Residual Fragments Following Ureteroscopic Lithotripsy: Incidence and Predictors on Postoperative Computerized Tomography

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Abbreviations and Acronyms

BMI = body mass index

CT = computerized tomography

RF = residual fragment

SFR = stone-free rate

SWL = shock wave lithotripsy

URS = ureteroscopy

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Purpose: Residual fragments following ureteroscopy for calculi may contribute to stone growth, symptoms or additional interventions. We reviewed our experience with ureteroscopy for calculus disease to define the incidence and establish factors predictive of residual fragments.

Materials and Methods: Records associated with 667 consecutive ureteroscopic lithotripsy procedures for upper urinary calculi were reviewed. In 265 procedures (40%) computerized tomography was done between 30 and 90 days postoperatively. They comprised the study group. Residual fragments were defined as any residual ipsilateral stone greater than 2 mm.

Results: Included in the study were 121 men and 127 women with a mean age of 47 years. Mean target stone diameter was 7.6 mm. The stone location was the kidney in 30% of cases, ureter in 50%, and kidney and ureter in 20%. Residual fragments were detected on computerized tomography after 101 of 265 procedures (38%). Pretreatment stone size was associated with residual fragments at a rate of 24%, 40% and 58% for stones 5 or less, 6 to 10 and greater than 10 mm, respectively ($p < 0.001$). Additionally, stone location in the kidney ($p < 0.001$) or the kidney and ureter ($p = 0.044$), multiple calculi ($p = 0.003$), longer operative time ($p = 0.008$) and exclusive use of flexible ureteroscopy ($p = 0.029$) were associated with residual fragments. In a multivariate model only pretreatment stone diameter greater than 5 mm was independently associated with residual fragments after ureteroscopy (diameter 6 to 10 and greater than 10 mm OR 2.03, $p = 0.03$ and OR 3.74, $p = 0.003$, respectively).

Conclusions: Of patients who underwent ureteroscopic lithotripsy for calculi 38% had residual fragments by computerized tomography criteria, including more than 50% with stones 1 cm or greater. Such data may guide expectations regarding the success of ureteroscopy in attaining stone-free status.

Key Words: kidney; ureter; ureteroscopy; tomography, x-ray computed; lithotripsy

Ureteroscopy has increasingly evolved in the last 2 decades into a preferred, minimally invasive treatment modality for urolithiasis in patients with stones less than 2 cm.[1] Various technological advancements, including deflectable tip endoscopes, ureteral access sheaths, superior optics, and

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improved lasers and stone retrieval devices have expanded indications for ureteroscopic management to include renal and upper ureteral stones.[2–6]

The ideal goal of any stone procedure is a stone-free kidney and ureter. However, the increasing use of minimally invasive treatments for more complex nephrolithiasis has made complete stone clearance less of a certainty.[7,8] The literature on SWL introduced the concept of clinically insignificant RFs to refer to stones 4 mm or less that would presumably pass spontaneously.[9] However, longitudinal series that followed patients after SWL highlight that these fragments do not necessarily always pass and can often grow with resultant clinical sequelae.[10–12] Therefore, it is not surprising that even fragments less than 4 mm are also problematic after URS.

Recently, Rebuck et al examined the natural history of fragments 4 mm or less at a mean followup of 19 months after URS.[13] They reported that 20% of these patients had experienced a stone event (need for emergency room visit, hospitalization or additional invasive intervention) and 59% had retained RFs. Thus, while urologists often present URS to patients as a "one and done" approach compared to SWL, contemporary data suggest that this may not necessarily be accurate.[14]

Such observations underscore the importance of imaging to objectively define the residual stone burden following treatment. In that regard, the post-URS SFR has evolved based on imaging modality. Initial reports showed a radiographically determined post-URS SFR of 77% to 81% and 91% to 100% for renal and ureteral stones, respectively.[6,15–19] However, these initial rates were based on older, potentially less accurate imaging modalities, including plain film radiography, ultrasound and/or excretory urography. It is now well appreciated that CT is more sensitive for detecting small or radiolucent renal calculi[20,21] and it is clear that the SFR is lower when CT is used as postoperative imaging.[22,23]

To date a limitation of CT based studies after URS is a relatively small sample size that is not statistically powered to adequately determine the rate of or risk factors for residual calculi. Therefore, in this cohort of approximately 250 patients with renal or ureteral calculi who underwent URS with lithotripsy we defined the incidence and variables associated with post-URS RFs using strict CT criteria.

