In Vivo Evaluation of Chemical Composition of Eight Types of Urinary Calculi Using Spiral Computerized Tomography in a Chinese Population

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Background: This study was conducted to evaluate the chemical composition of eight types of urinary calculi using spiral computerized tomography (CT) in vivo. **Methods:** From October 2011 to February 2013, upper urinary tract calculi were obtained from 122 patients in the department of urinary surgery of the First Affiliated Hospital of Soochow University. All patients were scanned with a 64-detector row helical CT scanner using 6.50 mm collimation before ureterorenoscopy. Data from the preoperative spiral CT scans and postoperative chemical composition of urinary calculi were collected. **Results:** The chemical composition analysis indicates that there were five types of pure calculi and three types of mixed calculi, including 39 calcium oxalate calculi, 12 calcium phosphate calculi, 10 calcium carbonate calculi, 8 magnesium ammonium phosphate calculi, 6 carbonated

apatite, 21 uric acid/ammonium urate calculi, 10 uric acid/calcium oxalate calculi, and 16 calcium oxalate/calcium phosphate calculi. There were significant differences in the mean CT values among the five types of pure calculi ($P < 0.001$). Furthermore, we also observed significant differences in the mean CT values among three types of mixed calculi ($P < 0.001$). Significant differences in the mean CT values were also found among eight types of urinary calculi ($P < 0.001$). However, no statistically significant difference was observed between the mean CT values of magnesium ammonium phosphate calculi and uric acid/calcium oxalate calculi ($P = 0.262$). **Conclusion:** Our findings suggest that spiral CT could be a promising tool for determining the chemical composition of upper urinary tract calculi. J. Clin. Lab. Anal. 29:370–374, 2015. ©

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Key words: spiral computerized tomography; upper urinary tract calculi; chemical composition

INTRODUCTION

Upper urinary tract calculi are a global health problem occurring with increasing frequency in populations from almost every ethnicity and geographic location (1). According to previous statistics, the male-to-female ratio is 3:1, the peak age at presentation is in the third to fifth decades of life, and the clinical manifestation is typical of renal colic (2). As one of the world's three largest highest incidence districts, incidence of urinary calculi in China is up to 1~5%, and even up to 5~10% in South China (3). While regional differences are very obvious in the incidence of urinary calculi, the intrinsic and extrinsic factors involved in the development and progression of urinary calculi always include hyperparathyroidism, bedridden, obstruction, infection, etc. (4, 5). Frequently, the true prevalence of urinary calculi is underestimated

because many calculi remain asymptomatic and hence go undiagnosed (6). Generally, the great majority of patients with urinary calculi can be diagnosed, to some extent, through medical history, physical examination, ultrasound, or X-ray examination (7). However, several factors constraint diagnostic accuracy, including the size, amount and position of the calculi, bowel content of patient, obstruction and infection, as well as calculi composition, etc. (8). Furthermore, conventional imaging methods, such as

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Received 18 February 2014; Accepted 29 April 2014

DOI 10.1002/jcla.21781

Published online in Wiley Online Library (wileyonlinelibrary.com).

ultrasonography (US) and plain kidneys–ureters–bladder radiographs (KUB) used for urolithiasis are less reliable due to radiolucency of calculi, increased amount of bowel gas, and smaller stone size (9).

Spiral computerized tomography (CT), a relatively safe, rapid, and accurate diagnostic method, is now becoming a frequently used radiographic examination to establish the diagnosis and severity of upper urinary tract calculi and has been widely adopted to evaluate the calculi in patients with renal colic (10, 11). Consequently, the success of spiral CT in determining calculi in renal colic suggests that spiral CT may potentially be a reliable imaging method to diagnosis upper urinary tract calculi (12). The basic advantages of spiral CT are its high sensitivity and specificity in detecting urinary calculi (including nonopaque calculi), celerity, and safety (2, 13). Clinical evidence has confirmed that spiral CT may significantly contribute to the improvement in identifying the chemical composition of upper urinary tract calculi (14, 15). Spiral CT can be conducted to determine the composition and brittleness of upper urinary tract calculi and thus provides a reference standard for the choice of treatment (16). Notably, determination of the chemical composition of upper urinary tract calculi, which is of critical importance in the selection of optimal management, is positively associated with subsequent treatment outcomes (17, 18). In this study, we conducted an in vivo evaluation of the chemical composition of eight types of urinary calculi using spiral CT in a Chinese population, which may contribute to improving the therapeutic effect, reducing complications, preventing stone recurrence, and minimizing unnecessary trauma.

