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Surgical and radiological predictive factors for ureteric stricture formation in patients treated with ureteroscopy for ureteric stones

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ABSTRACT

Background: Ureteric stricture is a potential complication of impacted ureteric stones. This study investigates surgical and radiological factors that could predict ureteric stricture formation after ureteroscopic treatment of impacted ureteric stones.

Materials and method: Intraoperative and radiological data for patients who underwent ureteroscopic treatment of ureteric stones impaction over a 5-year period were reviewed retrospectively. Patients who had previous ureteroscopic treatment or strictures were excluded.

Results: Between January 2014 and May 2019, 1,340 patients presented as emergency renal colic secondary to ureteric stones. A total of 297 ureteroscopy procedures were performed for impacted calculi. The mean age was 53 years. The stricture rate was 3.3%. Analysis of radiological and surgical factors revealed that the degree of hydronephrosis, residual fragments and intraoperative ureteric injury were significant predictors for stricture formation ($p = 0.018$, 0.01 and 0.02, OR = 10, 47 and 1776, respectively). None of the other factors significantly predicted ureteric stricture formation.

Conclusion: Our study found the presence of severe hydronephrosis, residual stone fragments after surgery and intraoperative ureteric injury are significant predictive factors for ureteric stricture formation. The high-risk patients should be monitored with routine postoperative renal ultrasound.

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Introduction

Kidney stone disease is one of the most common diseases in modern urological practice. The incidence rate of kidney stone disease is around 114–720 per 100,000 individuals, with prevalence rates of 1.7–14.8%, and rates seem to be rising [1]. In the UK, the lifetime prevalence of kidney stone disease increased by 63% (from 7.14% to 11.62%) between 2000 and 2010. It's thought that this rising trend may be attributed to lifestyle changes, dietary habits and global warming [2]. Recent innovations in stone surgery, such as high power light amplification by stimulated emission of radiation (LASER) machines and single use digital uretrorenoscopes, has led to higher success and lower complication rates [3]. Nevertheless the development of ureteric stricture remains a recognized complication of impacted ureteric stones [4]. In general, an impacted ureteric stone has been defined as a ureteric stone that fails to progress after a period of observation [5]. The intraoperative diagnosis of impaction is often associated with the presence of ureteric wall oedema and inflammation associated with failure to pass a guide wire or catheter on initial attempt [6]. Patients with an impacted ureteric stone will have a less favourable outcome of the initial ureteroscopy and a higher complication rate [7]. The reported stricture rates in the literature were variable; however, in more recent studies the reported incidence was 1.5% [4]. Rates as high as 24% were reported in earlier studies [8]. The inflammatory changes caused by stone impaction and/or ureteric perforation can result in ureteric devascularisation, necrosis, fibrosis and scar tissue formation. Ureteric wall perforation and urinary extravasation has been linked to increase complication rate following ureteroscopy [9]. Furthermore, submucosal calculi within 4 mm of the lumen has also been linked to subsequent stricture formation [10].

Patients with ureteric stricture may be completely asymptomatic and their first presentation may be a non-functioning kidney. This emphasises the importance of obtaining routine postoperative imaging in patients treated for impacted ureteric stones [11].

There are a limited number of studies that have investigated the predictive factors of ureteric stricture formation in impacted ureteric stones [4,12].

In our study, we evaluate the surgical and radiological factors that could predict ureteric stricture formation after ureteroscopic treatment of impacted ureteric stones.

Materials and methods

This is a single center retrospective case control study. Data were collected for all patients who presented with

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emergency ureteric colic and underwent ureteroscopic treament and holmium LASER intervention for an impacted ureteric stone in the period between January 2014 to May 2019. Exclusion criteria were patients with bilateral ureteric stones, a previous history of ureteroscopy or ultrasound shock wave lithotripsy treatment and those who had a previous history of ureteric strictures. Impacted stones were defined as stones that failed to progress after a period of observation of 8 weeks, were adherent to the ureteric wall which prevents easy insertion of a guidewire or ureteric catheter and were associated with moderate-to-severe hydronephrosis [6,12]. All stones were diagnosed with non-enhanced computerised tomography (CT). All patients in the study were treated with ureteroscopy (semirigid and flexible) and holmium laser lithotripsy. In case of difficult first procedure a 6 Ch ureteric stent was left *in situ* for 6 weeks, after which stone removal was attempted for a second time, otherwise stents were left for 3–10 days where stone retrieval or fragmentation was achieved.

