INTRODUCTION

Urinary stones disease is a major health problem with increasing prevalence and incidence worldwide. The prevalence of urolithiasis is 1 - 20%, and it is higher (> 10%) in countries with high living standards such as Sweden, Canada or the US than the other countries. Moreover, recurrence of the urolithiasis was observed in 50% within 5-10 years, and in 75% within 20 years.

The treatment of ureteral stones has improved significantly over the last two decades and includes various treatment options such as extracorporeal shock wave lithotripsy (SWL), ureterolithotripsy (URS), percutaneous antegrade lithotripsy, and open/laparoscopic lithotomy. The size, composition, and location of ureteral stones have been recognized as predictive factors of success. Among these factors, stone composition has been shown to affect the outcomes of SWL and URS, using holmium: yttrium-aluminum-garnet (holmium: YAG) laser, and electrohydraulic lithotripter.

URS has been the accepted first-line therapeutic approach for the endoscopic treatment of ureteral stones. It can be used singly or with various types of lithotripters including pneumatic or laser. Following the first URS operations, which showed the efficacy of the procedure, the technological progress in ureteroscopes and related lithotripters, and in parallel with this advancement, the introduction of small caliber semi-rigid and flexible ureteroscopes with small diameter and laser lithotripsy has improved the outcomes while decreasing the complications, which are mostly self-limiting. Stone-free rates of up to 97%, with low complication rates of 3.5-25%, have been reported. Different types of lithotripters can be used for stone fragmentation including pneumatic, ultrasonic, electrohydraulic, and laser lithotripters. The most commonly used are holmium: YAG laser lithotripsy (LL) and pneumatic lithotripsy (PL). A few studies have been evaluated the relationship between stone composition...
and the outcomes of PL or LL.\textsuperscript{4,5} In these studies, it has been demonstrated that PL and LL are efficient on fragmentation of different stone compositions. To the best of authors' knowledge, there have been conducted no studies to date to compare the outcomes of PL and LL for the management of calcium oxalate (CaOx) and calcium phosphate (CaP), which are the most common types of urinary stones.

The present study was done to assess the effect of ureteral stone composition on the outcomes of URS using LL or PL for ureteral stones.

**METHODOLOGY**

This observational study was conducted between August 2010 and August 2015 at the Istanbul Training and Research Hospital, Turkey, over patients in whom ureteral stones were treated with URS using PL or LL. The patients who were at least 18 years old with solitary ureteral stones were included, the composition of which was identified as CaOx and CaP postoperatively. Patients with pregnancy, congenital urinary tract malformations, ureteral tumor or stricture requiring dilatation, history of previous URS or ureteral surgery or who had impacted stone, were excluded. An impacted stone was described as a stone that could not be skipped either by a wire or a catheter, or a stone causing ureteral obstruction and remaining in same position for over 2 months.

Patient data included age, gender, body mass index (BMI), the presence of preoperative hydronephrosis, stone surface area (SSA), stone location, operation time (OT) and hospitalization time, perioperative and postoperative complications, stone-free status were recorded. The patients were divided into two groups according to stone composition; and each group was further divided into two groups, according to the lithotripter type (Table I). The stones were considered CaOx or CaP, if they consisted of ≥51% of calcium oxalate or calcium phosphate. Those stones that did not have CaOx or CaP content ≥51% were excluded from the study.

Routine biochemical and urine analysis, and urine culture were preoperatively performed. Radiological imaging including IVU and/or non-contrast computerized tomography (NCCT) was preoperatively obtained to determine SSA, and location. NCCT was performed on patients with a known allergic reaction to intravenous contrast medium. The presence of hydronephrosis was evaluated with ultrasonography preoperatively.

SSA calculated from the radiographic images preoperatively, according to European Association of Urology (EAU) guidelines.\textsuperscript{2}

Patients with positive urine culture received antibiotics according to urine culture results at least 3 days prior to URS. Antibiotic prophylaxis has been applied for all patients on the day of the procedure, and was continued, if a double-J stent was inserted.

All procedures were applied under general anesthesia with same equipment during the study period. URS was performed by the same group of urologists with experience in standard fashion using a 9.5F semi-rigid ureteroscope (Karl Storz, Tuttlingen, Germany) with all patients in the dorsal lithotomy position.