MATERIALS AND METHODS

Ethics Statement

The Ethics Committee of the First Affiliated Hospital of China Medical University approved our study design. All patients had to sign informed consent in written form to undergo renal colic protocol spiral CT at the time of hospitalization.

Subjects

From October 2011 to February 2013, a total of 122 patients (73 males and 49 females) with upper urinary tract calculi admitted to the Department of Urinary Surgery in the First Affiliated Hospital of Soochow University for ureterorenoscopy were included in this study. These 122 patients included 80 patients with renal calculi and 51 patients with ureteral calculi. The mean age of patients was 48.3 years (range, 21~84 years).

Fig. 1. Spiral CT scanning of (A) pure calculi and (B) mixed calculi.

Methods

Before ureterorenoscopy, all patients were scanned with a 64-detector row helical CT scanner using 6.50 mm collimation at the energy level of 120 kV at 330 mA. All images were acquired by the picture archiving and communication systems (PACS), and stored for subsequent evaluation by two radiologists blinded to the chemical composition of the calculi during a consensus reading session. For each calculus, a region of interest (ROI) overlying the whole calculi on the slice was obtained for each plane for tissue and bone windows at 120 kV. The absolute Hounsfield units (HU) value of each stone is presented for the central ROI of the plane that passed through the maximum transverse diameter. The average, highest, and lowest CT-numbers of upper urinary calculi were assessed on the basis of differences in densities measured in HU, which were recorded within the ROI using a conventional soft-tissue window (window width, 250H; level,

TABLE 1. The CT Values of Eight Types of Urinary Calculi

Urinary calculi	<i>n</i>	Mean	SD	SE	95% CI		Min	Max
					LL	UL		
Calcium oxalate	39	1057.79	71.449	11.441	1034.63	1080.96	912	1185
Calcium phosphate	12	1125.92	67.353	19.443	1083.12	1168.71	1046	1210
Calcium carbonate	10	770.30	87.469	27.660	707.73	832.87	610	875
Magnesium ammonium phosphate	8	631.38	75.676	26.755	568.11	694.64	530	720
Carbonated apatites	6	948.33	90.608	36.991	853.25	1043.42	830	1080
Uric acid/ammonium urate	21	349.10	77.761	16.969	313.70	384.49	213	460
Uric acid/calcium oxalate	10	670.20	72.718	22.996	618.18	722.22	530	740
Calcium oxalate/calcium phosphate	16	1335.56	50.636	12.659	1308.58	1362.54	1263	1412

SD, standard difference; SE, standard error; 95% CI, 95% confidence interval; LL, lower limit; UL, upper limit; Min, minimum; Max, maximum.

45H) at 120 kV. The visual density of stones was studied using a three-level scale (level 1: low density; level 2: intermediate density; level 3: high density). Qualitative analysis of eight main components (urate, oxalate, phosphate, carbonate, calcium, magnesium, ammonium, and cystine) in upper urinary tract calculi were detected using the standard urinary calculi analysis kit provided by the Institute of Urolithiasis in the First Affiliated Hospital of Guangzhou Medical College.

Statistical Analysis

Data were presented as mean $\pm$ standard deviation (mean $\pm$ SD) or frequencies. The χ^2 test was used to compare frequencies. One-way analysis of variance (ANOVA) and Student's *t*-test were used for normally distributed variables, whereas the Mann-Whitney's *U* test was used for nonnormally distributed variables. Comparisons between the two groups for nominal variables were made using the least significant difference (LSD) post hoc test. All statistical analyses were performed using the SPSS 18.0 software (SPSS, Inc., Chicago, IL). $P < 0.05$ was considered statistically significant.

