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Ureteral stricture formation after endoscopic removal of obstructing stones: Could it be predicted with well assessed radiological parameters?

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Abstract

The possible role of well-assessed radiological parameters in the prediction of ureteral stricture formation in cases with impacted obstructive ureteral calculi has been evaluated

46 adult patients with or without ureteral stricture formation after ureteroscopic stone management were included. In addition to stone size and some certain radiological parameters including ureteral wall thickness (UWT) of the involved ureter at the impacted stone site was also measured and noted on computed tomography (CT) images. Parameters were evaluated in two subgroups of cases namely: Group 1: patients in whom a ureteral stricture formed after endoscopic stone removal and Group 2: patients normal ureteral anatomy without any stricture formation. The possible relationship between the UWT values and degree of hydronephrosis (HN) with subsequent stricture formation was comparatively evaluated.

All of the stones were proximal ureteral calculi in both groups. Both the degree of HN and proximal ureteral diameter (PUD) parench was higher in cases with stricture formation. Additionally, mean parenchymal thickness was lower and mean values of UWT measurements at the stone site were 3.70 ± 0.97mm and 2.17 ± 0.26 mm in Group 1 and 2 respectively. A cut off value 2.49 mm for UWT was found to be highly predictive for stricture formation.

UWT value calculated at the obstructing stone site was found to be predictive enough for the likelihood of ureteral stricture formation with high sensitivity and specifcity. This evaluation along with some other radiological parameters may enable the urologists to follow such cases on this aspect with necessary mesaures taken.

Introduction

Around 5–10% of the general populationsuffer form urolithiasis [1, 2] An urgent intervention is commonly required in the majority of the cases presenting with obstructive ureteralcalculi to preserve renal functional status well and limit the degree of possible anatomical alterations. Accumulated data so far has shown that if not removed with a rational approach on time, such stones may cause some irreversible changes in these renal units [3, 4, 5].

Regarding the management principles, obstructed upper tract system needs to be drained in aquick manner to avoid the formation of functional alterations and possiblesevere infective problems [6].To decompress the the obstructed collecting system effectively, although placement of a percutaneous nephrostomy tube or insretion of a double J (DJ) stent are the rational options to be applied; based on the anatomy and stone related factors, removal of the obstructing stone as early as possible is the ultimate therapeutic approach [7].

Although management of such calculi includes ureteroscopy (URS) with laser lithotripsy, extracorporeal shock wave lithotripsy (SWL) and percutaneous nephrolithotomy; majority of them are commonly treated

with URS in today's clinical practice[8].When compared with PNL, despite its evident minimally invasive nature, ureteroscopic manipulation may be associated with certain complications such as ureteral injuries and subsequent ureteral stricture formation [9]. Ureteral stricture is a rare, but an important complication of ureteroscopic manipulation for stones.Such procedure and/or stone related ureteral strictures can be highly morbid and recurrent which require possible several reconstructive procedures duringa close follow-upperiod [4, 7, 8]. Limited data could be derived from the literature and the incidence of stricture formation seem to range from 0.3%-3% [3, 7, 9].Regarding the pathogenesis of such strictures, due to the shift of management from SWL to URS, procedure related complications have been reported to bemore likely majority of which were found to be associated with traumatic, long-lasting proceedures performed by inexperienced surgeons [3, 9] However such strictures may also formbased on the tissue changes at the ureteral wall caused by an impacted stone [10, 11].

