

**Ureteric wall thickness as a novel predictor for failed retrograde ureteric stent placement**

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**ABSTRACT**

**Introduction:** We sought to identify predictors of failed retrograde ureteric stent (FRS) placement in the setting of obstructing ureteric calculi. In addition to patient- and stone-specific characteristics, we also considered computed tomography (CT) measures of ureteric wall thickness (UWT), as it has shown clinical potential in predicting outcomes of shockwave lithotripsy, ureteroscopy, and spontaneous stone passage.

**Methods:** We performed a retrospective, case-control study comparing patients who had successful retrograde stent (SRS) insertions with those who failed stent placement and ultimately required nephrostomy tube (NT) insertion (2013–2019). Patients were identified using administrative data from a shared electronic medical record (capturing all urology patients in our geographic area) and a prospective database capturing all institutional interventional radiology procedures. Patient demographics, as well as clinical and stone characteristics were then collected, and imaging manually reviewed. Statistical analysis was performed using univariate and multivariate logistic regression analysis in collaboration with a statistician.

**KEY MESSAGES**

- Ureteral wall thickness is a novel predictor of stone impaction and successful endourologic intervention.
- We found that an elevated ureteral wall thickness, as well as acute kidney injury, is predictive of failed retrograde stent and may benefit from upfront nephrostomy tube insertion.

**Results:** A total of 109 patients met inclusion for analysis (34 FRS, 75 SRS). The most common indication for stent insertion included sepsis (79%). On multivariate analysis both acute kidney injury as primary indication for stent insertion (odds ratio [OR] 9.16, 95% confidence interval [CI] 1.91–44.00,  $p=0.006$ ) and UWT (OR 0.34, 95% CI 0.15–0.74,  $p=0.007$ ) were found to be significantly associated with failed retrograde stent placement. A receiver operator characteristic curve analysis demonstrates an optimal UWT cutoff of 3.2 mm (sensitivity 60.6%, specificity 83.3%).

**Conclusions:** Elevated UWT and acute kidney injury as an indication for urgent urinary decompression in the setting of obstructing ureteric stones are predictive of failed retrograde stent placement. These patients may benefit from upfront nephrostomy tube insertion.

## INTRODUCTION

Nephrolithiasis is a common urologic condition in North America affecting 7 to 13% of the population and approximately one third of patients are likely to have a repeat symptomatic stone event in 10 years<sup>1,2</sup>. Obstructing ureteric calculi in the setting of urosepsis and acute renal injury often constitutes a medical emergency requiring urgent decompression with retrograde ureteral stent placement or nephrostomy tube (NT) insertion. Many centers with urology services will attempt retrograde stent placement via cystoscopy, under varying forms of anesthetic (general, sedation, local). If unable to place the stent, they will then request insertion by interventional radiology, often urgently after hours. Failing to place a stent not only results in wasted operative resources, but more importantly delays definitive urinary tract drainage – which can result in significant morbidity to the patient<sup>3</sup>.

Often stone size, location, and anatomic abnormalities are considered for triaging patients to either stent or NT placement. However, ureteral wall thickness (UWT) has recently been characterized on CT scan to aid in the prognostication of stone passage with and without intervention<sup>4–8</sup>. Considered a radiographic surrogate for tissue edema and ischemic ureteral mucosal segments UWT may also play a role in unsuccessful passage of a stent from bladder to kidney<sup>7–9</sup>. Therefore, the purpose of this study was to identify patient, stone and ureteral wall characteristics that predict failed retrograde stent placement.

## METHODS

Institutional ethics approval was obtained, and a retrospective chart review carried out. Patients with obstructing ureteral stones and an urgent indication for upper urinary tract drainage were identified from a prospective NT database, and cross referenced through our electronic medical record (EMR). Those requiring NT insertion, after failed stent insertion, were then compared to 75 consecutive successful retrograde stent insertions from 2019.

Patients were included within our study if they had an obstructing ureteric stone, pre-operative non-contrast CT scan, and an urgent indication for upper tract decompression. Patients

were excluded from our study if they had other etiologies accounting for their hydronephrosis (i.e. extrinsic compression from malignancy, renal transplant, unidentifiable ureteric orifice).

Data was retrospectively collected from patients' medical records and our province wide imaging repository. This included age and gender, indications for stenting (urosepsis or acute kidney injury (AKI)), time from diagnosis to stent insertion, ureteral stone characteristics (craniocaudal length, diameter, location, laterality) degree of hydronephrosis, ureteric density (HU), UWT (mm), number of stones (one or greater) and renal parenchymal atrophy were all documented.

