Acta Med. Okayama, 2016
Vol. 70, No. 1, pp. 25-29

Acta Medica Okayama
http://escholarship.lib.okayama-u.ac.jp/amo/

Original Article

Calcium Phosphate Composition Affects Ureteroscopic Laser Lithotripsy

Hideo Otsuki[a]*, Takashi Yoshioka[a,b], Toshihiro Shimizu[a], Yusuke Nakanishi[a], Kei Fujio[a,b], Wataru Murao[a], Shinya Uehara[a,b], Hirosato Kikuchi[c], and Koji Fujio[a]

Departments of [a]Urology, and [c]Anesthesiology, Abiko Toho Hospital, Abiko, Chiba, 270-1166, Japan, [b]Department of Urology, Okayama University Graduate School of Medicine, Dentistry and Pharmaceutical Sciences, Okayama 700-8558, Japan

The effects of stone composition on transurethral lithotripsy (TUL) have not been sufficiently elucidated. The purpose of this study was to identify how calcium phosphate stone composition impacts TUL. Two hundred eighty-nine cases of semi-rigid and/or flexible TUL for upper urinary tract calculi were reviewed retrospectively. Inclusion criteria were a preoperative assessment by noncontrast computed tomography (NCCT) and a stone composition analysis. Small stones and those without calcium composition were excluded. Stone core radiodensity (SCR) was measured by taking the average of the upper 3 of 5 points in the proximity of the center of the stone on NCCT. Fifty-three patients with calcium phosphate composition (CaP) and 118 patients with calcium oxalate and without phosphate composition were eligible for analysis. SCR was significantly higher in the CaP group ($p < 0.01$). The CaP patient group needed a significantly longer operation time ($p = 0.014$) and more laser energy ($p = 0.085$), and tended to have a lower rate of complete lithotripsy ($p = 0.096$) and higher incidence of postoperative pyelonephritis ($p = 0.181$). Stones containing calcium phosphate are harder, demand more laser energy, and require a longer operating time. NCCT evaluation can estimate stone composition preoperatively, and may be a useful tool for predicting operative outcomes.

Key words: ureteroscopic lithotripsy, stone composition, calcium phosphate, radiodensity, complication

Urolithiasis is an important health problem that affects all societies. Approximately 1-5% of the population in Asia experiences urolithiasis [1]. The stone size, chemical composition, and location can influence the efficacy of medical and surgical treatments for urinary stones. Transurethral ureteroscopic lithotripsy (TUL) has been increasingly performed for upper-urinary-tract calculi because of the increasing use of thin ureteroscopes, the preference for minimally invasive treatment, and its higher complete lithotripsy rate. About 90% of stones are composed of a calcium compound; however, it is unclear whether stone composition affects operative time, procedural difficulty, or complications of TUL. We investigated whether stone composition of calcium phosphate influences perioperative outcomes of TUL.

Patients and Methods

Patient characteristics. We identified 289 operative cases that had undergone semi-rigid and/or

Received May 14, 2015; accepted September 18, 2015.
*Corresponding author. Phone:+81-4-7182-8166; Fax:+81-4-7182-2905
E-mail:hideotsuki2004@hotmail.com (H. Otsuki)

Conflict of Interest Disclosures: No potential conflict of interest relevant to this article was reported.

flexible TUL for upper urinary calculi from April 2012 to October 2014. We recorded various patient characteristics, including age, sex, body mass index, medical comorbidities, stone size, stone location, SCR, stone history, and stone composition analysis. Operation time, preoperative stent placement, use of access sheath, use of laser, amount of laser energy, postoperative fever, and complete lithotripsy were obtained from medical reports. Patients were classified into two groups according to whether their stones contained phosphate or not. Stone composition was analyzed at a reference stone laboratory (SRL Co. Ltd., Tokyo, Japan).

Study design. A retrospective chart review was conducted on all procedures performed for upper urinary tract calculi at Abiko Toho Hospital after institutional review board approval. Inclusion criteria were patients with a preoperative assessment of non-contrast computed tomography (NCCT) and a stone composition analysis. Exclusion criteria were stone size less than 4 mm, stones without calcium composition and less than 3 months' follow-up. Axial and coronal images of stones were obtained with a helical CT using identical settings (120 kV, 250 mA) for both 5- and 3-mm-thick slices. Stone core radiodensity (SCR) was measured by a single urologist taking the average of the upper 3 of 5 points in the proximity of the center of a stone on NCCT; the region of interest was 1 mm^2. A single anesthesiologist evaluated the American Society of Anesthesiologists (ASA) status. Complete lithotripsy was defined as complete extraction of fragments or complete fragmentation into parts less than 3 mm.

