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Research Article

Risk Factors For The Development Of Ureteric Stricture Post Ureteroscopic Lithotripsy: A Retrospective Analysis From A Tertiary Care Centre.

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Running title: Risk factors for post URSL ureteric stricture

Abstract

Background: Urolithiasis is a globally prevalent disease with an increasing worldwide prevalence of 4 to 5%. A ureteral stricture is a common and serious complication of ureteroscopic lithotripsy (URSL) and was reported in the literature in the range of 0.2 to 24%. The incidence of laser lithotripsy has increased substantially in the past few years with their own advantages and complications.
Methods: This retrospective observational (case-control) study was conducted from January 2021 to December 2022, including patients undergoing URSL for ureteral stone disease. Post-operative follow up was done for 12 months using ultrasound. Patients developing hydronephrosis on ultrasound and/or pain during the follow up period were subjected to Computed Tomography Urography to confirm the diagnosis. Multiple logistic regression analysis was done to measure the risk factors, Odd's ratio was calculated, and p-value of <0.05 was considered statistically significant.
Results: The mean stone burden was 10.2 mm with mean hardness of 970 HU. 189 patients had impacted stones with various degrees of impaction; smooth stone surface was present in 134 patients. The mean duration of lithotripsy was 30 minutes. The overall post operative complication rate was 17% with stricture formation in 5.9% of patients.
Conclusion: Stone burden, stone surface characteristic, energy source used (Holmium Laser vs Pneumatic), and impacted nature of calculi with degree of impaction were found to be associated with development of ureteric strictures post URSL.

Keywords : hydronephrosis, laser, stricture, ureteral stone disease, ureteroscopic lithotripsy.

INTRODUCTION

Urolithiasis represents a globally prevalent pathological condition, with an estimated worldwide prevalence ranging from 4% to 5% (1,2). Among the various surgical interventions available for the management of urolithiasis, ureteroscopic lithotripsy (URSL) has emerged as one of the most commonly performed day-care procedures within contemporary urological practice. Accumulating evidence has demonstrated that URSL offers superior stone-free rates and lower re-treatment rates when compared to extracorporeal shock wave lithotripsy (ESWL) (3). URSL may be performed utilizing a variety of energy modalities, including pneumatic lithotripters, holmium:YAG lasers, and thulium fiber lasers. Despite its efficacy, the development of ureteral stricture remains a well-recognized complication of URSL, with incidence rates reported in the literature varying from 0.2% to 24% (4,5). The pathogenesis of ureteral stricture formation following ureteroscopic stone extraction is multifactorial and incompletely understood. Proposed contributing factors

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include direct intraoperative ureteral injury and chronic inflammation secondary to prolonged stone impaction (6). Long-standing ureteral strictures have been associated with significant adverse outcomes, including moderate to severe hydronephrosis and ipsilateral renal functional deterioration, with some cases demonstrating estimated glomerular filtration rates (eGFR) less than 10 mL/min, indicative of non-functioning renal units. Previous investigations have identified several potential risk factors contributing to ureteral stricture formation post-URSL, such as increased stone size, prolonged operative time, and stone impaction (4,7,8,9). However, the majority of these studies have been retrospective in nature and have produced conflicting results regarding the relative importance of these factors. In light of the existing ambiguity and paucity of high-quality evidence, the present study was undertaken with the objective of retrospectively analyzing a large cohort of patients who underwent URSL. These patients were systematically followed over a 12-month period to evaluate and identify independent risk factors associated with the development of ureteral strictures within this study population

MATERIALS AND METHODS

This retrospective observational case-control study was conducted in the Department of Urology and Renal Transplant Surgery at Gauhati Medical College and Hospital, encompassing a total of 372 patients who underwent ureteroscopic lithotripsy (URSL) utilizing pneumatic lithotripters and/or holmium:YAG laser for the management of ureteral calculi between January 2022 and December 2023. All patients were followed up for a period of 12 months postoperatively. Follow-up evaluations were performed using ultrasonography (USG) of the abdomen at 3, 6, and 12 months. Patients presenting with abdominal pain and/or radiological evidence of hydronephrosis during follow-up were further evaluated using computed tomography with intravenous urography (CT-IVU) to confirm the presence of ureteral strictures. The following parameters were evaluated as potential risk factors for the development of ureteral strictures: patient age, sex, stone burden, stone density measured in Hounsfield units (HU), presence of stone impaction (defined by non-visualization of contrast excretion distal to the calculus, presence of peri-calculous oedema, or inability to negotiate a guidewire across the stone), stone surface morphology (categorized as smooth or irregular/ragged), energy source employed for lithotripsy, and the duration of lithotripsy.