Stone was fragmented with a PL (Lithoclast; EMS, Nyon, Switzerland) using a 3F pneumatic probe with either single or continuous pulses, whose frequency was 10 Hz and pressure was set at 2 bars. Holmium: YAG LL was performed using a laser generator (Sphinx 30; Lisa; Katlenburg, Germany) in combination with 200 µm laser fiber. The settings of LL were 0.6 - 1.4 J per pulse, and the frequency 5 - 8 Hz. Stones were fragmented small enough to pass spontaneously (≤4 mm).\textsuperscript{9} A double-J stent or a ureteral catheter was used according to surgeon's recognition. The ureteral stent was removed after first day of operation and double-J stent was extracted after 4 weeks of operation. Stone fragments were extracted during and after operation, and were sent for stone composition analysis, using an infrared spectroscopy analyzer. All stones were analyzed in the biochemistry laboratory, using infrared spectroscopy technique. Dry stone fragments were weighed and inspected visually before crushing to reveal internal structure and characteristics. Thereafter, stone samples were analyzed by FTIR Spectrometer Frontier (PerkinElmer, Waltham, Massachusetts, USA).

The OT was characterized as the time between insertion of the URS into the urethra and removal of URS at the end of the procedure. Patients were usually discharged within 24 hours unless complications or comorbidity demanded prolonged hospitalization.

Perioperative complications included ureteral bleeding, and mucosal injury. Postoperative complications included fever, and infection. Stone migration was also recorded.

The treatment success was evaluated with direct visualization of the involved ureter intraoperatively or radiological images (NCCT) 4 weeks after surgical procedure. According to the EAU guideline 2014, stone-free status was defined as the absence of stones or residual stone fragments smaller than 4-mm in size, which are asymptomatic and clinically insignificant.\textsuperscript{2}

The groups were compared regarding demographic characteristics of patients, BMI, SSA, presence of hydronephrosis, lateralization and localization of stone. Furthermore, stone-free rate, OT, hospitalization time, and perioperative and postoperative complication rates were also compared between the groups.

SPSS version 18 software (SPSS Inc, Chicago, USA) was used for statistical analysis. Normally distributed data were showed as the mean ± standard deviation,
and abnormally distributed data were expressed as median (interquartile range). Continuous variables were analyzed using either Student t-test (normally distributed data) or Mann-Whitney U-test (abnormally distributed data). Chi-square or Fisher’s exact test was used for the comparison of categorical variables. A p-value < 0.05 was accepted as statistical significance.

**RESULTS**

Patients’ characteristics were summarized in Table I. The CaOx stone location and lateralization were not statistically different among the lithotripter groups (p=0.083, and p=1.000, respectively) (Table I). The median SSA of LL and PL groups was 88 (77), and 70 (49) mm², respectively (p=0.196). However, the CaOx stones treated with LL were in more hydronephrotic ureter than the stones treated with PL (p=0.047). The mean OT of LL group was shorter than PL (p=0.009). The stone-free rates were 95% in LL group and 92% in PL group (p=0.679). The total number of perioperative complications and stone migration rates were similar in both groups (p=0.998, and p=0.133, respectively). No postoperative complications were found in both groups. The median postoperative hospitalization time of the patients in the PL group was significantly longer than the LL group (p<0.0001).

### Table I: Baseline demographics and clinical characteristics of stone composition groups.

<table>
<thead>
<tr>
<th></th>
<th>CaOx (n=58)</th>
<th>CaP (n=56)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>All (n=58)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Age [mean ± SD (range), years]</strong></td>
<td>43.66 ±11.66</td>
<td>45.18 ±12.60</td>
<td>0.171*</td>
</tr>
<tr>
<td><strong>Gender (male/female)</strong></td>
<td>37 (63.8%) / 21 (36.2%) / 21 (39.5)</td>
<td>36 (64.3%) / 20 (35.7%) / 8 (27.6%)</td>
<td>0.476**</td>
</tr>
<tr>
<td><strong>BMI [mean ± SD (range), kg/m²]</strong></td>
<td>27.24±4.23</td>
<td>26.85±3.86</td>
<td>0.707*</td>
</tr>
<tr>
<td><strong>Stone surface area [median (IQR) (range), mm²]</strong></td>
<td>70 (55)</td>
<td>88 (77)</td>
<td>0.196***</td>
</tr>
<tr>
<td><strong>Lateralization of stones (R/L)</strong></td>
<td>26(44.8%) / 32 (55.2%) / 21 (55.3%) / 1.000**</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Localization of stones</strong></td>
<td>48 (82.8%)</td>
<td>40 (71.4%)</td>
<td>0.083****</td>
</tr>
<tr>
<td><strong>Presence of hydronephrosis (+/-) [n (%)]</strong></td>
<td>2 (3.4%) / 56 (96.6%) / 4 (7.1%) / 0.047****</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
| **BMI: body mass index; SD: standard deviation; IR: interquartile range**

