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Flexible Ureterorenoscopy and Holmium Laser Lithotripsy for the Management of Renal Stone Burdens That Measure 2 to 3 cm: A Multi-Institutional Experience

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Abstract

Background and Purpose: Percutaneous nephrostolithotomy (PCNL) is the current standard of care for management of large renal stones (>2 cm). Recent studies have evaluated flexible ureterorenoscopy (URS)/holmium laser lithotripsy as an alternative treatment for patients with contraindications to or preference against PCNL. Stones in an intermediate size range (2–3 cm) may be most amenable to URS/laser lithotripsy as definitive treatment in a single stage. We report a multi-institutional series of URS/laser lithotripsy for renal stone burdens that measure 2 to 3 cm.

Patients and Methods: Patients who underwent URS/holmium laser lithotripsy for renal stones that measured 2 to 3 cm were identified retrospectively at three tertiary care centers. Demographic information, disease characteristics, and perioperative and postoperative data were gathered. Patients with renal stone burdens of 2 to 3 cm who were treated by URS/laser lithotripsy and had at least one postoperative visit and imaging study were included. Stone clearance was evaluated using 0–2 mm and < 4 mm residual stone burden on postoperative imaging.

Results: One hundred and twenty patients underwent URS/holmium laser lithotripsy for renal stones of 2 to 3 cm. Mean stone burden was 2.4 cm, and mean body mass index was 29.3 kg/m^2. Indications for URS/laser lithotripsy *vs* PCNL included patient preference (57), technical or anatomic factors (24), patient comorbidities (17), failed shockwave lithotripsy (9), patient body habitus (3), solitary kidney (3), chronic renal insufficiency (3), and strict anticoagulation (2). Thirty-one (26%) patients had stent placement preprocedure, and 94 (78%) patients underwent outpatient surgery. A ureteral access sheath was used in 67%. One hundred and one (84%) patients underwent single-stage procedures. There was one intraoperative complication (ureteral perforation), and there were eight minor postoperative complications (6.7%). The reoperation rate through the mean 18-month follow-up was 3/120 or 2.5%. Seventy-six (63%) patients had residual stone burden of 0 to 2 mm, and 100 (83%) patients had residual burden of <4 mm.

Conclusions: We demonstrate that single-stage URS/holmium laser lithotripsy is effective for management of renal stones that measure 2 to 3 cm through intermediate follow-up. Staged procedures can be used selectively for technical reasons or disease factors. Although PCNL achieves superior stone clearance overall, URS/laser lithotripsy is a viable treatment option for selected patients.

Introduction

Percutaneous nephrostolithotomy (PCNL) is the current first-line recommended treatment for patients with large renal stones (>2 cm).[1,2] While PCNL achieves superior stone clearance compared with endoscopic or extracorporeal therapies, it is also associated with increased morbidity and requires an inpatient stay.[3] Recent studies have demonstrated that flexible ureterorenoscopy (URS) with holmium laser lithotripsy can be effective and safe as an alternative management option for larger stones.[4–7] These studies have typically included a range of stone sizes from 2 to 6 cm as well as multistage procedures. Stones in an intermediate size range (2–3 cm) may be most amenable to URS/laser lithotripsy in

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fewer stages. Multistage procedures may improve short-term stone clearance but also introduce the morbidity and cost of another procedure.

While PCNL achieves superior stone clearance for large renal stones, URS/laser lithotripsy may be a reasonable or preferred option in patients with contraindications to percutaneous surgery.[8] These contraindications may be absolute (eg, strict anticoagulation, severe cardiopulmonary disease) or relative (eg, large body habitus, anatomic factors). Also, patients may have a strong preference against PCNL based on a higher major complication rate and the need for inpatient hospitalization.[3] These risks and inconveniences need to be weighed against the benefit of maximal stone clearance that is obtained with PCNL. As experience with URS/laser lithotripsy has grown and technology of ureteroscopes has improved (eg, digital and dual flexion capabilities), URS/laser lithotripsy has become an increasingly considered option for these patients.