PATIENTS AND METHODS

Study Population

Institutional review board approval was obtained to review the medical records and radiographic data associated with a total of 667 ureteroscopic procedures at our 2 institutions performed between April 2007 and May 2009. Of these cases 265 (40%) were followed by CT between 30 and 90 days (median 42) after the procedure. They comprised our study cohort. We specifically restricted our study group to this interval to minimize the consideration of early RFs (detected within 30 days of URS), which may spontaneously pass, or de novo calculi that would form greater than 90 days following primary stone therapy. Furthermore, our study cohort only included patients who underwent URS with laser lithotripsy, excluding those with simple basket extraction procedures. Baseline characteristics and indications for imaging by CT between 30 and 90 days posttreatment in 265 cases was no different than the remaining 402, who were imaged by plain x-ray of the kidney, ureters and bladder, excretory urogram or CT at less than 30 or greater than 90 days after URS (table 1).

RFs and Clinical Variables

RFs were defined as any residual ipsilateral renal or ureteral calculus greater than 2 mm, as determined by the official radiology interpretation on postoperative stone protocol, noncontrast 3 mm axial CT. When RF size was not provided by the radiology report, institutional imaging software was used to measure calculus size. When multiple residual calculi were present, the diameter of the largest RF is reported.

Preoperative patient characteristics queried were gender, race, BMI and age. Stone characteristics were 1) location, including kidney (lower and/or nonlower pole), ureter (proximal, mid or distal) or kidney and ureter, 2) number of calculi, 3) diameter of the largest target calculus (0 to 5, 6 to 10 or greater than 10 mm), 4) hydronephrosis and 5) stone composition. Operative data included operative time (less or greater than 60 minutes), ureteral access sheath use, ureteroscope type used (flexible and/or rigid) and postoperative stent use. Ureteral

Table 1. *Characteristics of 265 procedures imaged by CT between 30 and 90 days after URS vs remaining 402 imaged by other modality or at other interval*

	CT at 30–90 Days	Other*	p value
No. calculus (%):			
Single	164 (62)	269 (67)	0.19
Multiple	101 (38)	133 (33)	
Mean ± SD largest target stone diameter (mm)	7.6 ± 4.0	7.9 ± 3.9	0.76
No. largest target stone diameter (%):			
0–5 mm	82 (31)	133 (33)	
6–10 mm	143 (54)	225 (56)	
Greater than 10	40 (15)	44 (11)	
No. stone location (%):			
Kidney	78 (30)	129 (32)	0.57
Ureter	133 (50)	185 (46)	
Kidney + ureter	54 (20)	88 (22)	
No. imaging indication (%):†			
Symptomatic	72 (27)	89 (22)	0.14
Routine	193 (73)	313 (78)	

* Plain x-ray of kidneys, ureters and bladder in 249 patients, excretory urogram in 37, and CT at less than 30 days in 44 and greater than 90 days in 72.
† Symptoms include pain, fever, urinary tract infection and hematuria.

stenting was performed at surgeon discretion at the completion of the case. Of our cohort 29 of 265 cases (11%) had ureteral stents preoperatively and 243 (92%) were stented after the procedure.

Time from surgery to CT (imaging interval) was also evaluated as a variable of interest. It was dichotomized as between 30 and 60, and between 60 and 90 days as well as by the median 42-day interval to imaging. Each patient treated with bilateral URS was considered 2 cases.