### Table II: Peri- and postoperative findings of lithotripter groups.

<table>
<thead>
<tr>
<th></th>
<th>Pneumatic (n=65)</th>
<th>Laser (n=49)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Operation time [mean ± SD (range), minutes]</strong></td>
<td>81.79 ±33.28</td>
<td>53.16 ±36.94</td>
<td>0.010*</td>
</tr>
<tr>
<td><strong>Stone-free [n (%)]</strong></td>
<td>60 (92%)</td>
<td>44 (90%)</td>
<td>1.000**</td>
</tr>
<tr>
<td><strong>Perioperative complication [n (%)]</strong></td>
<td>57 (87.7%)</td>
<td>44 (89.8%)</td>
<td>0.874****</td>
</tr>
<tr>
<td><strong>Stone migration (+/-) [n (%)]</strong></td>
<td>6 (9.2%) / 59 (90.8%) / 4 (7.1%) / 0.669****</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Postoperative complication [n (%)]</strong></td>
<td>61 (93.8%)</td>
<td>46 (93.9%)</td>
<td>0.050****</td>
</tr>
<tr>
<td><strong>Hospitalization time [median (IQR) (range), days]</strong></td>
<td>2.5 (1)</td>
<td>1.0 (0)</td>
<td>0.900***</td>
</tr>
</tbody>
</table>

*Student t-test; **Fisher’s Exact Test; ***Mann-Whitney U-test; ****Chi-square test; SD = standard deviation; IR = Interquartile range.
The CaP stone location and lateralization were also similar in the two lithotripter groups (p=0.660, and p=1.000 respectively). The presence of hydroureter was frequently in the LL group (p=0.045). The mean OT was shorter in LL group (p=0.012). The groups were similar with respect to stone-free rate (p=0.440). The perioroperative and postoperative complications were compared in both groups (p=0.800, and p=0.800, respectively). The stone migration rate was not different in both groups (p=0.440). The median postoperative hospitalization time of the patients in the PL group was significantly longer than the LL [1 (1) (range, 1-8) vs. 2 (3) (range, 1-14), p=0.001]. The results of patients with CaOx and CaP stones in lithotripter groups were not significantly different in study parameters out of OT and postoperative complications. The OT of CaP groups were significantly shorter than the CaOx groups in both lithotripter groups (Table-2). Postoperative fever and infection were more frequently in patients with CaP stones treated with PL than the patients with CaOx stones (p=0.050). However, the postoperative complications were not different between these two stone compositions treated with LL (p=0.332).

**DISCUSSION**

The OT was significantly longer in PL and CaOx stone composition groups. The postoperative complications were more frequent in PL, when it was used for the treatment of the patients with CaP stones. The urinary tract of the patients with CaOx and CaP stones treated with LL were more dilated than the others. Moreover, the hospitalization time of the patients with CaOx and CaP stones treated with PL was significantly longer than the other patients. However, there was no statistical significant difference in stone-free rate between all groups. The lithotripter and stone composition groups were similar in all patients and stone characteristics that can affect the results of operations. Therefore, the difference in complications would be explained by the difference of lithotripters and stone compositions.

