Development of a Scoring System From Noncontrast Computerized Tomography Measurements to Improve the Selection of Upper Ureteral Stone for Extracorporeal Shock Wave Lithotripsy

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Purpose: We investigated the role of noncontrast computerized tomography in predicting the treatment outcome of shock wave lithotripsy on upper ureteral stones to formulate a clinical algorithm to facilitate clinical management.

Materials and Methods: Adult patients with upper ureteral stones confirmed by noncontrast computerized tomography and scheduled for primary in situ shock wave lithotripsy were prospectively recruited. Standardized treatment was performed on each patient. The primary end point was stone-free status at 3 months. Pretreatment noncontrast computerized tomography was assessed by a single radiologist blinded to the clinical parameters. Predictive values of computerized tomography measurements on the treatment outcome were then assessed.

Results: Between October 2004 and July 2007 a total of 94 patients (60 male and 34 female) were recruited for the study. Logistic regression showed that stone volume, mean stone density and skin-to-stone distance were potential predictors of successful treatment. From ROC curves the optimum cutoff for predicting treatment outcomes for stone volume, mean stone density and skin-to-stone distance was 0.2 cc, 593 HU and 9.2 cm, respectively. A simple scoring system was constructed based on the 3 factors of stone volume less than 0.2 cc, mean stone density less than 593 HU or skin-to-stone distance less than 9.2 cm. The stone-free rate for patients having 0, 1, 2 and 3 factors was 17.9%, 48.4%, 73.3% and 100%, respectively (linear-by-linear association test 22.83, $p < 0.001$).

Conclusions: Stone volume, mean stone density and skin-to-stone distance were potential predictors of the successful treatment of upper ureteral stones with shock wave lithotripsy. A scoring system based on these 3 factors helps separate patients into outcome groups and facilitates treatment planning.

Key Words: ureter, calculi, lithotripsy, tomography

Abbreviations and Acronyms

BMI = body mass index
CT = computerized tomography
MSD = mean stone density
NCCT = noncontrast computerized tomography
SSD = skin-to-stone distance
SV = stone volume
SWL = shock wave lithotripsy

Submitted for publication July 14, 2008.

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URETERAL colic due to upper ureteral stones is a common urological problem. Traditionally an excretory urogram is the gold standard in the diagnosis of ureteral stones. However, NCCT has gained popularity and become the new standard for diagnosis.[1]

Although many treatment options are available, extracorporeal shock wave lithotripsy has remained one of the first line treatments for upper ureteral stones.[2] The advantages of SWL include its simplicity and noninvasiveness. However, the main drawback of SWL compared with ureteros-

0022-5347/09/1813-1151/0
THE JOURNAL OF UROLOGY®

Vol. 181, 1151-1157, March 2009
Printed in U.S.A.
DOI:10.1016/j.juro.2008.10.161

copy is its lower stone-free rate.[3] Unsuccessful treatment will result in prolonged ureteral obstruction and further suffering of patients. If we could identify the favorable factors underlying successful SWL a better treatment plan could then be formulated. There are many simple factors that may affect treatment outcome including stone size, stone localization and multiplicity.[4] Recently there has been increasing evidence that various NCCT parameters can predict SWL treatment outcome including MSD (measured in HU), SV, SSD and the microstructure of the stones, etc (table 1).[5–10] If decision guidelines could be formulated from these factors better treatment plans could be devised. Therefore, we performed a prospective study to determine factors that affect the outcome of SWL for upper ureteral stones to formulate clinical guidelines to facilitate future patient treatment.

MATERIALS AND METHODS

Adult patients (older than 18 years) with radiopaque upper ureteral stones diagnosed by NCCT and planned for primary SWL were recruited into the study. Upper ureteral stone was defined as a stone located in the ureter above the upper border of the sacroiliac joint on plain radiography. Exclusion criteria included contraindications for SWL such as pregnancy, active urosepsis or coagulopathy, patients with percutaneous nephrostomy or ureteral stent and suspected distal ureteral obstruction.