Statistical Analysis

Analyses were performed using STATA®, version 8.2. Analyses were designed to 1) compare preoperative, stone and operative characteristics of patients undergoing URS with RFs on followup CT to patients without RFs and 2) quantify the risk associated with predictors of RFs while controlling for other risk factors. Categorical and continuous parameters were compared using the chi-square and Student t tests, respectively. Logistic regression was used to quantify the OR for RFs on followup CT while adjusting for covariates determined by univariate analysis.

RESULTS

A total of 265 ureteroscopy procedures were done in 248 patients between April 2007 and May 2009. Of the patients 15 underwent 2 ureteroscopies and 1 underwent 3. Multiple ureteroscopies in the same patient and bilateral URS in 7 during a single operation were considered separate procedures for data analysis. All other patients underwent only 1 procedure. In the 248 patients mean age was 47.1 years and mean BMI was 31.0 kg/m^2. Of the patients 49% were male. The mean size of the largest target stone was 7.6 mm, while 31% were 5 mm or less, 54% were 6 to 10 and 15% were greater than 10 mm. Stones were located in the kidney, ureter, and kidney and ureter in 30%, 50% and 20% of patients, respectively. The mean number of stones per renal unit was 1.4, and 38% of renal and/or ureteral units contained multiple calculi.

Overall, RFs greater than 2 mm were identified after 101 of the 265 procedures (38%) with a mean RF size of 4.1 mm (range 3 to 12). Another 13 patients had RFs between 1 and 2 mm. Pretreatment stone size was associated with RFs greater than 2 mm with a rate of 24%, 40% and 58% for stones 5 or less, 6 to 10 and greater than 10 mm, respectively. On univariate analysis the clinical and operative data associated with RFs on postoperative CT included location in the kidney (vs ureter $p < 0.001$) or the kidney and ureter (vs ureter $p = 0.044$), multiple calculi ($p = 0.003$), increasing stone size ($p < 0.001$), longer operative time ($p = 0.008$) and exclusive use of flexible ureteroscopy ($p = 0.029$, table 2).

Table 2. *Univariate analysis of potential factors associated with RF rate*

	No. No RF (%)	No. RF (%)	p Value
Overall	164	101	
Female	82 (50)	53 (53)	0.70
Race:			
White	118 (72)	70 (69)	0.96
Nonwhite	46 (28)	31 (31)	
BMI (kg/m^2):			
Less than 18.5	2 (1)	2 (2)	0.90
18.6–25.0	25 (15)	13 (13)	
25.1–30	34 (21)	20 (20)	
Greater than 30	103 (63)	66 (65)	
Age:			
18–39	49 (30)	40 (40)	0.25
40–59	78 (48)	43 (43)	
Greater than 60	37 (23)	18 (18)	
No. calculi:			
Single	113 (69)	51 (51)	0.003
Multiple	51 (31)	50 (49)	
Target stone size (mm):			
0–5	62 (38)	20 (20)	<0.001
6–10	85 (52)	57 (56)	
Greater than 10	17 (10)	24 (24)	
Stone location:			
Kidney	48 (29)	52 (51)	<0.001
Ureter	89 (54)	22 (22)	
Kidney +/or ureter stone location:			
Kidney or ureter alone	137 (84)	74 (73)	0.044
Kidney + ureter	27 (16)	27 (27)	
Preop hydronephrosis:			
Yes	93 (57)	48 (47)	0.24
No	71 (43)	53 (53)	
Operative time (mins):			
Less than 60	63 (38)	23 (23)	0.008
Greater than 60	101 (62)	78 (77)	
Ureteroscope type:			
Rigid +/or flexible	85 (52)	39 (39)	0.029
Flexible only	79 (48)	62 (61)	
Ureteral access sheath:			
Yes	81 (49)	56 (55)	0.41
No	83 (51)	45 (45)	
Post-URS days to imaging:			
30–60	114 (70)	77 (76)	0.24
61–90	50 (30)	24 (24)	
Stone composition:			
Calcium oxalate monohydrate	72 (44)	34 (34)	0.32
Calcium oxalate dihydrate	8 (5)	8 (8)	
Calcium phosphate	26 (16)	24 (24)	
Uric acid	9 (5)	5 (4)	
Mixed	49 (30)	30 (30)	