Inclusion and Exclusion Criteria: Patients who underwent URSL using available energy sources and subsequently developed clinical symptoms (such as abdominal pain) and/or radiological findings (hydronephrosis) during the 12-month follow-up period were included in the study. The diagnosis of ureteral stricture was confirmed using CT-IVU. Patients were excluded from the study based on the following criteria: incomplete stone clearance following URSL, presence of congenital anomalies of the urinary tract, forgotten or heavily encrusted double-J ureteral stents, and pre-existing renal insufficiency necessitating URSL. Additional exclusion criteria included patients with a prior history of pelvic irradiation or pelvic surgery for any other pathology, as well as those who failed to comply with the scheduled follow-up protocol.

Statistical analysis

SPSS Inc founded by Norman Nie, Dale Bent, Hadlai "Tex" Hull in 1968 and acquired by IBM Corporation (2010), Armonk, New York, United States of America. A comparative analysis of the variables predicted to be the risk factors for post URSL stricture development was conducted; Odd's ratio was calculated using univariate analysis. A p-value of <0.05 was considered statistically significant.

RESULTS

A total of 372 patients were included in the final analysis. The mean age of the study population was 39 years, with a male-to-female ratio of 2:3. There was no statistically significant association between patient sex and the development of ureteral stricture following URSL (p=0.825). The mean stone burden was 10.2 mm. Patients with a stone size greater than 10.2 mm were found to have a significantly higher incidence of post-URSL ureteral stricture compared to those with stones ≤10.2 mm (p=0.046). Stone hardness, assessed using Hounsfield Units (HU), did not demonstrate a statistically significant association with stricture formation (HU <970: 6.3% vs. HU ≥970: 5.2%, p=0.82). However, impacted calculi were significantly associated with a higher incidence of stricture formation when compared to non-impacted stones (9.1% vs. 2.2%, p=0.008). Additionally, stones with a ragged or irregular surface morphology were associated with a significantly higher rate of ureteral stricture (7.9%) compared to stones with a smooth surface (2.2%) (p=0.037). The energy source utilized during lithotripsy showed a significant influence on stricture formation. Patients undergoing lithotripsy with a holmium:YAG laser exhibited a higher stricture rate compared to those treated with pneumatic lithotripsy (8.6% vs. 1.9%, p=0.007). Duration of lithotripsy, whether less than 30 minutes (5.5%) or greater than 30 minutes (7.6%), was not significantly associated with stricture formation (p=0.568). Among the 22 patients who developed ureteral strictures, 18 patients (81.8%) had strictures measuring <1 cm in length, while 4 patients (18.2%) had strictures measuring ≥1 cm. All the parameters with their respective value and odds ratio is shown in **Table 1**. These findings suggest that larger stone

size, impacted nature of the calculus, irregular stone surface, and the use of holmium:YAG laser are independent risk factors significantly associated with the development of ureteral strictures following URSL. Univariate analysis of the following variables as significant predictors of post-URSL ureteral stricture formation is shown in **Table 2**.

Table 1. Post URSL strictures according to different parameters.

Parameters	Post URSL stricture	p-value	Odds Ratio
Mean stone burden (10.2 mm)			2.98
>10.2 [n=198]	17 (8.5)	0.046	
<10.2 [n=174]	5 (2.9)		
Hardness of stones (HU)			1.20
>970 [n=134]	7 (5.2)	0.820	
<970 [n=238]	15 (6.3)		
Impacted nature of calculus			3.99
Impacted calculus [n=197]	18 (9.1)	0.008	
Non-impacted calculus [n=175]	4 (2.3)		
Stone surface characteristic			3.56
Ragged [n=238]	19 (7.9)	0.037	
Smooth [n=134]	3 (2.2)		
Energy source			4.32
Holmium laser [n=221]	19 (8.6)	0.007	
Pneumatic [n=151]	3 (1.9)		
Mean duration of 30 minutes			1.36
<30 minutes [n=306]	17 (5.5)	0.568	
>30 minutes [n=66]	5 (7.6)		
Sex			-
Female [n=223]	14 (6.3)	0.825	
Male [n=149]	8 (5.4)		
Data presented as n (%).			

Table 2. Univariate analysis of different parameters

Parameters	Odds Ratio	95% CI	p-value
Mean stone burden (10.2 mm)	2.98	10.2 ± 3.8	0.046
Hardness of stones (HU)	1.20	970 ± 290	0.820
Impacted nature of calculus	3.99	Mean cannot be calculated	0.008
Stone surface characteristic	3.56	Mean cannot be calculated	0.037
Energy source	4.32	Mean cannot be calculated	0.006
Mean duration of 30 minutes	1.36	30 ± 14	0.568