With respect to the parameters which may cause a certain role in the formation of these strictures after ureteroscopic stone removal, in addition to the procedure related factors mentioned above, some stone (size, location, shape etc) anatomy related (hydronephrosis, impaction of the stone, ureteral diameter etc) factors may play an important role [3, 9, 10].Among these factors certain tissue alterations (inflammation, edema formation and subsequent fibrotic changes) on the wall of the ureter mainly caused by the impacted stone are among the important factors to be considered [10, 11]. Studies have revealed well that the thickness of the ureteric wall surrounding the stone could be a reliable sign of such alterations which seem to increase parallel to the severity of impaction [12]. Related with this issue, the possible predictive value of the ureteral wall thickness (UWT) has been well evaluated to assess the degree of stone impaction and in one of our studies, we were able to demonstrate a signifcant relationship between the UWT values and obstruction degree in patients with acute ureteral obstruction [12, 13, 14]. In addition, we were able to show the predictive value of UWT assessment on the outcomes of medical and interventional procedures for such stones [12, 15, 16]. Thus, UWT value could be used as a reliable parameter to predict the severity of stone impaction and the probability of subsequent stricture formation after removal procedures forthese stones. To our knowledge, this is the first study evaluating the possible predictive value of UWT on the formation of ureteric strictures.

In this present study, we aimed to evaluate the possible predictive role of the UWT values noted at the ureteral stone site on the likelihood of stricture formationafter ureteroscopic stone removal in cases with obstructing ureteral stones.

Patients and methods

The multicentric protocol of the study was approved by the ethical commitee of the our Hospital. Between January 2020 and May 2023, 1154 patients presenting with a single unilateral, obstructing ureteral stone (5–15 mm) treated with URS due to varying degrees of hydroneprosis in five different referral centers were searched. Patients with strictures developing following percutaneous nephrolithotomy with or without antegrade URS, with bilateral and multiple stones, previous stone related procedures, pregnancy, active urinary tract infection, congenital anomalies, and solitary kidneys, radiation, or other nonstone

related etiologies including endometriosis, retroperitoneal fibros, and psoas abscess were all excluded from the study program.

Of all these 1154 cases a total of 30 patients with a diagnosis of ureteral strictureformation after these stone removal procedures were initially included. However of these 30 patients, seven cases were excluded from further analysis because three were lost to follow-up and in the remaining four casesa ureteral stricture was identified and treated during the URS procedure prior to stone manipulation. Remaining 23 cases (out of 30) with stricture formation meeting the inclusion criteria were eligible for further analysis.Another 23 cases demonstrating no stricture formation after these procedures during the same follow-up period formed our control group.

In addition to the demographic data such as gender, age and body mass index (BMI) of the patients, detailed history, urogenital examination findings, biochemical evaluation, urinalysis and urine culture sensitivity test outcomes were all evaluated and recorded. Regarding the radiologic parameters, all on-contrast computed tomography (CT) studies performed prior to URS procedures were evaluated in detail on this aspect (Fig. 1). In addition to the stone related factors (size, location, position and hardness (HU)), the thickness of the ureteric wall surounding the impacted stone (UWT), diameter of the proximal ureter (PUD) above the stone, degree of hydronephrosis were carefully outlined and recorded from these images. Summary of the patient and stone related characteristics are being given in Table 1.

Table 1
Evaluation of the patient characteristics

		Overall (n = 46)	**Stricture (n = 23)**	**No stricture (n = 23)**	***p***
Gender; *n (%)*	*Male*	36 (78.2)	17 (73.9)	19 (82.6)	0.475
	Female	10 (22.8)	6 (26.1)	4 (17.4)	
Age; *(years)*	*Mean ± SD*	43.37 ± 14.28	51 ± 13.76	39.74 ± 12.7	0.409
BMI; *(kg/m2)*	*Mean ± SD*	26.08 ± 3.40	26.42 ± 4.01	25.73 ± 2.71	0.072
Hypertension; *n (%)*		9 (19.6)	8 (88.9)	1 (11.1)	**0.009**
Diabetes; *n (%)*		5 (10.9)	5 (100)	0 (0)	**0.018**
Body Mass Index (BMI)					