UWT (mm) was defined as the maximal thickness of the ureteral wall at the maximal stone diameter on axial CT scan, stone circumference measured in the axial plane and ureteric density was defined as the density of the ureter (HU) directly distal to the stone on axial non-contrast CT (Figure 1). These definitions are in keeping with the methods previous studies have described and were performed at eight times magnification<sup>4-7</sup>. Four independent evaluators (two urology residents and two medical students) measured both UWT and ureteral density directly from the CT axial images using our imaging software IMPAX Client 6.7 and were blinded to the result of a successful or failed stent placement. The mean of the four measurements was used for the analysis.

Baseline patient demographics and stone characteristics were compared between the failed and successful retrograde stent groups using Chi-square and Mann-Whitney U tests. Univariate logistic regression analysis and multivariate logistic analysis was then performed including the variables that were determined to be significant from univariate analysis. Statistical tests were two sided with a p-value of less than 0.05 being significant. Receiver operating characteristic curve analysis (ROC) was performed to determine an appropriate cut-off point for UWT. Statistical analysis was performed using STATA 16.

## RESULTS

109 patients were included in our study with 34 patients in the failed retrograde stent (FRS) group and 75 patients in the successful retrograde stent (SRS) group. Indications for urgent stenting included sepsis (79%) and AKI (21%). There was no significant difference between the groups in age ( $p=0.66$ ), sex ( $p=0.30$ ), laterality ( $p=0.71$ ), or ureteric density ( $p=0.45$ ). Significant differences between the two groups included the indication for stenting ( $p<0.001$ ), time since diagnosis of ureteral stone ( $p<0.001$ ), degree of hydronephrosis ( $p=0.02$ ), presence of renal atrophy ( $p=0.01$ ), stone craniocaudal distance ( $p<0.001$ ), stone circumference ( $p<0.001$ ), and UWT ( $p<0.001$ ) (Table 1).

Univariate analysis found significant difference between an AKI indication for stenting (OR 6.61, 95% CI [2.44-17.94]  $p<0.001$ ), time from diagnosis to urinary tract decompression (OR 0.92, 95% CI [0.85-1.00]  $p=0.05$ ), degree of hydronephrosis (OR 0.37, 95% CI [0.16-0.88]  $p=0.03$ ), presence of renal atrophy (OR 0.23, 95% CI [0.07-0.77]  $p=0.02$ ), craniocaudal distance (OR 0.87, 95% CI [0.80-0.94]  $p<0.001$ ), stone circumference (OR 0.97, 95% CI [0.95-0.99]  $p=0.001$ ) and UWT (OR 0.27, 95% CI [0.15-0.48]  $p<0.001$ ) (Table 2). Multivariate logistic

regression identified that an AKI indication for stenting (OR 9.16, 95% CI [1.91-44.00]  $p=0.006$ ) and ureteral wall thickness (OR 0.34, 95% CI [0.15-0.74]  $p=0.007$ ) were both significantly associated with a failed retrograde stent placement (Table 2).

ROC was performed to evaluate the predictive value of UWT and the failure of retrograde stent placement (Figure 2). The area under the curve for UWT was 0.815. The optimal cut-off for UWT from the ROC was determined to be 3.23 mm with a sensitivity of 60.6% and specificity of 83.3% in predicting failed retrograde stent insertion.

## DISCUSSION

From this retrospective review of patients with ureteral stones, undergoing stent insertion for urgent indications, our analysis suggests that increasing UWT and an AKI indication for urgent decompression may be useful predictors to identify patients that are more likely to fail retrograde ureteric stenting – thereby, potentially benefiting from upfront NT insertions.

Based on our ROC analysis we derived a ureteric wall thickness cutoff of 3.2 mm that can be utilized to guide the clinical decision to proceed with retrograde ureteric stent placement or upfront percutaneous NT drainage. We found that 75% of successful ureteral stent placements had a UWT of less than 3.2 mm and 74% of failed retrograde stent placements had a UWT of greater than 3.2 mm. Our findings suggest that a UWT of greater than 3.2 mm can be utilized as an objective measure that would support a patient proceeding with upfront nephrostomy tube insertion. Our estimated UWT cut off is similar to a independent studies by Yoshida et al. (2017) and Mishra et al. (2020) suggesting an optimal ureteral wall thickness cutoff of 3.49 mm and 4.8 mm to determine the success of ureteroscopic lithotripsy outcomes<sup>6,9</sup>.

