	Size in mm - mean (95% CI)	8.7 (8.3 - 9.0)
	Number of stones	1
		2
		3
		> 3
		336 (51.9%)
		112 (17.3%)
		60 (9.3%)
		139 (21.5%)
<i>Ureter</i> (n=460)	Size in mm - mean (95% CI)	7.4 (7.1 - 7.7)
	Number of stones	1
		2
		3
		> 3
	Location*	<i>proximal</i>
		<i>middle</i>
	<i>distal</i>	
		395 (85.9%)
		37 (8.0%)
		6 (1.3%)
		22 (4.8%)
		150 (32.6%)
		57 (12.4%)
		265 (57.6%)
<i>Obstruction prior to URS (dilatation on CT)</i>		330 (33.2%)
<i>Pre-stented with JJ</i>		140 (14.1%)

*Some patients had stones in multiple locations

Table 2 Comparison of characteristics related to the URS procedure

Characteristics	No stricture	Stricture	p-value
<i>Stone location</i>			
Renal pelvis	502 (54.6%)	10 (35.7%)	0.121
Ureter	318 (34.6%)	14 (50.0%)	
Both renal pelvis and ureter	99 (10.8%)	4 (14.3%)	
<i>Stone size in mm - mean (95% CI)</i>			
Renal pelvis	8.7 (8.3 - 9.1)	10.5 (6.3 - 14.7)	0.371
Ureteral	7.4 (7.1 - 7.7)	9.5 (6.9 - 12.1)	0.104
<i>Operator experience</i>			
Resident	242 (26.3%)	6 (21.4%)	0.476
Consultant	201 (21.9%)	4 (14.3%)	
Endourologist	476 (51.8%)	18 (64.3%)	
<i>Endoscopes</i>			
Semirigid only	202 (22.0%)	9 (32.1%)	0.155
Flexible only	56 (6.1%)	3 (10.7%)	
Semirigid and flexible	661 (71.9%)	16 (57.2%)	
<i>Safety guide wire</i>	18 (2.0%)	1 (3.6%)	0.438
<i>Access sheath</i>	32 (3.5%)	5 (17.9%)	0.004
<i>Stone fragmentation and retrieval</i>			
Dusting/fragmentation only	403 (43.9%)	6 (21.4%)	0.020
Fragmentation and retrieval	516 (56.1%)	22 (78.6%)	
<i>Intraoperative complications*</i>			
Total cases	74 (8.1%)	9 (32.1%)	< 0.0005
Disturbing bleeding	59 (6.4%)	5 (17.9%)	0.035
Perforation	25 (2.7%)	6 (21.4%)	< 0.0005
Mucosal abrasion	20 (2.2%)	2 (7.1%)	0.135
<i>Post endoscopic drainage with JJ-stent</i>	677 (73.7%)	26 (92.9%)	0.026
<i>Operating time - minutes (95%CI)</i>	51.5 (49.9 - 53.1)	72.1 (62.2 - 82.0)	< 0.0005

* Disturbing bleeding was registered as a complication when vision was impaired to an extent that hindered further endoscopy. Perforation was assessed endoscopically or as contrast leakage on retrograde pyelogram. Mucosal abrasion was defined as grade 2 or higher according to the classification of ureteral wall injuries presented by Traxer et al.¹⁵

Table 3 Multiple logistic regression analysis of potential risk factors for ureteral stricture development

Risk factor	OR	95% CI for OR	p-value
<i>Stone related factors</i>			
Stone location (ureter vs renal pelvis)	2.4	0.9 - 6.6	0.090
Stone burden	1.5	0.7 - 3.6	0.333
<i>Preoperative factors</i>			
Obstruction prior to URS	1.1	0.4 - 2.9	0.801
<i>Factors related to the URS procedure</i>			
Previous URS for same stone	1.7	0.7 - 4.2	0.233
Operator experience (resident vs urologist)	0.6	0.2 - 1.6	0.275
Access sheath	4.6	1.4 - 14.6	0.011
Fragmentation and retrieval vs dusting	2.7	1.0 - 7.6	0.059
Perforation	11.8	3.8 - 36.6	< 0.0001
Operating time ≥ 60 minutes	5.7	2.2 - 15.2	< 0.0005