DISCUSSION

The global prevalence of urolithiasis continues to increase, with ureteroscopic lithotripsy (URSL) emerging as a widely adopted minimally invasive surgical modality for the management of ureteral calculi. Although URSL is associated with excellent stone-free rates and favourable clinical outcomes, the procedure is not without complications, of which ureteral stricture remains a potentially serious and challenging sequel. The exact etiopathogenesis of post-URSL ureteral stricture formation is multifactorial and incompletely elucidated, with factors such as direct ureteral trauma, thermal injury, prolonged inflammation, and ischemia being implicated. The present study aimed to delineate the risk factors associated with ureteral stricture formation following URSL through a retrospective analysis of a large patient cohort with a 12-month follow-up period. In the current series, post-URSL ureteral stricture was identified in 22 patients. This finding is consistent with the observations

of Tonayali S et al., who reported URSL as the second most common etiology for ureteral stricture, with an incidence of 0.95% in their study population (3). Brito et al. demonstrated a notably higher stricture rate of 14.2% among 42 patients with impacted ureteral calculi treated using pneumatic lithotripsy (10). Similarly, prior studies have reported variable stricture rates following URSL, ranging from 1.5% to 4.5%, depending on patient selection, stone characteristics, and operative variables (11,12). In the present study, the mean patient age was 39 years, with a male-to-female ratio of 2:3; however, patient sex did not significantly influence the risk of stricture formation (p=0.825). A higher stone burden was identified as a significant risk factor, with patients harboring stones >10.2 mm demonstrating an increased incidence of post-URSL stricture formation (p=0.046). This observation aligns with the findings of Taş et al., who noted an increased stricture risk in patients with stone size >2 cm, with rates escalating from 0.17% in stones of 1–2 cm to 4.4% in stones >2 cm (13). Stone impaction emerged as a particularly important risk factor in the current study, with a significantly higher incidence of stricture in impacted versus non-impacted stones (p=0.008). This is corroborated by previous studies, including a systematic review by Tonyali S et al., which reported stricture rates ranging from 2.2% to 80% in cases of impacted calculi (3). Although Fam XI et al. identified stone impaction as a potential risk factor, their results did not reach statistical significance, likely due to a smaller sample size (n=5) (14). In contrast, Taş et al. reported a significantly higher stricture incidence in impacted stones (13.3%) compared to non-impacted stones (5%) (15). Notably, in the present study, stones with a ragged or irregular surface morphology were significantly associated with stricture formation when compared to stones with a smooth surface (p=0.037). The energy source employed for lithotripsy also demonstrated a significant association, with holmium:YAG laser lithotripsy exhibiting a higher risk of stricture formation compared to pneumatic lithotripsy (p=0.031). However, this finding is contrary to that of prior literature, where complication rates between laser and pneumatic energy sources were reported to be comparable (16). Stone density, measured in Hounsfield Units (HU), was not found to have a statistically significant association with stricture formation in the current study (p=0.83), consistent with existing literature. Similarly, the duration of lithotripsy, whether <30 minutes or >30 minutes, did not significantly influence the risk of stricture formation (p=0.568). Multivariate analysis revealed that among all the factors evaluated, the impacted nature of the stone was the most significant independent predictor of ureteral stricture formation following URSL. This finding underscores the critical role of stone impaction in the pathogenesis of stricture development. In contrast, a study by Lai D et al. identified stone burden (OR: 2.5; CI: 0.7–3.6; p=0.333) and prolonged operative time exceeding 60 minutes (OR: 5.7; CI: 2.2–15.2; p<0.0005) as significant predictors of stricture formation (17). In conclusion, this study identified several independent risk factors significantly associated with the development of ureteral stricture following ureteroscopic lithotripsy. A stone burden exceeding 10.2 mm, impacted calculi characterized by peri-ureteral wall edema and/or inability to advance a guidewire beyond the stone, irregular or ragged stone surface morphology and the use of laser energy as the lithotripsy modality were all significantly associated with an increased risk of post-URSL ureteral stricture formation. Conversely, patient sex, stone hardness and prolonged lithotripsy duration exceeding 30 minutes did not demonstrate a statistically significant association with ureteral stricture development in this cohort. Future prospective studies with larger sample sizes, longer follow-up durations, and comprehensive evaluation of additional intraoperative variables are warranted to further validate these findings and elucidate the pathophysiological mechanisms underpinning ureteral stricture formation post-URSL.

This study is not without limitations. Foremost, its retrospective design inherently predisposes to selection bias and precludes the establishment of definitive causal relationships between risk factors and ureteral stricture formation. Moreover, the exclusive reliance on radiological imaging modalities for the diagnosis of ureteral strictures may have led to underestimation of asymptomatic cases or strictures identified through alternative diagnostic methods, such as ureteroscopy or functional studies. Additionally, the study did not account for certain potentially influential variables, including surgeon experience, intraoperative technical variations, and specific procedural nuances, all of which may influence the incidence of ureteral strictures. Lastly, the relatively short duration of follow-up (12 months) may not have been sufficient to capture late-presenting strictures or long-term complications, potentially limiting the generalizability of the findings.

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