Flexible ureterorenoscopy and Ho: YAG laser fragmentation for stones with a mean density greater than 900HU: An alternative to extracorporeal shockwave lithotripsy

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Abstract

Background: A number of patient and stone characteristics predict SWL failure. When one or more of these factors are present, therapies such as flexible ureterorenoscopy and holmium: YAG lasertripsy (FURSL) have been promoted, with improved stone free rates (SFRs). There has been no study of FURSL efficacy in the treatments of stones with a density greater than 900 Hounsfield units (HU), another predictor of treatment failure with SWL. We aimed to assess the efficacy of FURSL in such cases.

Patients and methods: Patients undergoing FURSL from April 2012 - April 2014, under the care of a single surgeon were identified, and cases with at least one stone with a mean stone density greater than 900HU were assessed retrospectively. Patient and stone characteristics were recorded. Treatment outcomes and complications were detailed. Analysis of the differences in patient and stone qualities related to SFR after the first procedure were made.

Results: Sixty - six patients were included. The mean age was 58 (35 - 78) years. The mean stone density was 1216 (902 - 1768) HU. The mean maximal stone diameter was 13.2 (6.3 - 33) mm. Most stones were either renal pelvic or lower calyceal in position, accounting for 18 (27.3%) patients each. SFR after the first FURSL treatment was 74.2%. Only 7 (10.6%) patients had procedure associated morbidity. When comparing patients who were stone free with one treatment of FURSL to those who were not, there was no significant difference in gender, mean age or mean stone density. There was however, a significant difference in maximal stone diameter (9.1mm and 15.1mm respectively, p< 0.001) and position of the stones (p< 0.001).

Conclusion: This study confirms FURSL is safe and effective for calculi with a mean density greater than 900HU. Improved SFR, and possibly favourable complication rate, compared with SWL has been shown and FURSL could be considered as the treatment of choice in such cases.

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Introduction

Urinary tract calculi are a significant problem affecting approximately 5% of the population in the United States with a worldwide increase in incidence and prevalence reported\textsuperscript{1,2}. Nephrolithiasis has well-recognised associated morbidity\textsuperscript{3-5}. Since extracorporeal shockwave lithotripsy (SWL) was introduced in 1980 it has become the treatment of choice for upper tract urinary calculi less than 20mm as recommended by the European Association of Urology (EAU)\textsuperscript{6}. It is important to consider treatment efficacy, safety and cost when deciding on the most appropriate treatment. A number of studies have reported both patient and stone qualities which adversely affect stone free rate (SFR) after SWL. These include abdominal obesity with resultant high skin - to - stone distance, lower calyceal stones, large stones and hard stones. There has been significant advancements in other minimally invasive treatment modalities such as flexible ureterorenoscopy and Holmium: YAG laser lithotripsy (FURSL) in recent years. As such FURSL has become an alternative option to SWL when one or more of these adverse predictive factors are present.

Comparisons of treatment efficacy between FURSL and SWL for those with larger stones or lower calyceal stones have been reported. However, there is little data on the outcomes of patients with stone density greater than 900 Hounsfield Units (HU), another adverse stone factor. As such, our aim was to assess the efficacy of FURS and Holmium - YAG laser stone fragmentation in upper tract stones with a density greater than 900HU.

Patients and Methods

All patients with renal calculi requiring treatment are referred to a single surgeon in our institution for consideration of SWL, FURSL or percutaneous nephrolithotomy. Patients with a stone of density greater than 900HU are recommended for FURSL provided there are no contraindications and the patient agrees after counselling. All cases of FURSL performed between April 2012 and April 2014 were identified retrospectively from theatre logs.

Stone qualities for each of these patients were assessed by reviewing the pre - operative non - contract computed tomography of the kidneys, ureters and bladder (CTKUB). Stone burden and location were assessed on the soft tissue window. Stone size and density were calculated in the magnified bone window\textsuperscript{6}. Stone size was reported as maximal diameter in mm. Stone density was calculated as a mean two dimensional surface area density in Hounsfield units (HU) by selecting an elliptical region that incorporates the largest possible cross - sectional area of stone without including the adjacent soft tissue.

