ORIGINAL PAPER

Predicting negative ureteroscopy for stone disease – Minimizing risk and cost

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Summary *Introduction: Urolithiasis is common worldwide, with ureteric stones being a particular burden. Ureteroscopy (URS) is one of the most useful procedures in treating ureteric stones not passed spontaneously; this procedure has a complication risk of 4%. Negative URS, with described rates up to 15%, represents an avoidable patient risk and use of medical resources.*
Objectives: To describe rates and identify predictive factors for negative URS and to define strategies which would minimize patient and financial burden from these unnecessary procedures.
Materials and methods: A retrospective cohort study analyzed patients who underwent URS in our Center to treat ureteric stones over a period of 2 years. Patient age, gender, and comorbidities, as well as laboratory and imaging findings, were analyzed.
Results: 262 patients underwent URS for ureteric stones. The female population was 50.8% with a mean age of 56.89 years. A total of 78 (29.8%) URS procedures were negative. Univariate analysis showed a higher prevalence of negative URS in female patients, as well as in primary, smaller, and radiolucent stones. At multivariate analysis, a logistic regression model correctly classified 76% of patients, with smaller stone size and radiolucency being significant predictors of negative URS.
Discussion and conclusions: Our Center showed a high rate of negative URS, higher than commonly described in the literature. Female patients tend to have an even higher rate, possibly due to unnoticed passage of stones. Patients with small, radiolucent stones showed the highest rates of negative URS.

KEY WORDS: *Urolithiasis; Ureteric; Stone; Ureteroscopy; Negative.*

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INTRODUCTION

Urolithiasis is very common worldwide, with prevalence rates described in general population of 1-20% (1-4); countries with high standard of life show increasing rates over the past decades, with over 10% reported prevalence (5-7). Ureteric stones pose a particular burden with frequent need of emergency visits and possible need for admittance and invasive procedures (7, 8).
Ureteroscopy (URS) is one of the most useful methods for treating ureteric stones not passed spontaneously (4, 10, 11). This procedure is generally considered safe, involving a complication risk of 4%, with many being performed in an outpatient basis (12-14).
A mean overall cost of $2801 per procedure has been described in a systematic review (13).

When a patient is offered a URS for a ureteric stone, the possibility of spontaneous expulsion still exists before the procedure, eventually unnoticed by the patient. If no other measures are taken to detect persistence of stones before surgery, a "*stoneless*" or "*negative*" procedure (hence, unnecessary) would be performed (14). Negative URS, with described rates up to 15%, represents a avoidable patient risk and use of medical resources (15-18). Predicting negative URS preoperatively and cancelling the procedure would prevent this unnecessary burden (14).
Several factors predicting negative URS have been studied. Smaller stone size is associated with increased probability of unnoticed expulsion and negative URS (15, 17); other reported factors include distal stone positioning (17) and female gender (15, 16). Time since last imaging study does not appear to influence stoneless procedure rates (17). Other potential influencing factors showed varying results (15-18). The objective of this paper is to describe rates and identify predictive factors of negative URS and to define strategies which would minimize patient and financial burden of these unnecessary procedures.

MATERIALS AND METHODS

A retrospective cohort study analyzed all patients who underwent URS in our Center over a period of 2 years. Only procedures to treat ureteric stones were included; all were performed in the same Center, with similar surgical equipment. Several factors were reviewed, including patient age, gender and comorbidities, previous procedures, as well as clinical, laboratory and imaging findings. To comply with the purpose of the study, patients with negative URS were identified, and a potential correlation with the above-mentioned factors was investigated. Patients who had negative URS were followed with ultrasound or *computerised tomography* (CT), and those with presence of stone suspected of retrograde migration were not included; patients in which complete URS was not feasible were also not included. Statistical analysis was performed using SPSS 23®, including univariate Mann-Whitney and Kruskal-Wallis tests, and a multivariate logistic regression model.

RESULTS

During the defined period, 262 patients underwent URS as planned treatment for ureteric stones while meeting the selection criteria. The population was 50.8% female,

Table 1.

Patient/stone characteristics and acute episode clinical variables; frequencies represented in percentage of valid results and absolute number of cases excluding missing values in brackets.

Patient and stone characteristics		Frequency in valid % (n) excluding missing
Sex	Female	50.8% (133)
	Male	49.2% (129)
Age in years	20-34	7.3% (19)
	35-49	22.9% (60)
	50-64	37% (97)
	65-80	24.4% (64)
	80 or more	8.4% (22)
Number of episodes *1	Primary	81.5% (203)
	Recurrent disease	18.5% (46)
Stone anatomical location	Upper ureter	22.0% (52)
	Mid-ureter	23.7%(56)
	Lower ureter	54.3% (128)
Radiopacity *2	Radiopaque	86.3% (202)
	Radiolucent	13.7% (32)
Medical expulsive therapy	Alfa-blockers	53.8% (141)
	Corticosteroids	11.5% (30)
Perc. nephrostomy in acute episode	(performed)	11.8% (30)
JJ stenting in acute episode	(performed)	57.5% (146)

*1 missing value in 12 cases with dubious history of stones (patient unsure and no previous imaging available);
*2 based on KUB; missing value in 26 cases that did not undergo KUB and 2 cases for which KUB was not available to the authors (from other institutions).

with a mean age of 56.89 years (SD +/- 15.705 years). Patients had a mean stone size of 7.7 mm (SD +/- mm); 47.8% of patients had stones between 5 and 9 mm. According to pre-procedure imaging, the lower ureter was the most common stone location (54.3%), followed by mid (23.7%) and upper ureter (22%). Approximately 86.3% of stones studied were radiopaque on plain X ray of *Kidney-Ureter-Bladder* (KUB). Regarding imaging techniques applied at initial diagnosis, renal ultrasound was most used (99.2% of patients); KUB X-ray was performed in 90.2% of cases and CT in 78.6%.