Informed consent was obtained from each patient and background information was collected before treatment. All patients were treated with Sonolith 4000+ (Technomed, France) with a standard protocol. They received prophylactic antibiotics and intravenous injection of 0.5 mg alfentanil as premedication. The shock wave was delivered at an asynchonized rate of 100 shocks per minute or at electrocardiogram triggering mode with a power of 80% to 90%. The positioning of the stone was checked by fluoroscopy after every 1,000 shocks. Treatment was stopped after a maximum of 3,000 shocks if the stone could not be located or if the patient could not tolerate the procedure. After SWL x-ray was performed at 2 weeks, 6 weeks and 3 months to assess the progress. All films were assessed by a single urologist (CFN) who was blinded to the NCCT information. Plans for further treatment including observation, repeat SWL or other auxiliary procedures were decided based on the x-ray findings with patient benefit as the sole factor considered. Stone clearance was further documented by excretory urogram in all patients.

All pretreatment NCCTs were performed with a multidetector row CT scanner at 120 KV and 150 mA with 4 cm collimation and 0.625 mm slide thickness. They were reviewed by a single radiologist (DS) who was blinded to the clinical results. Information was measured on stone factors such as SV, MSD, stone level, the rim sign around the stone and SSD. The radiologist also attempted to classify the internal structure through different viewing windows into hyperdense center, hypodense center and homogeneous.[11] Stone level was defined as the vertical distance of the center of the stone from the upper border pubic symphysis. The rim sign was used to reflect any tissue reaction around the stone. SSD was defined as the vertical distance from the center of the stone to the skin measured on a supine NCCT film (fig. 1).

The primary outcome of the study was the stone-free rate at 3 months after 1 SWL session. Stone-free was defined as no radiopacity detected on good quality plain radiography and confirmed by excretory urogram. The crude odds ratio was calculated to investigate the effect of possible independent factors on the outcome and the adjusted odds ratio was then obtained after controlling for confounders using backward stepwise logistic regression. Because of the possible interaction between SV and the measurement of MSD, the confounding effect between SV and MSD was also assessed.[12]

ROC curves were plotted to obtain the optimum cutoff for significant predictors for treatment outcome. Backward stepwise logistic regression was then performed again with these factors regrouped according to the ROC curves to develop a clinical algorithm. All statistical analysis was performed using SPSS® 14.0 with a significance level of 0.05.

RESULTS

Between October 2004 and July 2007 a total of 94 patients (60 male and 34 female) with a mean age of 52.4 years (range 24 to 94) were recruited. The characteristics of patients and the NCCT measurement of stones are summarized in table 2. The treatment parameters for the patients are listed in table 3. There were significantly fewer shocks, a lower energy level and less total energy received for those successfully treated stones. This finding probably related to our protocol that treatment would be

Table 1. *Summary of main literature on the role of NCCT stone measurement in treatment outcomes*

References	No. Pts	Stone Sites	Predictors of Successful Treatment			
			MSD	SV	SSD	Other
Joseph et al[5]	30	Renal	Yes	—	—	—
Pareek et al[6]	64	Lower pole	No	—	Yes	—
Gupta et al[7]	112	Renal or proximal ureteral	Yes	—	—	—
Yoshida et al[8]	62	Renal or proximal ureteral	Yes	Yes	—	Hump existence
Perks et al[9]	76	Renal or ureteral	Yes	—	—	—
El-Nahas et al[10]	120	Renal	Yes	No	No	