Procedural factors. We adopted a non-guidewire method for the ureteroscopic procedure [2, 3]. First, cystoscopy was done under general anesthesia. The ureter was inspected using a 6/7.5 Fr dual-channel semi-rigid ureteroscope (Richard Wolf, IL, USA) without a guide wire. Ureteral lithotripsy was performed *in situ* for patients with fixed ureteral stones. Movable ureteral stones were pushed up into the renal pelvis. An initial guidewire was placed to the level of inspection. Special caution was exercised not to advance the guidewire into the renal pelvis to avoid hemorrhage. A Flexor 14.4/12 Fr ureteral access sheath (COOK, Tokyo, Japan) was passed over the guidewire gently to the level of inspection; then the guidewire was removed. The flexible ureteroscope (URF-V, 12 Fr, OLYMPUS, Tokyo, Japan) was then inserted into the renal pelvis. After inspecting all renal calyces to confirm location, size, and number of stones, holmium laser lithotripsy (MM niic, Tokyo, Japan) was started. Intermittent irrigation was controlled at the lowest pressure manually with a 50-ml syringe. A P-5 flexible ureteroscope (OLYMPUS, Tokyo, Japan) was used without an access sheath for patients with a narrow ureter. Active fragment retrieval using N-CIRCLE (COOK, Tokyo, Japan) was repeated as long as graspable fragments existed. Laser lithotripsy was completed when the fragment sizes were all less than 3 mm (complete fragmentation) or when complete extraction of fragments was attained. The maximal lasing time was set at 60 min without regard to complete lithotripsy. Prophylactic antibiotics (ceftriaxone) were administered within 2 days to patients without urinary tract infection. A ureteral stent was placed after surgery and removed at 2 weeks. All data were analyzed using Student's *t*-test, and p values < 0.05 were considered statistically significant.

Results

Of 289 cases of TUL, 53 patients with calcium phosphate composition (CaP group) and 118 cases with calcium oxalate but without phosphate composition (CaOx group) were eligible for analysis. Backgrounds of patients are listed in Table 1. In 14 cases, prior shock wave lithotripsy (SWL) had failed. The percentage of females was significantly higher in the CaP group; however, age, body mass index, ASA score, and prevalences of diabetes mellitus, hypertension, hyperlipidemia, and hyperuricemia were not significantly different between the 2 groups. A comparison of operative results is shown in Table 2. Stone size and rate of preoperative ureteral stent were not significantly different; however, SCR was significantly higher in the CaP group ($p < 0.01$). Patients in the CaP group needed significantly longer operation time ($p < 0.05$) and more laser energy ($p = 0.085$). There was a tendency for a lower complete lithotripsy rate ($p = 0.096$) and a higher incidence of postoperative pyelonephritis ($p = 0.181$) in the CaP group. As a surgical complication, all pyelonephritis cases were classified as Clavien grade 2. Eighteen and eleven R2 stones were identified in the CaOX group and the CaP

Table 1 Background of the patients

	CaP	CaOX	*P* value
Number of patients	53	118	
Age (years)	58.9	61.4	0.349
Rate of female (%)	54.7%	30.5%	0.004
BMI	24.7	24.0	0.424
ASA score	1.83	1.68	0.141
Diabetes mellitus	11.3%	19.5%	0.165
Hypertension	43.4%	35.0%	0.31
Hyperlipidemia	18.9%	10.3%	0.163
Hyperuricemia	3.7%	11.0%	0.067
Stone location			
R2	7	12	
R3	5	11	
U1	23	47	
U2	5	16	
U3	8	26	
Multiple	5	6	

BMI, body mass index; ASA, American Society of Anesthesiologists.