The ureteroscopic stone removal procedures were performed by using a semirigid endoscope (8F/9.8F tapering shaft, Richard Wolf Medical Instruments Corporation, Vernon Hills, IL). A safety guide wire (0.032 in) was used in all cases. A holmium laser (Ho-YAG) was utilized for stone disintegration and the fragments formed were removed with forceps or baskets. With respect to the course of the operative procedures, no evident operative related injury to the ureteral mucosa was noted during and/or after the intervention which may be resposible for such alterations after the procedure. Ureteroscopic stone

removal procedures were performed by the same experienced surgeons in all centers with the same Ho-YAG laser settings. The JJ stents were removed in patients after two weeks and all cases were closely followed during a period of three months for the presence and degree of upper tract dilation as done routinely in all these departments. Ureteral stricture formation was diagnosed with the presence of persistingupper urinary tract dilatation on CT imagingduring this follow-up period or demonstration of the stricture directly on a planneddiagnostic URS performed in the same period. Pre-and post operative above mentioned data of cases in both groups were evaluated in a comparative manner.

Independent-samples t-tests were performed comparing continuous variables, such as stone size and operating time. Categorical variableswere compared using exact chisquared 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.

Results

Evaluation of our data in both group of cases revealed following findings;

While the mean patient age of the 46 patients (36 men and 10 women) was 43.37 ± 14.28, with a mean BMI value of 26.08 ± 3.40 (Table 1); mean size of the stones was 9.38 ± 3.32 in this group and these values were 11.43 ± 3.08 and 7.33 ± 2.07 in the stricture group and control group respectively in Table 2. The incidence co-morbidities such as diabetes mellitus and hypertension was found to be higher in patients with stricture formation than in normal patients (P = 0.009 and P = 0.018, respectively). Patient and stone characteristics in both group of cases are being demonstrated in Table 1.

Table 2
Evaluation of the operative and radiological parameters in both groups

		Overall (n = 46)	Stricture (n = 23)	No stricture (n = 23)	*p*
UWT, *(mm)*	*Mean ± SD*	2.93 ± 1.04	3.70 ± 0.97	2.17 ± 0.26	**0.004**
PUD, *(mm)*	*Mean ± SD*	11.37 ± 6.40	15.49 ± 6.68	7.25 ± 1.93	**0.018**
Parenchimalthickness, *(mm)*	*Mean ± SD*	22.53 ± 6.64	20.45 ± 7.91	24.6 ± 4.32	**0.005**
Stone size, *(mm)*	*Mean ± SD*	9.38 ± 3.32	11.43 ± 3.08	7.33 ± 2.07	**0.042**
Stone density, *(HU)*	*Mean ± SD*	968.15 ± 305.08	864.39 ± 272.20	1071.91 ± 306.23	0.576
Laterality, %					
Right		19	12	7	0.134
Left		27	11	16	
Pre-operativehydronephosis					
Grade 1		9 (19.6)	0 (0)	9 (3.2)	**0.002**
Grade 2		13 (28.3)	6 (26.1)	7 (30.4)	
Grade 3		24 (52.1)	17 (73.9)	7 (30.4)	
Operation time, *(min)*	*Mean ± SD*	42.24 ± 10.50	45.13 ± 12.45	39.35 ± 7.28	0.059
Post-surgery JJ Stent, *(days)*	*Mean ± SD*	52.71 ± 110.5	80.82 ± 145.1	20.16 ± 13.6	0.067
SFR in 3 stmonth, (%)		43(93.5)	20(87.0)	23(100)	0.073

Body Mass Index (BMI), Hounsfieldunit(HU), Ureteralwallthickness (UWT), Diameter of theureterproximaltothestone (PUD), Stone free (SFR)

Table 2
Logistric regression analysis of the radiological parameters

	P	Odds	%95 CI	
			Lower	Upper
UWT, *(mm)*	**< 0.0001**	2.81	2.18	3.84
PUD, *(mm)*	**0.009**	4.53	1.45	14.19
HN	**0.002**	4.79	1.82	12.64
Parenchimalthickness, *(mm)*	**0.042**	0.90	0.81	1.00
Hounsfieldunit(HU), Ureteralwallthickness (UWT), Diameter of theureterproximaltothestone (PUD)				

As a possible operative risk factor for the development of ureteral strictures evaluated in our present study, operating time was longer in cases forming strictures (above 60 minutes, all 4 cases) than the other cases without any stricture formation.