Intraoperative ureteric perforation was detected by direct observation and retrograde pyelography. A renal ultrasound was used to assess the patients at increased risk of stricture formation at 3 months. When the ultrasound showed hydronephrosis, a contrast enhanced CT and diuretic mercaptoacetyltriglycine (MAG3) was used for further assessment of the patients to confirm the formation of ureteric strictures. The diagnosis of ureteric stricture is subsequently confirmed on reterograde studies.

Stone related risk factors for ureteric stricture formation that were taken into consideration were stone size (largest dimension), site of impaction, degree of hydronephrosis, ureteric oedema and perinephric stranding. Intraoperative risk factor that were considered are urothelial damage, ureteric perforation, preoperative stenting and/or nephrostomy insertion, the presence of residual or intramural stone fragments and duration of impaction.

Data analysis was performed by using Statistical Product and Service Solutions version 16.0 (SPSS Inc., Chicago, IL) software. Student's *t*-test was used to compare numerical variables and Fisher's exact test was used to compare categorical variables. A multivariate analysis (logistic regression) was used to study risk factors for the development of ureteric stricture. Odd ratios and 95% confidence intervals are reported. *p*-values under 5% ($p < 0.05$) were considered statistically significant.

Results

Between January 2014 and May 2019, just over a 5 year period, 1,340 patients presented to our center with emergency renal colic secondary to ureteric stones. A total of 297 were diagnosed with an impacted ureteric stone that required ureteroscopy and LASER treatment. The mean age was 52 years (range = 20–86 years old). The male-to-female ratio was 3:1. Patient's demographic characteristics are shown in Table 1.

Out of 297 impacted stones, 10 patients (3.3%) developed ureteric stricture that required further intervention. Strictures were suspected on post-operative ultrasound 3 months after primary surgery and confirmed with contrast enhanced CT, diuretics MAG3 renogram and retrograde studies. Stone characteristics are summarized in Table 1. Intraoperative factors are shown in Table 2.

The largest stone size was 25 mm in the longest diameter. Mean stone diameter was significantly larger in the stricture group compared to non-stricture group (11.5 vs 7.6 mm respectively, $p = 0.002$). Approximately half of the stones were impacted in the upper ureter in both groups. There was no significant difference in the time for definitive surgery between the two groups. The degree of pre-operative hydronephrosis differed significantly between the two groups and up to 40% of the stricture group patients had severe hydronephrosis compared to 2% in the non-stricture group ($p = 0.00001$). The stricture group showed more ureteric oedema and were more likely to require nephrostomy tube insertion which may reflect a higher degree of impaction compared to the non-stricture group. Intraoperative complications such as mucosal damage and ureteric perforation correlated significantly with ureteric stricture formation. In total, 70% of the ureteric stricture group patients had residual fragments after treatment, and half, had embedded stones in the ureteric wall compared to 5.5% and 2% respectively in the non-stricture group, (Table 2).

Table 1. Patients' demographics and stone characteristics.

	Without ureteric stricture ($n = 287$)	Stricture group ($n = 10$)	*p*-value
Mean age	53 years	58 years	0.25
Gender			0.27
Male	215 (75%)	6 (60%)	
Female	72 (25%)	4 (40%)	
Mean stone size (largest diameter)	7.6 mm	11.5 mm	0.002
Side (right)	115 (40%)	5 (50%)	0.73
Site of impaction			0.24
Lower ureter	125 (43.5%)	2 (20%)	
Middle ureter	43 (15%)	3 (30%)	
Upper ureter	119 (41.5%)	5 (50%)	
Degree of hydronephrosis			<0.00001
No	37 (13%)	2 (20%)	
Mild	154 (53.5%)	1 (10%)	
Moderate	90 (31.5)	3 (30%)	
Severe	6 (2%)	4 (40%)	
Ureteric oedema	46 (16%)	5 (50%)	0.023
Periureteric stranding	159 (55%)	7 (70%)	0.5

Table 2. Intraoperative variables.