Table 2 Comparison of operative results

	CaP	CaOX	*P* value
Stone size (mm)	10.1	8.7	0.058
(range)	4.2–24.5	4.4–41.1	
Stone core radiodensity (HU)	1,186	1,034	0.009
(range)	326–2,028	391–1,717	
Preoperative ureteral stent	37.7%	28.2%	0.232
Operation time (min)	84.9	71.4	0.014
(range)	30–202	20–153	
Laser energy (kj)	6.12	3.57	0.085
(range)	0.21–28.8	0.15–30.2	
Complete lithotripsy rate	79.3%	89.8%	0.096
Postoperative pyelonephritis	15.1%	7.6%	0.181

HU, hounsfield unit.

group, respectively. Of them, failures of complete lithotripsy were noted in 4 and 2 cases, respectively. Statistical analysis was difficult to perform due to the small sample; however, no obvious association was observed between stone position in calyces and operative outcome.

The percentages of stones with a core attenuation < 1,000 HU were 50.8% and 34.0% for CaOX and CaP stones, respectively. Urinary stones with SCR > 1,300 HU were seen in only 25.4% of patients in the CaOX group compared to 43.4% of patients in the CaP group.

Discussion

Surgical indications for flexible TUL have been expanding because recent technological advances have enabled thinner ureteroscopes that produce clearer images to be manufactured. Large renal stones such as staghorn stones can be treated with TUL instead of percutaneous or shock wave lithotripsy. Due to the existence of a clear visual field and the adequate deflection of recent flexible ureteroscopes, we can access almost all calyces to treat stones. In the current study, no obvious association was observed between stone position in calyces and operative outcomes. We often experience a stone that is so hard that it breaks into pieces during TUL. SCR on NCCT is related to the hardness of calculi; however, its effects on TUL or relation to stone composition have not been sufficiently elucidated. This is the first investigation to our knowledge of the impact of calculi containing calcium phosphate and SCR on the operative outcome of TUL.

Compared to uric acid and cystine stones, calcium-containing stones are heterogeneous with higher attenuation at the core, which decreases towards the periphery [4]. Torricelli *et al.* reported stone core and periphery attenuation values; CaOX core 1,099 (range 635 to 1,522 HU) and periphery 514 (range 304 to 827 HU): uric acid core 523 (range 285 to 759 HU) and periphery 382 (244 to 582 HU): cystine core 648 (257 to 798 HU) and periphery 479 (204 to 776 HU) [4]. We recorded 5 points of CT attenuation in the proximity of the center of the stone, and adopted the upper 3 points to reflect the hardest area of the stone because that portion was sometimes displaced from the center of the stone.

Many researchers have attempted to identify stone composition preoperatively. A stone of attenuation < 500 HU, > 4 mm in size and urine pH < 5.5 has a high predictive value for uric acid composition [5]. According to our investigation, the average stone attenuation level in the 3 excluded cases of uric acid stone was 371.7 HU, and that of one case of struvite was 496 HU. Previously reported CT attenuation values in uric acid, struvite, and cysteine stones are approximately 390, 470, and 510 HU, respectively [4–6]. Thus, it is relatively easy to distinguish these 3 stones from calcium-containing stones, whose SCR is > 700 HU [4]. Not only the CT attenuation level but also the radiolucency on roentgenogram, past history, urine pH, urine culture, and blood tests are helpful for predicting stone composition before treatment.

Our study demonstrated that SCR is significantly higher in the CaP group. This suggests that calculi containing calcium phosphate are harder than those containing calcium oxalate. The stone size in the CaP group (10.1 mm) was slightly larger than that in CaOX group (8.7 mm), although the difference was not significant ($p = 0.058$). The longer operation time in the CaP group was probably caused not only by the hardness of the stone, but also by the size of calculi. The higher laser energy and lower rate of complete lithotripsy may also have been influenced by size. Ito *et al.* reported that TUL for high stone radiodensity demands a longer operative time [7], which supports our results. Molina *et al.* concluded that calcium phosphate stones require less laser energy to fragment [8]; however, they only analyzed 22 calcium phosphate stones, giving their conclusions less validity. Wiener et al studied the effects of stone composition on TUL [9]; however, they did not focus on phosphate stones due to the small number of samples. A higher tendency of postoperative pyelonephritis in the CaP group was possibly the result of the larger stone burden and longer operating time. Urologists should pay attention when identifying urinary stones with a high SCR on NCCT.

Interestingly, the rate of females was significantly higher in the CaP group. The reason is unknown, but menopause or changes in the hormonal environment in women might be related. Other preoperative backgrounds do not explain this sexual specificity. No relationships between stone composition and lifestyle diseases (diabetes, hypertension, hyperlipidemia, obesity, and hyperuricemia) were found in this investigation.