Demographic factors, including gender, race, age and BMI, were not associated with RFs. Additionally, hydronephrosis, post-URS stent placement, ureteral access sheath use and stone composition were not associated with RFs. Analysis of the effect of the specific sublocation in the ureter (proximal, middle or distal) and the kidney (lower or nonlower pole) on the RF rate showed no statistical significance ($p = 0.53$ and 0.71, respectively). Finally, the interval to imaging, dichotomized as between 30 and 60 vs 61 and 90 days (p = 0.24) or by the median imaging interval of 42 days (p = 0.41) after URS did not appear to impact the SFR.

A multivariate model was constructed that incorporated the 5 significant variables identified on univariate analysis. On multivariate analysis only pretreatment stone diameter 6 to 10 mm (OR 2.03, p = 0.03) and target stone diameter greater than 10 mm (OR 3.74, p = 0.003) were independently associated with RFs (table 3).

DISCUSSION

In this study we defined an RF as any ipsilateral renal or ureteral calculus greater than 2 mm on CT performed between 30 and 90 days after URS. Using this relatively strict RF definition, imaging modality and interval, our overall RF rate in a cohort of almost 250 patients was 38%. In other words, 62% of patients in our study population were stone-free or had RFs 2 mm or less. Such values are clearly lower than the success rate reported in studies of nonCT imaging for postoperative assessment.[6,15–19] However, the sensitivity of nonCT imaging modalities has been questioned.[20,21]

Conversely, our results compare quite favorably to previous reports of smaller patient cohorts in which post-URS outcomes were assessed by CT.[22–24] Specifically, Macejko et al noted a 63% stone clearance rate at a 2 mm threshold after URS for renal and ureteral calculi.[23] Pearle et al reported a 50% SFR and a 72% stone clearance rate at a 4 mm threshold, although this analysis was restricted exclusively to lower pole renal calculi.[22] Portis et al observed a similar 54% SFR but the stone clearance rate at a 2 mm threshold was higher at 84%.[24]

Initial size of the target stone had a significant effect on the RF rate, which is not surprising. Indeed, it is well accepted that larger stone size correlates with a decreased SFR.[25] However, to our knowledge ours is the first such study to quantify the SFR based on the size of the initial stone using exclusively CT for followup. We found an almost fourfold greater risk of RFs for stones greater than 10 mm compared to those less than 5 mm. This distinction is clinically useful for the practitioner in the current setting of CT based followup and assessment. Importantly, our analysis confirmed statistical significance even after controlling for other covariates related to stone size, ie the need for multiple types of ureteroscopes and operative time.

Additionally, although stone location appeared to be an important factor on univariate analysis, its impact decreased in the multivariate model and only trended toward significance. In particular, the comparison of RF rates stratified by stone location revealed a higher RF rate for renal vs ureteral calculi (52% vs 20%). This observation was also reported in series using older methods of radiological assessment, although with much higher overall SFRs.[16–19] Our results appear somewhat better than the contemporary CT based series by Macejko et al, which showed an SFR of 35% and 80% for renal and ureteral stones, respectively.[23] A possible explanation for the discrepancy between our study and that by Macejko et al in terms of the renal stone SFR (48% vs 35%) could be the interval to imaging. They reported CT assessment at a mean of 3 months but with a range of 1 day to 16.9 months. We chose a relatively confined interval of between 30 and 90 days after the procedure in which to evaluate for RFs. We thought that the lower end of this window would allow for potentially insignificant fragments to pass, while the upper end of the selected period would preclude the inclusion of de novo stone formation.