Emergency ureteroscopy	77 (27%)	1 (10%)	0.28
Preoperative stenting	106 (37%)	5 (50%)	0.5
Nephrostomy insertion	3 (1%)	3 (30%)	0.003
Mean time to definitive surgery	76 (range = 1–305)	127 (range = 2–273)	0.11
Mucosal injury	3 (1%)	6 (60%)	<0.00001
Ureteric perforation	2 (0.7%)	3 (30%)	0.003
Residual stone fragments	16 (5.5%)	7 (70%)	<0.00001
Embedded stone fragments	6 (2%)	5 (50%)	<0.00001

Table 3. Multiple logistic regression model for predictors of stricture formation.

		95% confidence interval		
Risk factor	Odd ratio	Lower	Upper	*p*-value
Size of the stone	0.961	0.681	1.350	0.82
Site of impaction	0.60	0.151	2.44	0.60
Severe Hydronephrosis	10	1.469	68.137	0.018
Time to surgery	1.01	0.997	1.03	0.08
Ureteric perforation	1776	2.677	78343	0.02
Residual fragments	47.66	2.50	906.84	0.01

Multivariate logistic regression analysis (Table 3) was conducted to evaluate the predicting factors for stricture formation. Out of all parameters tested, only the degree of hydronephrosis, residual fragments and intraoperative ureteric damage were significant predictors for stricture formation ($p = 0.018$, OR = 10; $p = 0.01$, OR = 47; and $p = 0.024$, OR = 1776, respectively). This suggests that ureteric stricture is more likely to occur as the degree of hydronephrosis increases, the presence of residual fragments post-treatment or intraoperative ureteric damage occurs. None of the other factors tested contributed significantly to the formation of ureteric strictures.

Discussion

Ureteric stricture is a recognised complication of impacted ureteric stones. It is a significant complication which may ultimately lead to loss of the kidney. Historically, the incidence rate of ureteric strictures secondary to impacted stones was reported to be as high as 24% [8]. However, newer and contemporary studies suggest that the incidence rate is much lower. Darwish et al. [4] Fam et al. [12] and El-Abd et al. [13] reported the incidence rate of ureteric stricture secondary to impacted stones as 1.5%, 7.8% and 0.6%, respectively. Elashry et al. [14] reported the lowest incidence rate of 0.23%. In comparison, our study suggests an incidence rate of 3.3%.

The low incidence rate of ureteric stricture is primarily attributed to the advances in the science and technology in ureteroscopes, intracorporeal lithotripsy devices and especially the holmium: YAG LASER technology [15]. Today, urologists have relatively easy access to small caliber modern ureteroscopes and powerful laser lithotriptors to treat ureteric stones endoscopically more safely and efficiently than ever before.

Several studies have been conducted previously to identify factors that cause ureteric strictures following endoscopic treatment for ureteric stones. However, the results have been mixed. More recently, Fam et al. [12] have explored intraoperative factors and stone related factors in their study of 77 patients, they were not able to identify any significant contributing factor. However, one of the significant drawbacks of this study is the small sample size of 77 patients.

The pathogenesis of ureteric stricture secondary to impacted stones formation is not fully understood. However, it is hypothesized to be multifactorial, but likely to include a sustained inflammatory response caused by the stones, and intraoperative ureteric injury.

Long-term irritation and inflammation caused by the impacted stone can lead to the formation of ureteric lesion around the impacted stone. Yamaguchi et al. [16] identified two types of ureteric lesions associated with impacted stones. Type 1 lesions were oedematous or cystic hemispheric lesions; while type 2 lesions had a villous appearance. Under the microscope, type 1 lesions appeared as submucosal oedema without specific findings; while type 2 lesions appeared as columnar mesenchymal tissue surrounded by several layers of transitional epithelium. The authors were not able to find factors that determine the type of ureteric lesion formed. Chronic granulomatous inflammation in the ureter has also been observed by Mugiya et al. [17].