Stenting in the acute setting was performed at physician discretion, with Center policy including best practice guidelines; stenting was performed in cases with associated infection, compromised renal function or long-standing pain (over 14 days) irrespective of planned URS or not. A significant proportion of patients underwent ureteric stenting in the acute setting (57.5%; n = 146); of those proposed to URS after stenting, 67.8% (n = 99) underwent KUB, 15.1% (n = 22) underwent CT, with 2.7% (n = 4) having both exams; 29 patients (19.9%) had no imaging between stenting and surgery. Cases where no evidence of stones was found were not considered for URS.

The mean time between the acute episode and subsequent URS was 61.8 days (+/- 27.076). In patients who underwent stenting prior to URS, mean time from stenting to surgery was 65.3 days (+/- 28.278). Patient and stone characteristics are displayed in Table 1.

A total of 78 URS procedures were negative for stones, representing 29.8%. Several factors were investigated in univariate analysis, which showed a higher prevalence of negative URS in female patients (p = 0.023), as well as in primary (p = 0.001), smaller (p = 0.010), and radiolucent stones (p = 0.035). These results are displayed in Table 2.

Several other factors were analyzed, but not found to be predictors of negative URS (Table 3). Namely, anatomical stone position (p = 0.646), mean time between the acute episode and subsequent URS (p = 0.207) and mean time from stenting to surgery (p = 0.614) did not appear to influence the risk of negative ureteroscopy. There was also no significant difference between patients who did or did not undergo CT scan (negative URS rates of 28.6% *vs* 33.9%, p = 0.139).

At multivariate analysis, a logistic regression model correctly classified 76% of patients, with smaller stone size (p = 0.026) and radiolucency (p = 0.011) being significant predictors of negative URS, and accounting for 47.7% of the variance. Each mm increase in stone size, showed an impact on OR for negative URS of 0.815 (expB=-0.204), while radiopaque stones showed an OR

Table 2.

Significant variables in univariate analysis with respective rates of negative URS in each subgroup and corresponding p values. Negative URS was more common in females, primary cases, small and radiolucent stones.

Clinical Variables	% negative URS	p value
Primary	32.5%	< 0.001
Recurrence	8.7%	
Female	36.1%	0.023
Male	23.3%	
0-4.9 mm	56.3%	0.010
5-9.9 mm	33.7%	
10 mm or more	15.5 %	
Radiopaque	19.8%	0.035
Radiolucent	43.8%	

Table 3.

Non-significant variables which did not show influence on the rate of negative URS.

Univariate non-significant patient and stone characteristics		Frequency of negative URB (%)	p value
Age in years	20-34	47.4%	0.442
	35-49	26.7%	
	50-64	30.9%	
	65-80	28.1%	
	80 or more	22.7%	
Stone anatomical location	Upper ureter	25%	0.646
	Mid-ureter	28.6%	
	Lower ureter	27.3%	
Diagnosis Imaging	Including CT	28.6%	0.139
	No CT	33.9%	
Medical expulsive therapy	Alfa-blockers	33.1%	0.282
	Corticosteroids	40%	
	None	27%	
Time from acute episode to URS	0-29 days	28.6%	0.207
	30-59 days	33.1%	
	60-89 days	27.9%	
	≥ 90 days	21.4%	
Time from stenting to URS	0-29 days	35.7%	0.614
	30-59 days	36.8%	
	60-89 days	37.9%	
	≥ 90 days	29.4%	
Percutaneous nephrostomyin acute episode	Yes	30%	0.777
	No	28.6%	
JJ stenting in acute episode	Yes	36.3%	0.464
	No	21.3%	

Table 4.

Logistic regression model accounting for 47.7% of the variance in the dependent variable (probability of negative URS), correctly classifying 76% of patients; each mm increase in stone size with OR of 0.815 and radiopaque stones with OR of 0.240 for negative URS.

Applied variables	Significance (p)	B	exp (B)
Sex	0.234		-
Stone size (absolute value in mm)	0.026	-0.204	0.815
Primary vs Recurrence	0.198		-
Radiopacity	0.011	-3.716	0.240

for negative ureteroscopy of 0.240 (expB=-3.716). Table 4 summarises these results.

DISCUSSION AND CONCLUSIONS

Our Center showed a high rate of negative URS, more than previously described in the literature. A recent systematic review suggests that a publication bias may exist, resulting in series with higher rates of URS not being submitted for peer review, leading to underestimation of its prevalence (19).

Stone position has been described in one previous study as an influencing factor, with distal stones resulting in higher negative URS rates (17); this did not seem to be the case with our population. In accordance with previously reported data (17) time to surgery from last imaging study or stenting also did not influence negative URS rates. Of note, our series presents a significant number of pre-stented patients, more than in previously reported retrospective studies (15) and 19.9% of those did not undergo further imaging before URS.

Female patients tend to have a higher rate of negative URS, as described in two recent studies (15, 16). This is possibly explained by frequent unnoticed passage of stones (due to shorter urethral length and lower voiding pressure) or by a higher frequency of pelvic phleboliths mistaken as ureteric stones (19).

Patients with small, radiolucent stones showed the highest rates of negative URS; this is also in accordance with previously described series (15, 17). These patients would benefit the most from pre-operative repeat imaging studies, eventually with non-contrast CT, to identify and preclude unnecessary treatments and costs (14). Prospective studies could help identify more precisely which imaging studies, in which patients and in what timeframe would impact the most in terms of change in planned treatment, to suggest clear guidelines regarding this matter.

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