In this study, we hypothesized that stones that measuried 2 to 3 cm might be amenable to URS/laser lithotripsy in a single stage, and that results would be comparable to those in published studies of smaller stone burdens (<2 cm) that were managed with URS/laser lithotripsy from the standpoint of clinical success (ie, stone clearance, low risk of complications, and subsequent stone events). Thus, we reviewed our large multi-institutional experience with URS/laser lithotripsy for stones in this larger size range. This series is the largest to evaluate URS/laser lithotripsy for >2 cm renal stones in general and is the first to specifically address stones that measure 2 to 3 cm.

Patients and Methods

A retrospective chart review was performed at three university medical centers to identify patients who underwent URS/holmium laser lithotripsy for renal stones of 2 to 3 cm. All URS/laser lithotripsy procedures were performed by one of three surgeons between 2004 and 2009. Inclusion criteria included undergoing URS/laser lithotripsy for an initial renal stone burden of 2 to 3 cm and a postoperative evaluation including at least one office visit and imaging study. Stone burden was measured using greatest total diameter of renal stones on CT imaging. Demographic, perioperative, and postoperative data were collected. Statistical analysis, including the Fischer exact test, was performed using JMP software (Cary, NC).

Technique

URS/laser lithotripsy was performed in standard retrograde fashion; a safety guidewire was used on a routine basis. Flexible ureteroscopes included Storz Flex X, Flex X2, and ACMI DUR 8 Elite. At the discretion of the surgeon, a ureteral access sheath was used and placed over a 0.038 inch guidewire or a 0.035 inch Amplatz super stiff wire. Holmium laser lithotripsy was performed using a 200 or 365 micron laser fiber. All stones were fragmented into small particles (“dust”) and small fragments that could be retrieved with small caliber nitinol baskets. For lower-pole stones, fragments were displaced to the renal pelvis and upper pole when feasible to facilitate the laser procedure and decrease scope fatigue and loss of deflection. Diligence in extracting fragments was made on an individualized basis by the surgeon. A ureteral stent was placed at the conclusion of the procedure.

Patients were either held for observation or discharged to home the same day. Patients underwent imaging and stent removal in the outpatient clinic typically 1 to 2 weeks postoperatively. If patients were thought to have a large residual stone burden or visualization was obscured during the first stage, a second stage was scheduled approximately 1 to 2 weeks postoperatively. Imaging modalities to assess residual fragments (RF) included radiography of the kidneys, ureters, and bladder (KUB), ultrasonography, and/or CT.

Results

One hundred and twenty patients who underwent URS/holmium laser lithotripsy for renal stones of 2 to 3 cm were identified. Each site treated between 22% to 42% of patients. Mean body mass index was $29.3 \pm 5.1\,kg/m^2$. Patient demographic data and comorbidities are listed in Table 1.

Disease characteristics are included in Table 2. The mean stone size was 2.4 ± 0.3 cm. Thirty-one (26%) patients had stent placement preprocedure for reasons including clinical obstruction in 10 (8%), shockwave lithotripsy (SWL) attempts in 10 (8%), infection in 5 (4%), acute renal failure in 2 (2%), presence of a solitary kidney in 1 (1%), retained stent from an outside hospital in 1 (1%), and unknown/referred from outside hospital in 12 (10%). Documented reasons for URS/laser lithotripsy included patient preference in 57 (48%), technical or anatomic in 24 (20%), patient comorbidities in 17 (14%), failed SWL in 9 (8%), patient body habitus in 3 (3%), solitary kidney in 3 (3%), chronic renal insufficiency in 3 (3%), strict anticoagulation in 2 (2%), and other/unknown in 2 (2%). Technical or anatomic factors included failed percutaneous access, multiple previous percutaneous interventions, thin renal parenchyma, and positioning difficulty including history of contractures or spinal cord injury.