FURSL for calculi with a mean density greater than 900HU were selected for analysis. When multiple calculi were present, at least one must have a mean stone density greater than 900HU.

All patients were seen in a surgical pre - assessment clinic within a week of planned surgery and had serum biochemistry measured and a mid - stream sample of urine sent for culture. Any patients with a positive urine culture were treated with a course of appropriate antibiotics prior to surgery. All patients were subsequently admitted on the day of operation, anaesthetised and given prophylactic treatment dose antibiotics based on previous positive urine culture or gentamicin empirically when no previous positive culture was available, as per local microbiology guidelines. The patient was then positioned in lithotomy. Flexible cystoscopy and ureteric intubation with a guide wire was performed. The guide wire was exchanged for a 12/14Fr ureteric access sheath. FURS was performed with a 7.5 Fr Storz\textsuperscript{\textregistered} flexible uretero - renoscope and laser fragmentation was conducted with a holmium - YAG laser using a 273µm fibre at a setting of 0.6 - 1.2J and 6Hz. When basketing was required a 3Fr zero - tip basket was used. Stone fragments were sent for analysis in 54 patients. A ureteric stent or ureteric catheter was placed routinely, and removed between 7 and 21 days or the first post - operative day respectively, following plain X - ray of kidneys, ureters and bladder (KUBXR). This was used to assess residual stone burden and plan further treatment as required. Those patients not listed directly for further FURSL were reviewed in clinic at three months with repeat KUBXR. Stone free was defined as no radio - opaque calculi greater than 2mm in diameter on KUBXR.

Treatment outcomes and complications were as-
Flexible ureterorenoscopy and hard stones, p. 45 - 51

Results

In 250 patients underwent FURSL during the study period. Of these, 66 patients, 41 male and 25 female, had mean stone densities greater than 900HU. Patient and stone qualities are shown in Table 1. The mean patient age was 58 years (range 35 - 78 years). The mean stone density was 1216HU (range 902 - 1,768 HU). The mean maximal stone diameter was 13.2mm (range 6.3-33.0mm). There were 43 patients with stones treated on the left and 23 on the right. Most stones were either renal pelvic or lower calyceal in position, accounting for 18 (27.3%) patients each. The distribution of stones based on location is seen in Figure 1.

Stone clearance rates are seen in Figure 2. 49 patients (74.2%) were stone free after their first procedure. A further 12 patients (18.2%) required a second procedure. Post-operative complications were recorded using the Clavien - Dindo classification. Analysis of differences in patient and stone qualities related to stone free rate after the first procedure were made. Continuous variables were compared using an unpaired t-test and categorical variables were analyzed using chi-square test. Correlations were assessed with pearson correlation. Statistical analysis was performed using SPSS version 19.0 (SPSS Inc., Chicago, IL, USA), p< 0.05 was taken to indicate significance.
session of FURSL for clearance. Two patients (3.0%) have had a third session of FURSL for complete clearance, while 3 patients (4.5%) with asymptomatic fragments less than 5mm are being managed conservatively at present. Stone analysis was performed for 54 patients (82%) and 50 of these were primarily calcium oxalate monohydrate or calcium oxalate dehydrate stones, the remaining being mixed composition. Only 7 patients (10.6%) had procedure associated morbidity. Six patients developed post-operative pyrexia, treated empirically with antibiotics without positive cultures (Grade II complication). One patient developed multi-resistant *E. coli* sepsicaemia following their second FURSL (Grade IVa complication). This was managed in the high dependency unit with conservative measures. No invasive intervention was required. There were no ureteric injuries encountered and there was no associated 30 day mortality.