RESULTS

The analysis of chemical composition indicated that there were five types of pure calculi ($n = 90$) and three types of mixed calculi ($n = 37$, Fig. 1), including 39 calcium oxalate calculi (29%), 12 calcium phosphate calculi (9%), 10 calcium carbonate calculi (8%), 8 magnesium ammonium phosphate calculi (6%), 6 carbonated apatite (5%), 21 uric acid/ammonium urate calculi (16%), 10 uric acid/calcium oxalate calculi (8%), and 16 calcium oxalate/calcium phosphate calculi (12%).

The mean CT values of each type of urinary calculi were as follows: calcium oxalate calculi (1058 ± 71 HU); calcium phosphate calculi (1126 ± 67 HU); calcium carbonate calculi (770 ± 87 HU), magnesium ammonium

TABLE 2. Differences in the Mean CT Values of Eight Types of Urinary Calculi

<i>P</i> -value	Urinary calculi							
	1	2	3	4	5	6	7	8
1	–	0.000	0.000	0.000	0.000	0.000	0.000	0.000
2	0.000	–	0.005	0.000	0.000	0.001	0.000	0.000
3	0.000	0.005	–	0.000	0.000	0.000	0.000	0.000
4	0.000	0.000	0.000	–	0.000	0.000	0.003	0.000
5	0.000	0.000	0.000	0.000	–	0.000	0.262	0.000
6	0.000	0.001	0.000	0.000	0.000	–	0.000	0.000
7	0.000	0.000	0.000	0.003	0.262	0.000	–	0.000
8	0.000	0.000	0.000	0.000	0.000	0.000	0.000	–

1, uric acid/ammonium urate calculi; 2, calcium oxalate calculi; 3, calcium phosphate calculi; 4, calcium carbonate calculi; 5, magnesium ammonium phosphate calculi; 6, carbonated apatites calculi; 7, uric acid/calcium oxalate calculi; 8, calcium oxalate/calcium phosphate calculi.

phosphate calculi (631 ± 76 HU); carbonated apatites calculi (948 ± 90 HU), uric acid/ammonium urate calculi (349 ± 78 HU); uric acid/calcium oxalate calculi (670 ± 73 HU), and calcium oxalate/calcium phosphate calculi (1335 ± 51 HU). The CT values of each type of urinary calculi are shown in Table 1.

There were significant differences in the mean CT values among five types of pure calculi ($P < 0.001$). Furthermore, we also observed significant differences in the mean CT values among three types of mixed calculi ($P < 0.001$). Significant differences in the mean CT values were also found among eight types of urinary calculi ($P < 0.001$). However, no statistically significant difference in the mean CT values was observed between magnesium ammonium phosphate calculi and uric acid/calcium oxalate calculi ($P = 0.262$, as shown in Table 2).

DISCUSSION

Spiral CT is a type of three-dimensional CT that is becoming frequently used for radiographic examination and

is a relatively safe, rapid, and accurate diagnostic method for urinary calculi (12, 19). Clinically, spiral CT has been suggested to have a positive effect on density resolution and contrast, and to be unaffected by interference from overlapping bone and intestinal contents, features that are particularly helpful for obtaining the desired measurements of upper urinary tract calculi (13, 20). Particular in cases where patients have nonfunctioning kidney or iodine allergies, the use of spiral CT performs significantly better on excluding upper urinary tract obstruction or urolithiasis, as well as determining the stone size, location, and values (21). Furthermore, in view of the fast and continuous development of medical science and technology, accompanied by increasingly sophisticated two-dimensional CT images and 3D reconstruction techniques, the use of spiral CT has become central to a new noninvasive examination method for successfully diagnosing urinary system diseases (14, 15). Previous technologies, including US, necessary X-ray examination, and plain KUB radiographs, have been demonstrated to be limited by several constraining factors in accurately diagnosing upper urinary tract calculi and in determining the size, composition, amount and position of the calculi, bowel content, obstruction, and infection, etc. (7–9). Theoretically, 90% of stones can be found by X-ray and KUB, however the actual display rate of both have been shown to be lower than actual rates, thereby seriously hindering the diagnosis of calculi (22). Therefore, there is strong reason to believe that spiral CT is more powerful in determining the clinical treatment of upper urinary tract calculi. (23). More specifically, spiral CT can be conducted to determine the composition of calculi by measuring stone location, size, and average CT value, which provide a reference for analyzing the composition of upper urinary tract calculi since different calculi components may show different CT values (24). Interestingly, a previous experimental study revealed that the analysis outcome of X-ray spectroscopy for calculi from a performed percutaneous nephrolithotomy was only able to evaluate several calculi, including struvite, uric acid, cystine stones, and calcium stones (23). However, with spiral CT, a total of 11 categories of stone composition are able to be obtained through chemical analysis (23). Therefore, spiral CT may be a more feasible method for accurately determining the chemical composition of the upper urinary tract calculi (25). Indeed, determining calculi composition is of great importance in providing information for appropriately treating urinary calculi, reducing complications, preventing recurrent calculi, and decreasing unnecessary trauma (17, 18). Therefore, we conducted a correlation study on the efficacy of spiral CT in identifying the chemical composition of upper urinary tract calculi.