A urinary calculus with a core attenuation value > 700 HU could be considered a calcium-containing stone [4-6, 10]. The hardness of the stone is one of the important factors when making a decision on the treatment strategy: namely, selection of TUL or SWL. Preliminary NCCT information on a stone is very helpful when planning treatments for patients because of the likelihood of a poor outcome from SWL when the SCR > 970 HU [10]. In our series, stone attenuation levels of 14 TUL patients after SWL failure were 1,190 HU around the core and 1,066 HU on average. Upper urinary stones with SCR > 1,000 HU can be considered to be an active indication for TUL. According to our results, the percentages of stones with a core attenuation < 1,000 HU are 50.8% and 34.0% for CaOX and CaP stones, respectively. A urinary stone with SCR > 1,300 HU was seen only in 25.4% of the CaOX group; however, it was seen in 43.4% of patients in the CaP group. Thus, a urinary stone with a higher CT attenuation level has a higher probability of having a phosphate composition. Furthermore, stones with TUL in patients whose CT attenuation level was > 1,300 HU seemed very difficult to treat. We suggest that urinary stones with SCR > 1,300 HU have a relatively high probability of being a CaP stone and require extra caution during TUL.

The limitations of this study include its being a retrospective, single-center investigation, and the small number of stones examined. The phosphate composition might have been overlooked in some cases because not all fragments were collected at the time of surgery. Operation time indicates overall operative time; it does not necessarily represent lasing time. The stones examined in the study cohort numbered no more than 170; however, this study found a significantly higher SCR in stones containing calcium phosphate, and thus our study has a certain level of reliability.

In conclusion, stones containing calcium phosphate are harder, demand more laser energy, and require a longer operating time. NCCT evaluation can estimate stone composition preoperatively, and may be a useful tool for predicting operative outcomes. Calcium phosphate-containing stones were more often seen in females.

References

1. Costa-Bauzá A, Ramis M, Montesinos V, Grases F, Conte A, Pizá P, Pieras E and Grases F: Type of renal calculi: variation with age and sex. World J Urol (2007) 25: 415-421.
2. Kumon H, Tsugawa M, Matsumura Y and Ohmori H: Endoscopic diagnosis and treatment of chronic unilateral hematuria of uncertain etiology. J Urol (1990) 143: 554-558.
3. Araki M, Uehara S, Sasaki K, Monden K, Tsugawa M, Watanabe T, Monga M, Nasu Y and Kumon H: Ureteroscopic management of chronic unilateral hematuria: a single-center experience over 22 years. PLoS One (2012) 7: e36729.
4. Torricelli FC, Marchini GS, De S, Yamaçake KG, Mazzucchi E

and Monga M: Predicting urinary stone composition based on single-energy noncontrast computed tomography: the challenge of cystine. UROLOGY (2014) 83: 1258–1263.
5. Spettel S, Shah P, Sekhar K, Herr A and White MD: Using Hounsfield unit measurement and urine parameters to predict uric acid stones. UROLOGY (2013) 82: 22–26.
6. Wisenbaugh ES, Paden RG, Silva AC and Humphreys MR: Dual-energy vs conventional computed tomography in determining stone composition. UROLOGY (2014) 83: 1243–1247.
7. Ouzaid I, Al-qahtani S, Dominique S, Hupertan V, Fernandez P, Hermieu JF, Delmas V and Ravery V: A 970 Hounsfield units (HU) threshold of kidney stone density on non-contrast computed tomography (NCCT) improves patients' selection for extracorporeal shockwave lithotripsy (ESWL): evidence from a prospective study. BJU Int (2012) 110 (11 Pt B): E438–442.
8. Ito H, Kawahara T, Terao H, Ogawa T, Yao M, Kubota Y and Matsuzaki J: Predictive Value of Attenuation Coefficients Measured as Hounsfield Units on Noncontrast Computed Tomography During Flexible Ureteroscopy with Holmium Laser Lithotripsy. J Endourol (2012) 26: 1125–1130.
9. Molina WR, Marchini GS, Pompeo A, Sehrt D, Kim FJ and Monga M: Determinants of holmium: yttrium-aluminum-garnet laser time and energy during ureteroscopic laser lithotripsy. Urology (2014) 83: 738–744.
10. Wiener SV, Deters LA and Pais VM Jr: Effect of stone composition on operative time during ureteroscopic holmium: yttrium-aluminum-garnet laser lithotripsy with active fragment retrieval. Urology (2012) 80: 790–794.