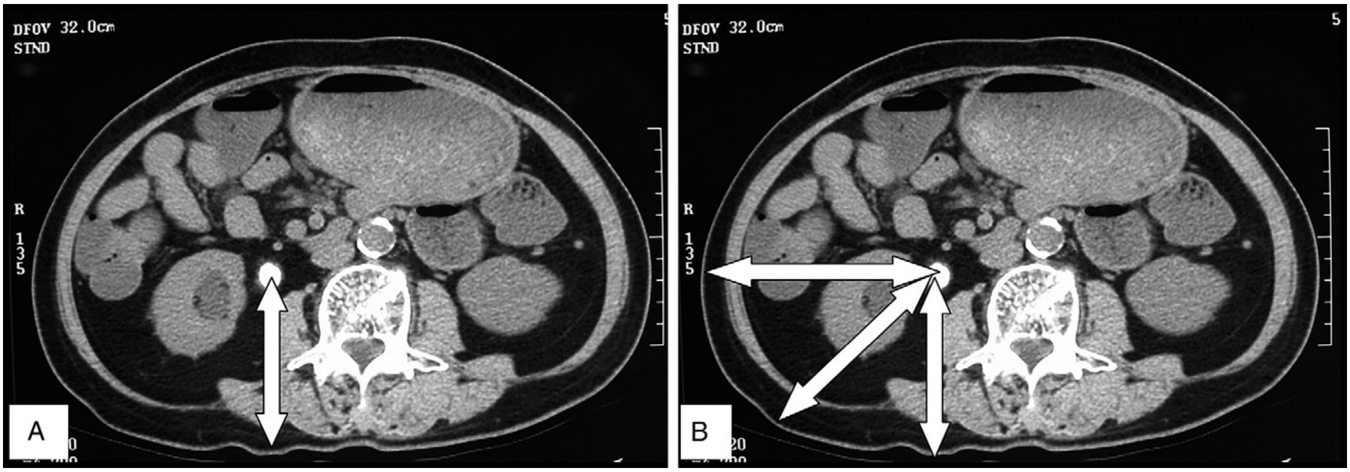

Figure 1. *A*, definition of SSD (white arrow) in study. *B*, definition of SSD distance, mean of 3 measurements at 0, 45 and 90 degrees as suggested by Pareek et al.[6]

stopped once the stone was not detectable, thus fewer shocks and less total energy were given to these successfully treated stones. The overall complication rate for SWL was low (2.13%). Steinstrasse developed in 1 patient and required ureteroscopy, and vomiting developed in another patient shortly after SWL which subsided within a few hours after treatment. Only 6 patients had stone analysis results available for review, and all contained a mixture of calcium oxalate (69% to 92% of stone composition) and calcium phosphate (8% to 31% of stone composition).

The overall stone-free rate was 50% (47/94). Univariate analyses demonstrated that a greater SV (OR 0.028; 95% CI 0.003, 0.234; $p = 0.001$) and a greater MSD (for every 10-unit increase in MSD, OR 0.932; 95% CI 0.932, 0.971; $p = 0.001$) were associated with a lower likelihood of success (table 4). Logistic regression was used to assess the effect of all potential predictive factors including age, sex, BMI, SV, MSD, SSD, stone level and rim sign. Because of the interaction between SV and the measurement of MSD the confounding effect was adjusted by adding interaction parameters between SV and MSD in the analysis (fig. 2).[12] The results showed that greater SV (OR 0.89; 95% CI 0.10, 0.89; $p = 0.033$) and MSD (for every 10-unit increase in MSD, OR 0.947; 95% CI 0.9, 0.996; $p = 0.035$) were significant predictors of a lower stone-free rate. The stone-free rate was marginally smaller for a longer SSD (OR 0.716; 95% CI 0.492, 1.041; $p = 0.08$). There was no significant association between interaction parameters of MSD and SV on the outcome (OR 1.013; 95% CI 0.922, 1.033; $p = 0.226$) (table 4).

The ROC curves of these factors were plotted to find the optimum cutoff points for developing an algorithm to predict the treatment outcome of a ureteral stone with SWL. The optimum cutoff points

Table 2. *Patient characteristics and stone parameters measured with NCCT*

	Successful		Unsuccessful		Overall		p Value
No. pts	47		47		94		
Mean age (range)	51.4	(30–82)	53.5	(24–94)	52.4	(24.0–94.0)	0.424
No. sex (%):							
Male	27	(57.4)	33	(70.2)	60	(63.8)	0.200
Female	20	(42.6)	14	(29.8)	34	(36.2)	
Mean BMI (range)	23.67	(17.72–31.81)	24.37	(18.15–36.12)	24.0	(17.72–36.12)	0.332
Mean cc SV (range)	0.25	(0.07–1.09)	0.50	(0.09–2.11)	0.38	(0.07–2.11)	0.001
Mean HU stone density (range)	534	(340–961)	626	(412–842)	580	(340–961)	0.001
Mean cm stone level (range)	18.99	(12.3–23.9)	18.97	(14.5–24.2)	18.97	(12.3–24.2)	0.957
Mean cm SSD (range)	10.23	(6.9–13.0)	10.44	(7.7–13.5)	10.34	(6.9–13.5)	0.456
No. presence of rim-sign (%):							
Yes	33	(70.2)	30	(63.8)	63	(67.0)	1.000
No	14	(29.8)	17	(36.2)	31	(33.0)	
No. internal structure (%):							
Homogenous	47	(100)	47	(100)	94	(100)	Not applicable
Hyperdense or hypodense center	0	(0)	0	(0)	0	(0)	