On the hand, regading the radiological risk factors evaluated.logitic regression analysis dempnstrated well that renalparenchymal thickness, diameter of the ureter proximal to the stone (PUD) and especially the ureteral wall thickness (UWT) were the important risk factors in predicting stricture formation after ureteroscopic stone management (P = 0.0001, P = 0.009 and P = 0.042, respectively) in Table 3. Mean parenchymal thickness was significantly higher in control group casescompared to the ones formingstricture (20.45 ± 7.91mm vs 24.6 ± 4.32mm,p = 0.005) in Table 2. Comparative evaluation of the PUD values againdemonstrated a significant difference in favor of the cases with stricture where the mean value was higher than control group patients (15.49 ± 6.68 vs7.25 ± 1.93, p = 0.018) in Table 2.Last but not least, presence of hydronephosis was more frequent in the stricture group compared to the non-stricture group (p = 0.002) in Table 2.

As the most important factor in predicting the possible ureteral stricture formation after these procedures, in our study, evaluation of the mean ureteric wall thickness values demonstrated a statistically signifcant difference between the two group of cases. While the mean UWT value was 3.70 ± 0.97 mm in stricture group cases, this value was noted to be 2.17 ± 0.26 mm in cases with no stricture group (p < 0.004) in Table 2.A cutof value of 2.49 mm was highly predictive and in stricture cases with a value higher than this calculation. In the receiver operating characteristic (ROC) curve, the best cutof point of ureteral wall thickness was 2.49 mm with a sensitivity value of 100%, specifcity value of 100% (area under the curve: 1.00 AUC 95% (1.00–1.00), p < 0.0001). Figure 2 demon strates well the relevant values and ROC curve.

Discussion

Ureteric stones comprise 73.0% of all calculi and a considerable percentage of these stones particularly the large ones induce varying degrees of upper tract obstruction [7]. Due to the impaction and evident flow hindrance, an urgent decompression of the collecting system is required to avoid possible renal

alterations. Similar to those cases again, prompt relief of the obstruction may also be necessary in ureteral stone cases whodo not reply well to the conservative treatment for the relief of symptoms and spontaneous passage [4, 5].

Regarding the effective relief of obstruction in such cases apart from the urgent cases requiring a quick on time, elective ureteroscopy with Ho-YAG disintegration of the stone(s) is the commonly performed theraputic approach applied in the vast majority of these cases (16,17). However, despite its a minimally invasive nature in today's clinical practice, published data so far has pointed out that this approach may be associated with certain complications such as ureteral injuries and subsequent ureteral stricture formation. Ureteral stricture is a rare, but an important complication of ureteroscopic manipulation for Stones [4, 6, 8].

Among the underlying causes of stricture formation following endoscopic stone removal procedures ureteral injury during stone manipulation and inflammatory alterations in ureteral wall at the impacted stone site could be contributing factors [6, 7, 9]. In fact, any process resulting in ureteral wall injury could be regarded as a potential risk factor for this problem. Within this frame, the large and impacted stones are the ones which may cause stricture formations [3, 9].

In most cases, the level of the strictures coincided with the location of the stones and majority of such strictures seem to develop following removal of the stones. Thus, the inflammatory response to the presence of the stone for a certain period of time coupled with the trauma induced during stone removal may be the resposible factors for stricture formation[3, 6, 9]. Additionally prolonged operative duration which may cause reduced blood flow to the ureteric wall coupled with the insertion of a bigger UAS could promote such stricture formations [18].

Taking the risk of prolonged obstruction due to such a stricture formation and the need of several procedures for its management into account, it may provide a distinct advantage for the practicing urologist being able to predict the probability of stricture formation in such cases [3].