Perioperative data are included in Table 3. There was one intraoperative complication (1%) (ureteral perforation with extravasation necessitating prolonged ureteral stent placement). Nineteen (16%) patients underwent second-stage procedures including URS/laser lithotripsy in 17 (14%), percutaneous nephrolithotomy in 1(1%), and laparoscopic pyelolithotomy in 1 (1%). One patient underwent a third stage URS/laser lithotripsy to clear residual fragments.

There were eight postoperative complications (6.7%) as noted in Table 4. Additional postoperative complications necessitating surgical intervention included obstructive pyelonephritis necessitating ureteral stenting (1) and Steinstrasse necessitating URS/laser lithotripsy (1). The former

Table 1. Demographic Information

Sex	
Male	72 (60%)
Female	48 (40%)
Age (years)	55.7 ± 12.8
BMI (kg/m^2)	29.3 ± 5.1
Comorbidities	
Hypertension	66 (55%)
Diabetes mellitus	23 (19%)
Coronary artery disease	15 (13%)
Chronic kidney disease	11 (9%)
Solitary kidney	2 (2%)

BMI = body mass index.

Table 2. Disease Characteristics

Size (cm)	2.4 ± 0.3
Mean number of stones	2.5 (1–15)
Partial staghorn	9 (8%)
Stone position	
Pelvis	65 (54%)
Upper pole	13 (11%)
Lower pole	43 (36%)
Midpolar	23 (19%)
Preprocedure stent placement*	31 (26%)
Previous ipsilateral SWL	35 (29%)

*Ureteral stent placed before ureterorenoscopy for temporization of fever/colic/renal insufficiency, or before referral to the present surgeon.
SWL = shockwave lithotripsy.

patient was noncompliant with postoperative imaging and represented 6 months later with flank pain and fever. The latter patient presented 2 weeks postoperatively with renal colic and was treated without complications. An additional patient underwent URS/laser lithotripsy for enlarging stone burden approximately 2 years postoperatively. This patient had a residual fragment postoperatively that was <4 mm and was noncompliant with medical and dietary therapy. Thus, the reoperation rate during the mean 18.3 month (range 1–64 mos) follow-up was 3/120 or 2.5%.

Ureteral stents were left in place for a mean of 12 days. Postoperative imaging to assess stone clearance was performed at mean 2.0 months. The type of postoperative imaging included CT in 57 patients (48%), ultrasonography in 54 (45%), and KUB in 9 (8%). Seventy-six (66%) patients had a residual stone burden of 0 to 2 mm, and 100 (83%) patients had aresidual burden of <4 mm (Table 3). Fifty-six (47%) patients were truly stone free. Subgroup analysis was performed using the Fischer exact test to evaluate relative stone

Table 3. Perioperative and Postoperative Information

Use of access sheath	80 (67%)
Operating room time (min)	102.7 ± 20.6
Surgical time (min)	74.3 ± 20
Intraoperative complications	1[a] (1%)
Admission status	
Ambulatory surgery	94 (78%)
23 hour admission	17[b] (14%)
Inpatient	9[c] (8%)
Number of stages	
One	100 (83%)
Two	19[d] (16%)
Three	1 (1%)
Stone clearance	
Stone free	56 (47%)
0–2 mm	76 (66%)
<4 mm	100 (83%)

[a]Ureteral perforation with extravasation necessitating prolonged ureteral stent placement.
[b]Telemetry monitoring for significant cardiac disease, sleep apnea monitoring, pain control, and/or convenience for patients with evening cases.
[c]Current inpatients on other services.
[d]Ureterorenoscopy (17), percutaneous nephrolithotomy (1), and laparoscopic pyelolithotomy (1).