Currently the radiographic finding of UWT and its correlation with the endoscopic findings of ureteric edema, inflammation, and mucosal ischemia have yet to be demonstrate within histopathologic studies<sup>4</sup>. FRS patients displayed higher proportions of renal atrophy, severe hydronephrosis and larger stone sizes, suggesting chronicity and possibly more complete obstruction.

UWT is a practical measure that is easy to use. Prior to the study we created a six-minute video based on the instructions by Yamashita et al. (2019) demonstrating how UWT is measured on our imaging software<sup>4</sup>. After the initial twenty patients – our evaluators consistently took less than 90 seconds to measure both UWT and ureteric density regardless of their training level. The majority of patients will have a CT scan prior to urologic intervention and other than the initial learning curve there are no barriers to the utilization of UWT in clinical practice.

There are several limitations with this present study that should be noted. This study was a retrospective design with a small sample size from a single center. Given the low rate of failed stent insertion we required two separate cohorts of patients (failed and successful stent placement) retrospectively selected by their outcomes. Although these groups had no differences in their age or sex it is possible that there are intrinsic differences in these groups of patients that could not be accounted for. Furthermore, surgeon and operative factors are surely to play a part but are difficult to control for in this analysis. Finally, the measurements of UWT were the mean

of 4 evaluators who completed the measurement manually. To this date there are no studies assessing the inter-user reliability and reproducibility of this measure. Utilizing software-based measures or an automated UWT measurement system would help ensure reliability and reproducibility of the UWT measurements. One of the strengths of this study include a blinded multiple evaluator measure of both UWT and ureteric density therefore likely improving the reliability and reproducibility of our study. To our knowledge this has not been a part of any of the previous studies examining UWT<sup>4-7</sup>.

### **CONCLUSIONS**

Our study suggests patients presenting with an AKI requiring decompression and an elevated UWT (> 3.2 mm) may be at higher risk of stent placement failure, thereby benefitting from upfront NT insertion.

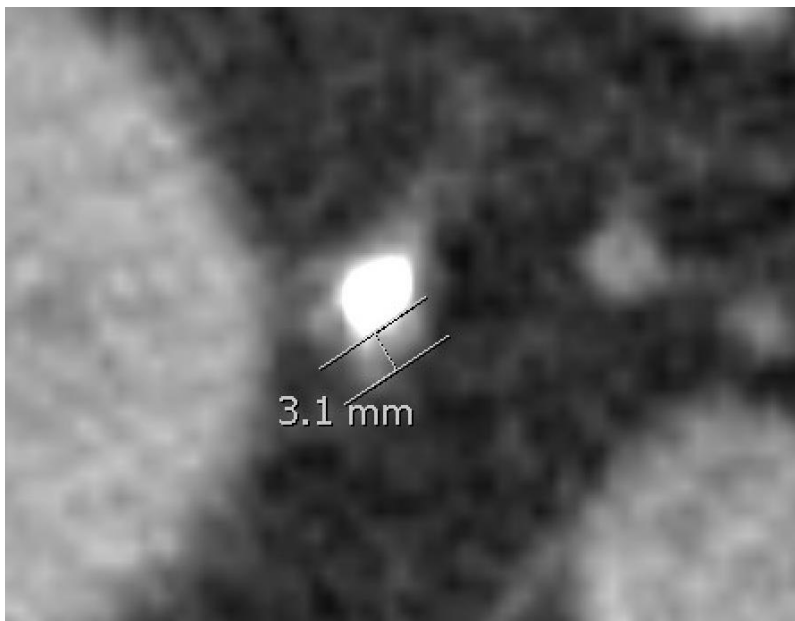
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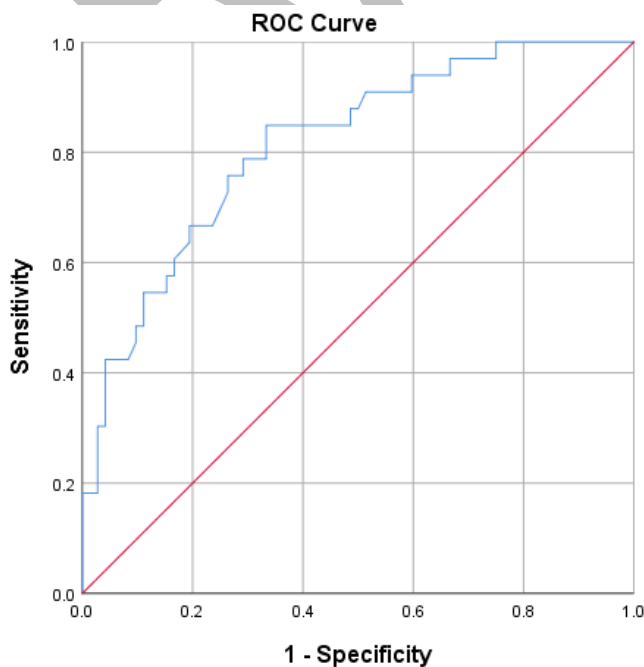
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FIGURES AND TABLES