As mentioned above the presence and the degree of stone impaction into the ureteral wall is an highly important parameter from this aspect. Vast majority of obstructing stones are being detected in NCCT and some indirect radiological parameters have been evaluated to assess the presence of impaction and related alterations in the ureteric wall which may play a certain role insubsequent stricture formation in the affected ureteric wall [9–12,15). Parameters such as degree of hydronephrosis, diameter of the dilated proximal ureter have been used with this aim [19].

On the other hand, published studies revealed that the thickness of the ureteric wall just around the stone could also increase parallel to the severity of ureteral obstruction depending on the time elapsed and the degree of infammatory reactions formed [20]. Related with this issue, the possible predictive value of the UWT has been evaluated in a number of studies to assess the degree of stone impaction. This parameter has been defined as the noninvasive way to assess the degree of stone impaction (embedment). In some of our studies, we demonstrated a signifcant relationship between the value of UWT and the severity of

the obstruction in patients with ureteral stones [12, 14, 17, 21–23]. In addition, UWT was also used to predict the outcomes of medical and interventional management of ureteric stones [24–27]. Thus, it will be rational to think that this parameter could also be used as a reliable tool to predict the probability of stricture formation alongside the stone in cases with obstructing ureteral stones.

It is a well known that not all of the cases undergoing endoscopic stone management for impacted upper ureteral calculi develop stricture formation at the stone site, but some do. Thus, in this study, in addition to operative parameters we aimed to evaluate the possible role of some certain radiological parameters in predicting the likelihood of stricture formation after ureteroscopic stone management. Our data indicated well enough the predictive role of increased PUD, higher degrees of hydronephrotic changes and thinner paranchymal thickness values in cases presenting with ureteral stricture after these procedures. Additionally and more importantly, as a critical parameter indicating tissue changes at the stone bearing ureteral wall and a reliable indicator of stone impaction; we aimed to evaluate the predictive value of ureteral wall tickness (UWT) in ureteral stricture formation after endoscopic (uretroscopic –Ho-YAG laser disintegration) stone removal proceduers in obstructive, impacted upper ureteral calculi. Evaluation of the ureteric wall thickness values in both groups of cases demonstrated a statistically signifcant difference where the value of UWT was signifcantly higher in cases in whom a ureteral wall stricture has formed at the impacted stone site in the ureter. Further evaluation of our findings demonstrated that a cut-off value of 2.49 mm for UWT evaluation was highly predictive (with high sensitivity and specifcity) for the likelihood of stricture formation in such cases.

Our results and highly limited data published so far indicate that certain radiologic parameters could be useful in the prediction of a stricture formation following removal of an impacted, large stone located in proximal portion of the ureter. Among these parameters, specifically a UWT value higher than the cut-off value of 2.49 mm may be a reliable predictor of stricture formation. Prediction of such a rare but very critical complication which certainly will require several additional procedures to establish the urinary flow well again seems to be highly important for the endourologists in these cases. This will in turn enable the urologists to make the proper and rational plan for the close follow-up period by maintaining the effective drainage of upper urinary tract for a relatively longer period than the other non-complicated ones and let the inflammatory changes be healed well with an open ueteric lumen. This will also let us to avoid certain possible functional and morphologic changes in the collecting system during long-term obstruction with less risk of postoperative infective complications. To our knowledge, our current study is the first trial focusing on the possible predictive value of UWT assessment on the likelihood of stricture formation in the ueretric wall following the endoscopic removal of obstructing ureteric stones.

Our current study is not free of limitations. First of all, the retrospective design of our trial constitutes an important limitation. Another major limitation is the relatively lower number of cases with ureteral strictures included into the study program. However, taking the limited number of such cases reported for the stricture formation after endoscopic stone management; we believe that our serie from five referral centers seems to be one of the largest on this aspect and the findings reported will be contributive well enough to the existing literature.