Table 3. *Treatment parameters for cases of success and failure*

Stone Parameters	Mean (range)			p Value
	Successful	Unsuccessful	Overall	
Total No. shocks	2,657 (1,000–3,000)	2,957 (2,000–3,000)	2,807 (1,000–3,000)	0.002
Energy level (%)	81.28 (70–90)	85.43 (80–90)	83.35 (70–90)	<0.001
Total energy amount	659.02 (223–812.7)	755.51 (470–819.6)	707.27 (223–819.6)	<0.001
Treatment mins	47.49 (20–75)	52.47 (35–140)	50.0 (20–140)	0.348

were SV at 0.2 cc, MSD at 593 HU and SSD at 9.2 cm (fig. 3).

The variables SV, MSD and SSD were then regrouped into dichotomous variables based on the ROC curves, and logistic regression of these factors was performed to test their strength in predicting the SWL outcome. The adjusted ORs for SV 0.2 cc or less vs SV greater than 0.2 cc, SSD 9.2 cm or less vs SSD greater than 9.2 cm and MSD 593 HU or less vs MSD greater than 593 HU on the stone-free rate were 4.297 (95% CI 1.422, 12.985; p = 0.01), 3.497 (95% CI 1.073, 11.2391; p = 0.038) and 3.388 (95% CI 1.154, 9.941; p = 0.026), respectively (table 5).

An algorithm of these factors with equal weighting was formulated (table 6). The stone-free rate at 3 months for scores 0, 1, 2 and 3 was 17.9%, 48.4%, 73.3% and 100%, respectively (chi-square test p <0.001) (linear-by-linear association test 22.83, p <0.001).

DISCUSSION

Our results revealed that SV, MSD and SSD are significant predictors for successful SWL. Based on these factors we formulated a scoring system to stratify the treatment outcome of patients with upper ureteral stones. The stone-free rates at 3 months for scores 0, 1, 2 and 3 were 17.9%, 48.4%, 73.3% and 100%, respectively (p <0.001). This practical information is important for future pretreatment counseling and treatment plan formulation for patients with upper ureteral stones.

There is increasing evidence to suggest that stone measurement by NCCT can help in predicting treatment outcome of SWL. However, practical guidance on its use is still scant. Therefore, we wish that this study could help to generate practical guidelines. Although many articles in the literature report on the analysis of NCCT on renal stones, the clinical application is still not universal (table 1).[13] However, the application of NCCT in ureteral colic/ureteral stone is relatively well established and is a common practice worldwide.[1,14] Therefore, we decided to recruit only those patients who were confirmed by NCCT to have upper ureteral stones. As a result our findings are more applicable to centers that use NCCT for the diagnosis of ureteral stones. We also excluded patients with renal stones from analysis because the treatment outcome of renal stones can be affected by additional factors such as age[15] and lower caliceal anatomy.[16] All of these factors must be controlled during statistical analysis which makes the situation more complicated than analyzing only ureteral stones. After identifying the predictors of successful treatment a practical guideline was formulated to facilitate future patient treatment. Therefore, in the future when a patient presents with ureteral colic, after the diagnosis is confirmed by NCCT the success rate of treating with SWL can also be estimated. This process could facilitate decision making, and perhaps unnecessary delay and suffering due to failed stone clearance after SWL could be avoided.

Other preoperative practical guidelines were also available in the literature. Kanao et al performed a prospective study to assess the treatment outcome of more than 500 renal and ureteral stones.[4] Using logistic regression stone length, location and number were identified as significant predictors of treatment success, and a nomogram was formulated. The methodology was similar to that of our study. How-

Table 4. *Univariate and multivariate analysis of patient characteristics and stone parameters on outcome of SWL*

	Crude OR (95% CI)	p Value	Adjusted OR (95% CI)	p Value
Age	0.987 (0.956, 1.019)	0.424	*	*
Sex (male vs female)	1.746 (0.745, 4.091)	0.200	*	*
BMI	0.943 (0.837, 1.062)	0.332		
Stone vol	0.028 (0.003, 0.234)	0.001	0.089 (0.010, 0.819)	0.033
MSD	0.993 (0.989, 0.997)	0.001	0.995 (0.990, 1.000)	0.035
Stone level	1.005 (0.853, 1.182)	0.957	*	*
SSD	0.895 (0.668, 1.198)	0.456	0.716 (0.492, 1.041)	0.080
Presence of rim-sign (no vs yes)	1.366 (0.564, 3.166)	0.511	*	*