When comparing patients who were rendered stone free with the first episode of FURSL to those who were not, there was no significant difference in gender (59.2 and 70.9% male respectively, p= 0.296) or mean age (56.4 and 61.2 years respectively, p= 0.366). There was no significant difference in mean stone density between these groups (1224.8HU and 1193.5HU respectively, p= 0.530). Nor was there any difference in laterality (70.9% and 63.7% left respectively, p= 0.407) between the two groups. There was however, a significant difference in distribution of stone by location between the two groups (*Figure 3*, p< 0.001). Furthermore, there was a significant difference in maximal stone diameter between those that were stone free and those who were not after the first treatment (9.1mm and 15.1mm respectively, p< 0.001). When mean stone diameter was grouped as less than 10mm, 10 - 20mm and greater than 20mm, Pearson correlation confirmed failed stone clearance after the first treatment with FURSL was associated with a maximal stone diameter greater than 10mm (p= 0.012). There was no correlation found between the stone location and reduced SFR when examined individually.

### Discussion

SWL efficacy has been reported as between 46 - 91%. There have been a number of studies reporting the favourable outcome with FURSL compared to SWL in patients with adverse stone qualities such as increased size or lower calyceal location. However, we believe this to be the only study to date to assess the efficacy of FURSL in a cohort of patients with dense upper urinary tract calculi, another independent factor for predicting poor outcome in SWL treatment. We have shown a single treatment stone free rate of 74.2% with a complication rate of 10.6% with FURSL for treatment of renal calculi with a density of greater than 900HU.

The correlation between stone density and fragmentation with SWL was initially shown *in vitro*. Since then there have been a number of retrospective clinical studies confirming an increased median number of shocks required for successful stone fragmentation and higher incidence of SWL failure with higher stone densities. Our results confirm a favourable SFR for stones with a mean density greater than 900HU treated with FURSL compared to the published outcomes for SWL.

This inferior SFR is important to consider as it not only increases the likelihood of requiring further treatment for stone clearance but residual fragments following SWL are also associated with a higher compli-

### Table 1

**Patient and stone characteristics for patients who were treated with flexible ureterorenoscopy**

<table>
<thead>
<tr>
<th>Patient or stone characteristics</th>
<th>No</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean age (years)</td>
<td>58 (range 35 - 78)</td>
</tr>
<tr>
<td>Gender (male: female)</td>
<td>41:25</td>
</tr>
<tr>
<td>Stone laterality (left: right)</td>
<td>43:23</td>
</tr>
<tr>
<td>Mean maximal stone diameter (mm)</td>
<td>13.2 (range 6.3 - 33.0)</td>
</tr>
<tr>
<td>Mean stone density (HU)</td>
<td>1768 (range 902 - 1768)</td>
</tr>
</tbody>
</table>
cation rate. Streem et al. demonstrated a 43% risk of having a symptomatic episode and/or needing an intervention, after a mean 26-month follow-up in patients with residual calculi less than 4 mm post SWL.

Complication rate, as well as SFR, is important when counselling patients and advising on the most appropriate treatment strategy for their urinary calculi. Overall complication rate up to 40% have been reported for SWL. Pain during and after SWL is common but usually manageable with oral analgesics in the community and normally settles within seven days. Haematuria is the most widely reported complication following SWL, due to direct trauma to the renal tissue and vasculature. However, many would consider this routine and it too usually settles spontaneously. Significant haematuria or other bleeding related complications such as peri-renal or subcapsular haematoma are fortunately much rarer at less than 1% with SWL. In our cohort of FURSL treated stones there were no reported cases of severe pain or significant haematuria.

Urinary tract infection is another relatively common complication of SWL. Symptomatic bacteruria has been reported in 7.7% - 23.5% of patients who undergo SWL. The rate of bacteraemia after SWL is reportedly as high as 14% converted into sepsis in <1% of cases, although for staghorn calculi, the rate is elevated to 2.7%. These are largely comparable to our infection rate of 10.6% and sepsis rate of 1.5%.