Conclusions

Ureteral stricture is a rare, but serious complication following ureterorenoscopic removal of large/impacted ureteral stones. Prediction of this critical problem prior to the procedure with the help of some reliable radiological parameters could be highly helpful for the post-operative decision making of endourologists. As a noninvasive parameter assessed in CT images, mean value of UWT surrounding the stone in this portion of the ureter seemed to be a reliable parameter to predict the likelihood of stricture formation with great sensitivity and specifcity. Evaluation of UWT value could help the responsible urologist to make a rational follow-up plan to avoid possible anatomic as well as infective complications and be ready for further auxiliary procedures. However, we believe that further clinical trials with larger series of cases are certainly needed to support our current findings.

Declarations

Author contributions KS: project development and manuscript writing. CS: project development and manuscript YK: data collection. writing. RS: data collection and manuscript writing. OA: data collection. FB: data collection. MU: data collection. EBS: data collection.

Compliance with ethical standards

Conflict of interest The authors have no confict of interest to declare.

Ethical approval This retrospective study was conducted after receiv- ing approval from the institutional review board.

Informed consent All the participants have given informed consent before inclusion in the present study

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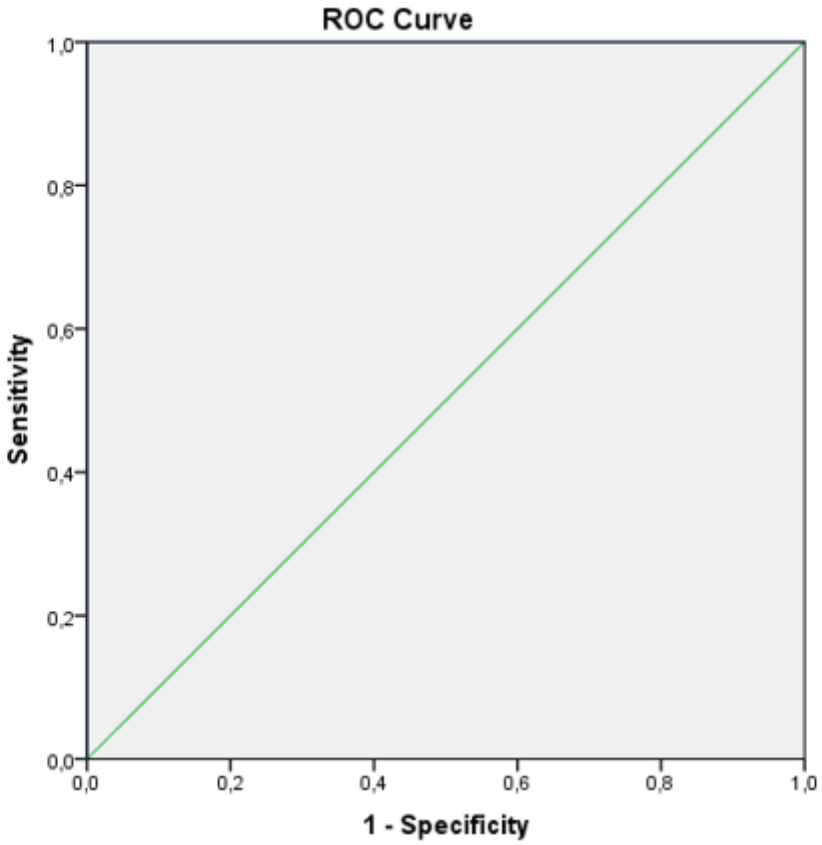
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Figures



Risk factor	AUC(95%)	Cutoff	P value	Specifity (%)	Sensitivity (%)
Ureteralwallthickness		2.40		83	100
		2.46		96	100
	1.00(1.00-1.00)	2.49	<0.0001	100	100