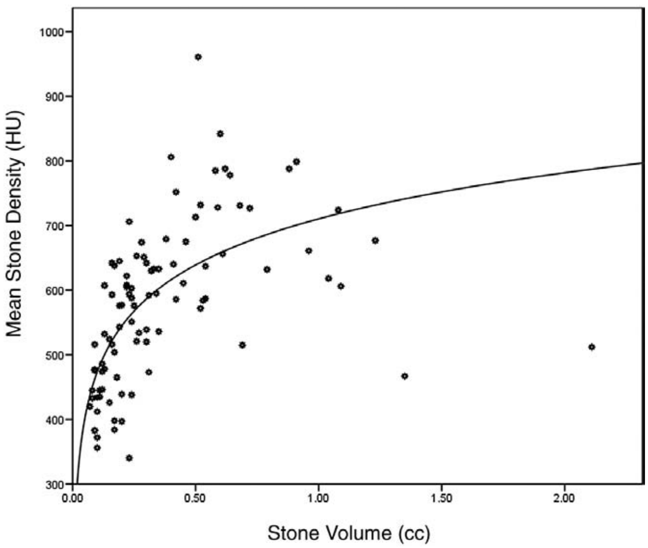

Figure 2. Scatterplot of SV and MSD as measured by NCCT for individual ureteral stones.

ever, we recruited only patients with solitary proximal ureteral stones prospectively for analysis, and we used NCCT to provide more accurate measurement of stone size (stone volume) and other parameters. Kacker et al also reported on practical guidelines to facilitate patient selection for SWL.[17] In this retrospective study the authors preselected several parameters including maximum, average and standard deviation of stone attenuation, stone size and SSD as potential radiographic parameters of interest. These parameters were then measured in 325

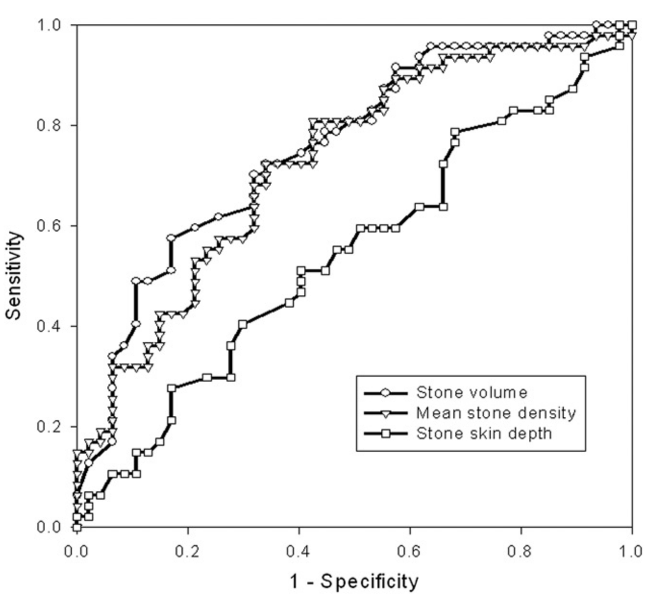

Figure 3. ROC curve of SV, MSD and SSD for prediction of stone-free status.

Table 5. *Multivariate analysis of prognostic factors on outcomes of SWL*

	Adjusted OR (95% CI)	p Value
SV 0.2 cc or less vs greater than 0.2 cc	4.297 (1.422, 12.985)	0.01
MSD 593 HU or less vs greater than 593 HU	3.497 (1.073, 11.391)	0.038
SSD 9.2 cm or less vs greater than 9.2 cm	3.388 (1.154, 9.941)	0.026

stone cases. The ROC curves for each parameter were plotted and average attenuation was selected as the parameter of interest. By using statistical calculation with the results from Kanao et al a refined probability of treatment success was calculated.[4] They concluded that SWL was effective in treating solitary stones 6 to 10 mm with an average stone attenuation of less than 1,000 HU for proximal ureteral stones and less than 640 HU for renal pelvis stones. However, the retrospective nature and complicated statistical calculations of this study were drawbacks. A summary of the comparison of these 2 studies with our study is provided in table 7.