Table 4. Postoperative Complications

Febrile UTI	2
Acute urinary retention	1
Subcapsular hematoma	1
Fever	1
Steinstrasse	2[a]
Obstructive pyelonephritis	1[b]

[a]One case treated conservatively, one case treated surgically (ureterorenoscopy).
[b]Treated surgically (ureteral stent placement with delayed ureterorenoscopy.
UTI = urinary tract infection.

clearance (0–2 mm, <4 mm) in single *vs* multiple stones, use of ureteral access sheath *vs* none, stent placement preprocedure *vs* no stent placement preprocedure, and partial staghorn *vs* other. The only significant difference using a threshold of $P < 0.05$ for significance was that patients who had stent placement preprocedure were more likely to have RF of 0 to 2 mm compared with those who did not have stent placement preprocedure ($P = 0.008$). Patients who did have stent placement preprocedure, however, were not more likely to have RF <4 mm ($P = 0.20$).

Stone analysis included calcium oxalate in 89 (74%) patients, uric acid in 20 (17%), struvite in 5 (4%), calcium phosphate in 5 (4%), and cystine in 1 (1%).

Discussion

We demonstrate that URS/holmium laser lithotripsy is safe and effective for management of 2 to 3 cm renal stones. While we do not directly compare our results with PCNL controls, we demonstrate good stone clearance and a low rate of repeated stone events and reoperation during intermediate follow-up. The results are also comparable, if not superior to, previously published series of URS/laser lithotripsy for management of smaller stone burdens that report stone-free rates that range from 64% to 93% and also low rates of recurrence, although most series have limited follow-up.[9–12] While previous studies of URS/laser lithotripsy for management of large renal stones have also reported promising results, these studies have involved patients with a wide range of stone sizes >2 cm as well as multistage procedures.[4–7,13] Our series specifically examined patients with stones in the 2 to 3 cm range managed with single-stage URS/laser lithotripsy. All but 16% of patients in our study underwent a single procedure, and a second stage was performed primarily for poor visualization, struvite stones, and patient preference.

We have previously reported clinical outcomes of URS/laser lithotripsy *vs* PCNL for 2 to 3 cm renal stones matched by size.[8] Although PCNL achieved superior stone clearance, there was a low rate of subsequent stone events for URS/laser lithotripsy, as well as a significantly lower estimated cost. Approximately 20 patients in each arm were followed through 13-month follow-up. The higher estimated cost with PCNL related primarily to the need for inpatient hospitalization and the frequent performance of a second-stage procedure. Long-term follow-up and formal cost analysis are necessary to clarify the relative benefits of these procedures, although there appears to be a tradeoff between stone clearance (favoring PCNL) and cost and invasiveness (favoring URS/laser lithotripsy).

While PCNL has been shown to be safe and effective for management of large renal calculi.[1,14] there can still be significant perioperative morbidity. This may include hemorrhage, sepsis, hydrothorax or pneumothorax, injury to intra-abdominal structures, and medical complications. The overall complication rate has been reported up to 50% with a major complication rate up to 20%. More recent series have reported lower complication rates; however, there has been lack of standardization in the reporting of complication severity (eg, Clavien grade).[3,15] Also there are data that there is functional parenchymal loss after PCNL, further study is needed.[16]

URS/laser lithotripsy has a universally low complication rate (12% overall and 1.5% major complication rate in one large series)[17] and is typically an outpatient procedure. While there have been case reports of outpatient PCNL, this is not presently the standard of care.[18] In one series that examined length of stay after PCNL, Matlaga and colleagues[19] demonstrated that 68% of their patients were discharged within 24 hours with a mean length of stay of 1.97 days. Technical improvements, including smaller caliber ureteroscopes with digital optics and dual deflection, have recently made URS/laser lithotripsy a more popular and feasible option.[20]

Because our study was retrospective, there was selection bias for patients who underwent URS/laser lithotripsy. The most common reported reason for proceeding with URS/laser lithotripsy was "patient preference," which may simply reflect lack of documentation of an underlying medical rationale. It may also reflect, however, the impact of lifestyle and/or employment factors on treatment choice.