Holmium: YAG LL fragments stones through photothermal mechanism. The stone migration is less likely than other laser types and PL, because of low power of holmium: YAG laser. PL uses compressed air that propels a projective against the probe tip, causing the probe to oscillate back and forth, and stone is fragmented with this ballistic impact. Therefore, stone migration is the main disadvantage of PL. Razzaghi et al. reported the incidence of stone migration as 17.9% in PL group; but, it was no stone migration in LL group. However, the studies by Salvado et al. and Manohar et al. did not find any significant difference in stone migration between two lithotripters. The highest rates of stone migration in this study were 10.5% in patients with CaOx treated with PL and 13.8% in patients with CaP stones treated with LL. Because CaOx stones are lighter than CaP stones, the possibility of migration of CaOx stones may be higher than CaP stones in PL group. In LL group, because of more dilated ureters of patients with CaP stones, but statistically insignificant, than the patients with CaOx stone, the migration rate of CaP stones was greater than CaOx stones. However, the difference in stone migration between CaOx and CaP stones was not statistically significant in PL and LL groups (p=0.668 and p=0.083, respectively). In addition, the stone migration rates of all stones were similar in PL and LL groups (9.2% vs. 8.2%, retrospectively, p=0.743).

It has been shown that LL is more advantageous from the aspect of the OT than PL, because the stones migrate less with laser, and are pulverized and debulked until a few fragments; thus, lesser ancillary procedures are required. The studies comparing the OT between PL and LL demonstrated the mean OT of LL between approximately 15 and 50 minutes. However, these studies reported the OT for all types of stones, despite the importance of the stone composition on the OT of any lithotripsy procedure. Because stone hardness is still the most important factor limiting the usage of holmium: YAG laser, it was demonstrated that the speed of CaP stones fragmentation is slower than CaOx stones. Teichman et al. demonstrated that when energy and fiber size were constant, the efficacy of holmium: YAG laser was greater on CaP than CaOx stones. In this study, because of these factors explaining the reason for the shorter OT with LL, especially for CaP stones, the total time consumed in fragmentation of CaP stones with LL was significantly shorter than the fragmentation of CaOx stones with LL or PL and the fragmentation of CaP stones with PL. These findings show the importance of stone composition on the OT, and are compatible with the results mentioned above. However, in a study by Wiener et al., it was shown that the composition of stones appears to have little effect on the overall OT for holmium: YAG LL. The stone-free status is an important factor for the comparison between the lithotripter groups, as well as stone composition groups. It is expected that LL is performed better than PL with respect to fragmentation under direct vision. As mentioned above, the stones tend to pass spontaneously with the pulverization effect of laser lithotripter. The studies, which compare two lithotripters, support these findings with results demonstrating that the LL has significantly higher stone-free rate than PL. However, the results from our study and the study by Akdeniz et al. showed no difference in stone-free rates between LL and PL. They presented that the stone-free rates for LL and PL were 75, and 74.2%, respectively. Although our results were higher than theirs, this insignificant difference between two lithotripters promotes their findings. In this study, no major complications were encountered and only minor perioperative complications occurred in lithotripter and stone composition groups, which did not
require any medical or surgical interventions. However, the postoperative fever and infection were determined only in patients with CaP stones of LL and PL groups. In PL group, the patients with CaP stones had more fever and infection than the patients with CaOx stones. But, it was not an effect of the lithotripter type on these complications; because in CaP group, postoperative complications were similar between the lithotripters. It has been suggested that the urease-producing bacteria play a critical role in the formation of CaP stones, and urinary tract infection is necessary for the urine pH be high enough for carbonate to form especially in the absence of tubular bicarbonate leak. The findings of the study by Gault et al., which support the relationship between urinary tract infection and CaP stone, demonstrated that, whereas 21% of CaP stone formers had positive urine cultures, 9.4% of CaOx stone formers had positive urine cultures.

The primary limitation of this study was the retrospective collection of data. The small number of patients and a lack of information on exact fragmentation time were other limitations of the study. However, the groups included entirely of consecutive patients with chronological difference. The groups were similar in patient and stone characteristics. Therefore, the comparison of our groups was acceptable. Another important limitation of the study was the lack of detailed presentation of composition of CaOX stones. The authors could not present CaOx stones as monohydrate and dehydrate, because the stone analysis revealed stone compositions as only CaOx. The same level of experience of surgeons may help exclude biases of the skills and experience differences of more than one surgeon. The lack of long-term follow-up of the patients may be another limitation of this study.

CONCLUSION

Both LL and PL are efficient with high success rate in the treatment of CaOx and CaP stones. However, the LL has advantage over PL in shorter OT. Moreover, the OT of CaP stone was shorter than CaOx stones. Despite the advantage of CaP stones in OT, PL in the treatment of CaP stones had more postoperative complications. Thus it is suggested that LL in the treatment of recurrent CaP stones is a safe and effective treatment modality.

REFERENCES