Of the 3 predictors identified in this study MSD is the most commonly identified factor in the literature.[5–10] However, there is an observation that MSD measurement is affected by stone size, which was also observed in our study (fig. 2).[12] Therefore, in our multivariate analysis we included an assessment of the potential interaction between these 2 factors. This could help control the confounding effect of SV on MSD measurement and assess the strength of the interaction. However, our results showed the interaction between SV and MSD was not a significant predictor of the outcome.

We did not follow the suggestions of Pareek et al in our measurement of SSD, that is the average of 3 measurements taken at 0, 45 and 90 degrees from the stone center to the skin (fig. 1).[6] In the Sonolith 4000+ the generator approaches the patient directly from below rather than from the lateral direction as in the Doli S lithotripter. Therefore, a vertical measurement of SSD correlates better with the actual distance of the shock wave path.

In our study BMI was not a significant predictor of treatment outcome while SSD was a marginally significant predictor, similar to the results of Pareek

Table 6. *Association between number of predictive factors and stone-free rate*

Score	% Stone-Free Rate (No./total No.)	p Value
0	17.9 (5/28)	<0.001
1	48.4 (15/31)	
2	73.3 (22/30)	
3	100 (5/5)	

Scoring system for prediction of SWL treatment outcome of upper ureteral stone. Score 1 point if upper ureteral stone has characteristics SV 0.2 cc or less, MSD 593 HU or less, SSD 9.2 cm or less.

Table 7. *Comparison of study design and guidelines*

	Kanao et al[4]	Kacker et al[17]	Present Series
Study design	Prospective	Retrospective	Prospective
Subject No.	507	325	94
Stone site	Renal + ureteral	Renal + ureteral	Upper ureteral only
Nature of predictive variables	Based on plain radiography or excretory urogram	NCCT	NCCT
Basic statistical methods	Multivariate analysis with logistic regression model	Best predictor assessed by ROC curve of preselected radiographic parameters, then refined probability of success determined with consideration of result of Kanao et al[4]	Multivariate analysis with logistic regression model
Final predictors for treatment success	Stone length, location + No.	Av stone attenuation	SV, MSD, SSD
Practical guidelines	Nomogram table	Simple guidelines for stones 6–10 mm	3-Point scoring system

et al.[6] However, El-Nahas et al found the opposite with BMI being a significant predictor of success instead of SSD.[10] In our opinion the effect of BMI on SWL outcome is probably related to the distance of the stone from skin, which reflects the shock wave path in the body. Since body fat distribution varies in different races, BMI may not truly reflect central body fat distribution, which is probably the main factor affecting the SSD.[18] Therefore, SSD is probably a more direct measurement of the effect of body build on SWL outcome than BMI.

In our initial study design we planned to follow the method suggested by Jacobsen et al to classify the internal structure through different viewing windows into hyperdense center, hypodense center and homogeneous to determine the effect of the internal structure on SWL outcome.[11] However, in the actual study setting we were unable to view the internal structure of the stone effectively (all cases were classified as homogenous). There have been some promising in vitro reports on the applicability of a micro-CT in assessing the internal structure of stones for the prediction of SWL results.[19] However, further clinical studies are needed to clarify its role.

The overall success rate after 1 session of SWL was only 50%, which was slightly lower than that of other studies.[3,4] This was probably partly related to the fact that there was no real-time fluoroscopic screening during treatment with the Sonolith 4000+. However, with the incorporation of a real-time fluoroscopic system in the latest version of the electroconductive generator, the reported success rate approached that of the HM-3 machine.[20]

Finally, we only tested our scoring system by using our own data set and proved that it was able to stratify cases into different success rates. Further verification of this scoring system with external data is important to confirm its general applicability.

CONCLUSIONS

The results of this prospective study showed that MSD, SV and SSD as measured by NCCT are predictors of successful SWL for upper ureteral stones. A simple scoring system can be constructed to stratify cases into prognostic groups. Therefore, for future patients who present with ureteral colic and suspected upper ureteral stones, NCCT can provide the diagnosis as well as an estimated success rate for SWL. This will facilitate the decision process for the patient and hopefully minimize unnecessary delay in treatment.

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