Our series reported RF of 0 to 2 mm in 66% and <4 mm in 83%. The clinical significance of RF is not well understood. Most literature reports regarding RF pertain to SWL and are mixed regarding their significance. Increasingly, small RF 4 mm that had been considered "clinically insignificant" are considered significant risk factors for future stone events. Streem and coworkers[21] found that among 160 patients with RF ≤ 4 mm after SWL, there was a 43% likelihood of a symptomatic episode or repeated intervention at a mean of 26 months postoperatively. Zanetti and associates[22] reported a 22% likelihood of symptomatic episodes within 2 years among 129 patients with RF < 4 mm. Osman and colleagues[23] reported that among 173 patients with RF ≤ 4 mm, 78.6% of RF cleared spontaneously and 21.4% necessitated ipsilateral treatment within 5 years. Overall, these data show that 20% to 40% of patients with RF ≤ 4 mm will have symptoms or regrowth after SWL, although the majority will not be affected. Buchholz and coworkers[24] reported that among 266 patients after SWL with a mean follow-up of 2.5 years, 12.7% of RF 5 mm had not passed, but all were clinically silent.

There have also been several studies that examined the significance of RF after PCNL. Raman and colleagues[25] evaluated 42 patients with RF after PCNL who were undergoing observation rather than second-look nephroscopy. These authors demonstrated that RF > 2 mm and location in the renal pelvis or ureter increased the risk of stone-related events through median 41-month follow-up. Stone-related events were defined broadly as growth of RF, emergency department visit, hospitalization, or additional intervention. Krambeck and coworkers[14] reported that RF after PCNL increased the risk of symptomatic stone disease through long-term (19 year) follow-up; however, these authors did not precisely define RF and defined stone events broadly as passage of stone material or symptomatic stone that was identified on imaging.

There is additional evidence that most small RF pass spontaneously after PCNL. Ganpule and Desai[26] reported that 65.5% of RF after PCNL passed within 3 months of surgery, particularly smaller fragments ($<25\ mm^2$). Other factors that affected fragment passage included stone position, previous stone surgery, metabolic abnormality, and placement of a Double-J stent. Nobody has studied the fate of RF after URS per se, but it is likely to parallel SWL and PCNL, with patient and disease factors affecting both likelihood of passage and risk of stone events.

Medical therapy may improve the efficacy of conservative management of small RF. Kang and associates[27] reported that selective medical therapy controlled stone formation and growth in 70 patients with and without RF after PCNL. Fine and colleagues[28] demonstrated decreased risk of recurrent stone formation or growth with medical therapy after SWL; only 16% of patients with RF < 5 mm had an increase in fragment size. Medical therapy may also improve passage of RF after treatment; Cicerello and coworkers[29] reported citrate therapy significantly improved stone clearance and prevented regrowth in patients without complete clearance after SWL.

The primary obstacle with medical therapy may be poor patient compliance.[23,28] although patients may be more amenable to treatments to prevent recurrent pain or surgical procedures than urologists have thought traditionally.[30] In patients who may be candidates to observe small RF, medical therapy has an integral role and physician/patient communication and education are critical.

There are also competing philosophies on how to address small fragments intraoperatively. While some surgeons routinely place access sheaths and attempt to visually clear all fragments, others "dust" a stone, create sub-mm fragments, and allow them to pass postoperatively. The latter approach is more likely to demonstrate small RF on early postoperative imaging, but a long- term difference in stone clearance or risk of stone events has not been evaluated. A comparative study would be useful to determine benefits of active extraction and access sheath use for larger renal stones.