Rarely considered complications of SWL include injury to adjacent organs. In a recent review, 62 of 3,423 (1.81%) patients experienced a documented gastrointestinal (GI) complication after SWL. One study examining specifically the incidence of GI injury after SWL with pre- and post-procedure endoscopy revealed 80% of patients sustained gastric or duodenal erosions. These adverse effects were associated with the increase in the number and energy of shockwaves delivered.

As it has already been demonstrated that dense calculi are likely to require more shocks, with a higher likelihood of unsuccessful fragmentation with SWL it could be possible that patients with these stones are at a higher risk of these and other complications. Furthermore, while long term complications such as hypertension as a result of SWL are still debated, animal studies have shown that renal injury is related to the number, energy and rate of shockwaves delivered and as such it is possibly that patients with dense stones could be considered at risk of long term complications. To our knowledge, there has been no study of the complication rate following SWL related specifically to the treatment of stones with density greater than 900HU. Clearly it would be important to investigate both the short and long term risk of adverse events in this group to allow accurate patient counselling and comparison to FURSL outcomes.

While we believe this to be the first reported outcomes for FURSL in a cohort of patients with calculi with a mean density greater than 900HU, outcomes for FURSL in other subgroups have been well reported. SFR have been shown to be as high as 98% with FURSL. However, this is highly variable, largely dependant on stone size and location. SFRs as low as 47 - 50% have been reported for lower calyceal stones and 43% for stones greater than 3 cm. Our cohort presented, has a high proportion of large stones and lower calyceal stones and as such our SFR of 74.2% would appear acceptable. We were able to confirm the correlation of stone size with SFR in FURSL although no particular stone position was predictive of reduced SFR. Our complication rate of 10.7% was also in line with the published literature which ranges from 10 - 25%, with a major complication rate in the region of 1%. However, we do acknowledge the relatively small cohort size of the study, resulting in possible under reporting of complications and associations with SFR.

We recognise the other limitations of this study including the retrospective design. Furthermore, the SFR may be subject to both over- and under-estimation. The use of KUBXR for confirmation of residual stone burden is known not to be as sensitive as CTKUB, risking over-estimation of the true SFR. It is also known that SFR continues to improve after 3 months due to spontaneous passage of small residual fragments, which may be a source of under-estimation of SFR. We also appreciate that other factors should be taken in to consideration when assessing the utility of FURSL for this cohort, including anaesthetic risks and costs; however this was out with the scope of this study. Further assessment of the optimal management of stones with a mean density greater than 900HU would be achieved from well powered randomised control trial.
Η πυκνότητα (density) των πυελοκαλυκικών λίθων αποτελεί έναν από τους κύριους παράγοντες που πρέπει να λαμβάνει υπόψιν ο ουρολόγος πριν καταλήξει στη μέθοδο αντιμετώπισης τους. Λίθοι με πυκνότητα πάνω από 900 HU είναι δύσκολο να αντιμετωπιστούν με τη χρήση υπερήχων, ακόμα και με πολλαπλές συνεδρίες, ενώ αντιθέτως η εύκαμπτη ουρητηροσκόπηση και η χρήση Laser Holmium είναι ασφαλής και οικονομική μέθοδος, που ίσως θα έπρεπε να θεωρηθεί θεραπεία εκλογής για «σκληρούς» λίθους.

Περίληψη

Η πυκνότητα (density) των πυελοκαλυκικών λίθων αποτελεί έναν από τους κύριους παράγοντες που πρέπει να λαμβάνει υπόψιν ο ουρολόγος πριν καταλήξει στη μέθοδο αντιμετώπισης τους. Λίθοι με πυκνότητα πάνω από 900 HU είναι δύσκολο να αντιμετωπιστούν με τη χρήση υπερήχων, ακόμα και με πολλαπλές συνεδρίες, ενώ αντιθέτως η εύκαμπτη ουρητηροσκόπηση και η χρήση Laser Holmium είναι ασφαλής και οικονομική μέθοδος, που ίσως θα έπρεπε να θεωρηθεί θεραπεία εκλογής για «σκληρούς» λίθους.

References