**Figure 1.** Ureteral wall thickness measured on non-contrast computed tomography scan.



**Figure 2.** Receiver operator characteristic (ROC) curve for ureteral wall thickness prediction of failed retrograde stent insertion



<b>Variable</b>	<b>Total (n=109)</b>	<b>Successful retrograde stent (n=75)</b>	<b>Failed retrograde stent (n=34)</b>	<b>p</b>
Age (years)	60 (19–92)	59 (19–89)	61 (26–92)	0.66
Sex				0.30
Male	56 (21.4%)	36 (48.0%)	20 (58.8%)	
Female	53 (48.6%)	39 (52.0%)	14 (41.2%)	
Indication				<0.001
AKI	23 (21.1%)	8 (10.7%)	15 (44.1%)	
Sepsis	86 (78.9%)	67 (89.3%)	19 (55.9%)	
Time since diagnosis (days)	33 (0–979)	2 (0–40)	102 (0–979)	<0.001
Hydronephrosis				0.02
Mild/moderate	77 (70.6%)	58 (77.3%)	19 (55.9%)	
Severe	32 (29.4%)	17 (22.7%)	15 (44.1%)	
Stone location				0.09
Proximal	61 (56.0%)	40 (53.3%)	21 (61.8%)	
Middle	18 (16.5%)	10 (13.3%)	8 (23.5%)	
Distal	30 (27.5%)	25 (33.3%)	5 (14.7%)	
Renal atrophy				0.01
No	96 (88.1%)	70 (93.3%)	26 (76.5%)	
Yes	13 (11.9%)	5 (6.7%)	8 (23.5%)	
Stone craniocaudal distance (mm)	11.1 (2.1–35.4)	9.6 (2.1–23.6)	14.4 (2.2–35.4)	<0.001
Stone circumference (mm)	48.6 (13.3–130.7)	43.2 (13.3–130.7)	60.3 (16.2–103.7)	<0.001
Ureteral wall thickness (mm)	2.94 (1.10–6.60)	2.57 (1.10–4.73)	3.76 (1.95–6.60)	<0.001
Ureteric density (HU)	34.9 (7.2–84.2)	34.1 (7.2–84.2)	36.6 (9.3–81.8)	0.45

Values shown as median (range) or number (%). AKI: acute kidney injury.

**Table 1. Univariate and multivariate analysis of patient and stone characteristics predicting failed retrograde stent insertions**

Variable	Univariate		Multivariate	
	OR (95% CI)	p	OR (95% CI)	p
Age (years)	0.99 (0.97–1.02)	0.63		
Sex (male vs. female)	0.65 (0.29–1.47)	0.30		
Indication (non-sepsis vs. sepsis)	6.61 (2.44–17.94)	<b>&lt;0.001</b>	9.16 (1.91–44.00)	<b>0.006</b>
Time since diagnosis (days)	0.92 (0.85–1.00)	<b>0.05</b>	0.95 (0.87–1.03)	0.19
Hydronephrosis (mild/mod vs. severe)	0.37 (0.16–0.88)	<b>0.03</b>	0.30 (0.07–1.28)	0.10
Number of stones (1, more than 1)	0.55 (0.22–1.41)	0.21		
Stone location				
Proximal	1.00 (reference)	1.00 (reference)		
Middle	0.67 (0.23–1.91)	0.67		
Distal	2.63 (0.88–7.85)	0.084		
Renal atrophy	0.23 (0.07–0.77)	<b>0.02</b>	0.35 (0.06–1.94)	0.23
Stone craniocaudal distance (mm)	0.87 (0.80–0.94)	<b>&lt;0.001</b>	0.93 (0.81–1.06)	0.25
Stone circumference (mm)	0.97 (0.95–0.99)	<b>0.001</b>	1.03 (0.99–1.07)	0.23
Ureteral wall thickness (mm)	0.27 (0.15–0.48)	<b>&lt;0.001</b>	0.34 (0.15–0.74)	<b>0.007</b>
Ureteric density (HU)	0.99 (0.97–1.02)	0.51		

CI: confidence interval; OR: odds ratio.