Due to these ureteric lesions, the view during ureterolithotomy may be suboptimal, which could potentially render the surgery increasingly difficult. Furthermore, these inflamed ureters may be more prone to perforation, even with the most gentle endoscopic manoeuvres. Therefore, iatrogenic ureteric injury and perforation are more likely to happen during treatment of impacted ureteric stones. Previous studies have shown that ureteric perforation could subsequently lead to ureteric stricture [13,18]. Indeed, prevention is better than cure and Dong et al. [19] have summarised some of the tips and tricks that a urologist can take to reduce the chances of ureteric perforation while treating an impacted ureteric stone.

Our research suggests that intraoperative injury and perforation is a significant predictor for subsequent formation of ureteric stricture in contrast to previous studies findings [4,12]. Ureteric injury is likely to occur in highly impacted stones with significant inflammation and oedema and this may explain the higher risk of stricture formation.

Understandably, it is easy to assume that a larger stone size is a risk factor for ureteric stricture formation. We have demonstrated that stone size does not increase the risk of stricture formation. Similar results were shown in other case series [12]. Nevertheless, the study by El-Abd et al. [13] found that ureteric stricture developed in 4.4% of patients with stones larger than 2 cm while compared to only 0.2% of patients with stones less than 2 cm in size. Greater pressure to the ureteric urothelium is exerted by stones with larger transverse diameters rather than its vertical length or volume, which may have a more significant effect on subsequent ureteric stricture formation [12].

Dretler and Young [20] have proposed that residual stone fragments in the ureteric could lead to 'stone granuloma'. Just like conventional granuloma, macrophages and foreign body giant cells were seen around the embedded calcium oxalate residual fragments, causing surrounding inflammation and fibrosis. Indeed, just like our study has shown, residual stone fragments after ureteroscopic laser lithotripsy is a significant predictor of ureteric stricture formation.

This standardized approach adapted in our unit helped in eliminating such intra-operative variables, this is highlighted with the usage of the same type and size of ureteroscopes in addition to the duration where ureteric stents were left *in situ*. In the same way, surgeon's experiences were standardized with on-call consultants taking over any failure to pass the impacted stones as part of our unit protocol.

The correlation between the degree of hydronephrosis and stricture formation were not fully evaluated in similar previous studies. It is known that the severe hydronephrosis is associated with poor treatment outcome of ureteric stones [21]. Tran et al. [22] evaluated the preoperative radiological findings that could predict stone impaction and they found that patients with impacted stones had a greater degree of hydronephrosis on univariate analysis. Our finding revealed that the degree of hydronephrosis is a significant predictor for stricture formation. The degree of hydronephrosis may reflect severe impaction and complete ureteric obstruction and hence a higher rate of stricture formation [21].

Some patients may develop silent ureteric strictures after ureteroscopic treatment for their impacted stones. It was shown that up to 25% of patients can develop silent stricture post-ureteroscopic treatment [13,23]. Therefore, routine postoperative imaging is important in patients with higher risk of stricture formation.

We acknowledge that this study is limited by short follow-up, the small number of patients who developed ureteric stricture and the lack of objectivity of defining impacted ureteric stones. A larger multi-institutional study with pre-agreed criteria for impacted stones is needed to define stricture formation rate and the salient predicting factors.

Our study suggests that the rate of stricture formation following ureteroscopic treatment of impacted ureteric stone is 3.3%. We identified severe hydronephrosis, residual stone fragments and intraoperative ureteric injury as significant predicting factors for stricture formation. Ureteric stricture can be a silent complication leading and presenting with a renal impairment. Therefore, arranging postoperative imaging after impacted ureteric stones ureteroscopic treatment, might be essential.

Ethics approval

Registered locally as QI4600, the principles of the Helsinki Declaration were followed.

Disclosure statement

The authors report no conflicts of interest.

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