Figure 1

ROC curve analysis of the sensitivity and specifity for UWT values

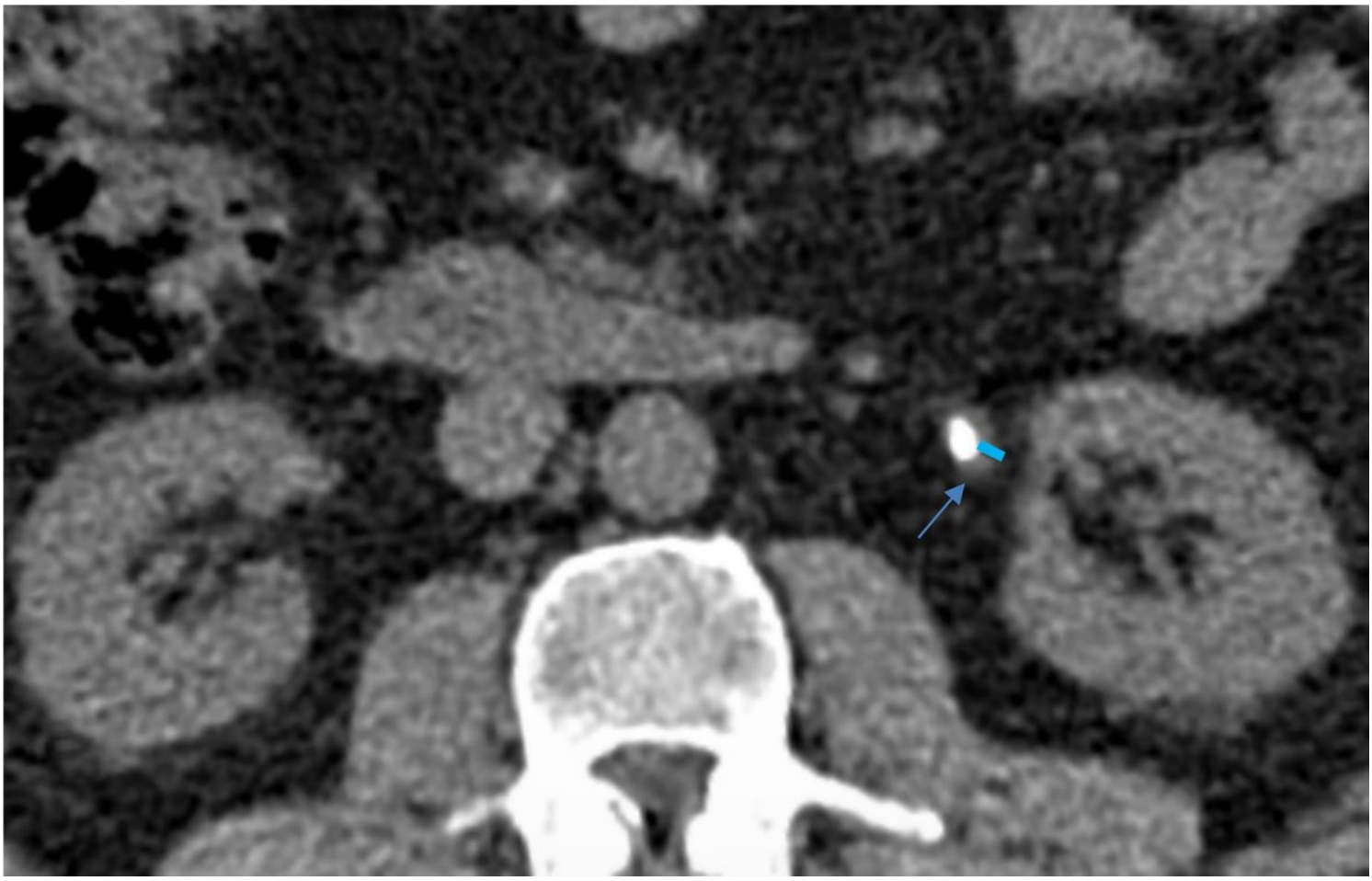


Figure 2

Assessment of ureteral wall thickness (UWT) value on CT imaging in a patient with large proximal ureteral stone