Lower pole renal calculi represent a unique challenge, in part due to difficulty accessing the lower pole with flexible ureteroscopes[2] and to pelvicalyceal anatomy that may preclude stone passage even with adequate fragmentation.[26] However, several recent studies showed no significant difference in SFRs between lower pole and nonlower pole renal stones.[23,24,27] Our results provide further evidence to suggest that lower pole renal stones carry no greater risk for RFs than nonlower pole calculi. A proposed explanation for this observation is an increasing trend toward relocating lower pole calculi to an interpolar or upper pole calyx before or after lithotripsy.[23]

Table 3. *Multivariate analysis of factors associated with RF after URS*

	OR (95% CI)	p Value
Target stone size (mm):		
0–5	Referent	—
6–10	2.03 (1.07–3.84)	0.03
Greater than 10	3.74 (1.57–8.94)	0.003
No. calculi:		
Single	Referent	
Multiple	1.57 (0.83–2.95)	0.23
Stone location:		
Kidney	Referent	—
Ureter	1.9 (0.98–3.8)	0.057
Kidney +/or ureter stone location:		
Kidney or ureter alone	Referent	—
Kidney + ureter	1.77 (0.90–3.51)	0.099
Operative time (mins):		
Less than 60	Referent	—
Greater than 60	1.10 (0.58–2.10)	0.77
Ureteroscope type:		
Rigid +/or flexible	Referent	—
Flexible only	1.20 (0.64–2.24)	0.56

Several other variables queried on univariate analysis did not maintain independent significance on multivariate analysis. Many study variables probably depended on each other to some degree. For example, it is likely that stone size or multiple stones affect operative time and ureteroscopy type. Nevertheless, our univariate findings provide useful information from a clinical perspective and our multivariate findings confirm the significant effect of stone size on the RF rate.

We acknowledge certain limitations to our study. 1) It is retrospective in nature. Therefore, our data collection and analysis likely did not consider variations in stone removal technique, eg antimigration device use, and/or the surgical objective, eg complete removal vs fragmentation with expected spontaneous passage.

2) Various size thresholds (0, 2 and 4 mm) have been used to assess post-URS efficacy. This presents some difficulty when comparing various studies. While some groups used a 4 mm threshold, the 4 mm cutoff for clinical significance has been strongly challenged and is likely not appropriate.[13,14] Thus, we chose a relatively stringent 2 mm threshold, which still permitted comparison to existing studies.[22–24] This criterion was further based on a prior series by our group on RFs after percutaneous nephrostolithotomy, in which stone size greater than 2 mm was a significant predictor of future stone related events.[28]

3) We included in our collection and analysis only procedures assessed by CT between 30 and 90 days postoperatively. As mentioned, our rationale was to allow adequate time for passage but not so much time as to risk de novo stone formation that would compromise the data. However, the exclusion of patients in whom CT was not performed during the specified interval or at all could have introduced bias into the analysis. Indeed, it is possible that CT was not ordered for some patients if the operating surgeon thought it was unnecessary, ie the surgeon was confident enough about stone-free status to preclude the need for imaging. Although we attempted to reconcile this bias by comparing baseline stone characteristics and indications for imaging in our cohort vs all others (265 vs 402 cases, each p not significant, table 1), excluding such patients could have altered our RF rates. Hopefully, future studies of the natural history of post-URS RFs will help further elucidate the most appropriate modalities and time frames with which to assess postoperative outcomes.

CONCLUSIONS

Of patients treated with URS for renal and/or ureteral calculi 38% had RFs by strict CT criteria. Pretreatment stone size was independently associated with RFs with an RF rate of 24%, 40% and 58% for stones less than 5, 5 to 10 and greater than 10 mm, respectively. There was no difference in the RF rate for lower pole compared to nonlower pole renal stones. This relatively large, contemporary cohort provides the clinician with data with which to help counsel patients on the success of URS in attaining stone-free status.

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