Only 16% of the patients in our study underwent multiple stages. Repeated URS/holmium laser lithotripsy improves short-term stone clearance but introduces additional perioperative risk, cost, and inconvenience. Because $>80\%$ of our patients had RF < 4 mm in a single stage and there was a low risk of stone events and reoperation, we believe second-stage procedures are not routinely necessary. Staged procedures after PCNL are more common,[8] because there is an established tract for flexible nephroscopy and greater motivation to achieve complete stone clearance. Ultimately the decision to proceed with second-stage URS/laser lithotripsy depends on patient and disease factors (eg, aggressive stone former, struvite stone) and discussion of risks/benefits. While PCNL does improve stone clearance in a single stage, we do believe that single-stage URS/laser lithotripsy can be sufficient therapy for many patients, depending on these individualized factors and based on the low incidence of subsequent stone events as discussed above.

Limitations of our study include its retrospective nature and selection bias that makes comparison with PCNL series difficult. The low risk of stone events and reoperation for a large patient sample, however, provides reasonable evidence for the safety and viability of this approach. Importantly, we do not support URS/holmium laser lithotripsy as the treatment of choice for 2–3 cm renal stones, rather as an option that offers benefits for selected patients. We report intermediate rather than long-term follow up; thus, additional stone events may not yet have occurred. We will continue to follow our patients and eventually report long-term outcomes.

A criticism of URS/holmim laser lithotripsy for stones of intermediate size can be made based on the cost of scope replacement and repair, because these cases can be more strenuous on the equipment. Proper use of ureteroscopes is essential to prevent scope fatigue and damage, including passing the laser fiber through the scope only when it is not deflected. Selecting patients who do not have lower pole stone burden primarily can also be helpful. We typically displace lower pole stones into upper pole calices as soon as technically feasible. Finally, use of an access sheath has been shown to extend the longevity of ureteroscopes.[31]

Different imaging modalities were used to assess RF postoperatively. This provides a practical, "real world" data set for this procedure. While CT is the most sensitive modality for assessing RF,[32,33] logistical and cost reasons may prohibit its routine use. In addition, radiation exposure with CT is undesirable, because stone formers will likely encounter future radiation, given the recurrent nature of their disease. Ultrasonography was used frequently as a postoperative imaging test based on its low cost, ready accessibility, and lack of radiation. Indeed, ultrasonography has less sensitivity for small fragments compared with CT, particularly in obese patients; however, an experienced ultrasonographer and high resolution ultrasonography can help to compensate for this shortcoming. Also the addition of KUB to ultrasonography can increase sensitivity for small stones. A randomized study with uniform postoperative imaging would be useful for obtaining more definitive conclusions regarding stone clearance. Unfortunately, the current nephrolithiasis literature contains extremely variable follow-up protocols and use of imaging modalities before and after stone treatment,[34] and it is critical that future studies standardize these factors to enable more meaningful comparisons.

Conclusions

URS/laser lithotripsy is a safe and effective management option for renal stone burdens of 2 to 3 cm, which can be treated typically in a single stage. Although PCNL achieves superior stone clearance, URS/laser lithotripsy is a viable treatment option for selected patients. Patients who are undergoing URS/laser lithotripsy have a low risk of stone events during follow-up and have a less invasive and less expensive procedure. Metabolic evaluation and appropriate medical therapy are important to prevent stone growth and prevent recurrence and future events. The decision to proceed with PCNL *vs* URS/laser lithotripsy for 2 to 3 cm renal stones will depend on weighing of risks and benefits in light of specific patient and disease factors. Long-term comparative study of these populations is needed to ascertain which treatments are ideal for specific patient subgroups.

Disclosure Statement

Ojas Shah, study investigator for Watson Pharmaceuticals; consultant for Boston Scientific. Vincent G. Bird, lecturer for Applied Medical. No competing financial interests exist for the other authors.

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Abbreviations Used

CT = computed tomography
KUB = kidneys, ureters, and bladder
PCNL = percutaneous nephrostolithotomy
RF = residual fragments
SWL = shockwave lithotripsy
URS = flexible ureterorenoscopy