In this study, we assessed whether spiral CT with advanced postimage processing can accurately differentiate the chemical composition of upper urinary tract calculi.

Nonenhanced spiral CT scans were performed on a total of 131 preoperative patients with upper urinary tract calculi. Our study results showed that we could differentiate the chemical composition of all pure calculi and mixed calculi with absolute HU values at 120 kV, suggesting that the measurement of absolute HU values and HU density via spiral CT scanning with a small collimation size can reveal significant differences among all pure urinary calculi and most of the mixed calculi. A study conducted by Mitcheson et al. and Newhouse et al. confirmed that the chemical composition of all pure calculi could be differentiated by spiral CT scan and found a similar association for mixed calculi (26, 27). Although we still do not fully understand the precise reasons why a spiral CT scan can differentiate the chemical composition of all pure calculi and mixed calculi, one possible explanation is that there were no significant differences between calculi volume and absolute HU values for most calculi in our study. Sheir et al. also found no obvious association between calculi volume and absolute HU values in their study (26). Another explanation may be that the spiral CT examinations used in our study were performed at 120 kV, which almost all previous studies found most useful. Mostafavi et al. also reported in their study that the best single CT parameter for assessing the chemical composition of calculi was the absolute CT-attenuation value at 120 kV (28). The results of our study also revealed that a spiral CT could differentiate the chemical composition of all calculi besides magnesium ammonium phosphate calculi and uric acid/calcium oxalate calculi. Our findings agreed with Motley et al. and Nakada et al., who found statistically significant differences between pure uric acid calculi and calcium oxalate calculi, but not between uric acid and calcium oxalate calculi, and magnesium ammonium phosphate calculi (29, 30). Although the precise reason why uric acid/calcium oxalate calculi and magnesium ammonium phosphate calculi could not be differentiated from all pure calculi and the mixed urinary calculi is still poorly understood, it may be caused to some extent by calculi composition and size. As Saw et al. concluded, calculi composition and size may influence CT attenuation independently (31). Our results demonstrated that absolute HU values and HU density derived from spiral CT scanning using a small collimation size could uncover statistically significant differences among all pure and most mixed urinary calculi, permitting greater accuracy in the prediction of calculi composition. Furthermore, this technique permits diagnostic conclusions on the basis of a single CT evaluation. In order to improve the accuracy of spiral CT to analyze the chemical compositions of upper urinary tract calculi and to reduce the selection of partial volume effect and interested regions, it is crucial to establish optimal scan parameters and reduce radiation doses to patients. More large-sample and multicenter

research data are needed to support our findings due to the current lack of large-sample studies and standard examination methods.

In conclusion, our findings provide empirical evidence that spiral CT could be a promising tool for determining the chemical composition of upper urinary tract calculi. Thus, spiral CT may be recommended before selecting a method of treatment for urinary calculi.

ACKNOWLEDGMENTS

We thank the reviewers for their helpful comments on this article.

REFERENCES

- Liu CC, Huang SP, Wu WJ, et al. The impact of cigarette smoking, alcohol drinking and betel quid chewing on the risk of calcium urolithiasis. *Ann Epidemiol* 2009;19:539–545.
- Niemann T, van Straten M, Resinger C, Bayer T, Bongartz G. Detection of urolithiasis using low-dose CT—A noise simulation study. *Eur J Radiol* 2011;80:213–218.
- Zeng G, Mai Z, Zhao Z, et al. Treatment of upper urinary calculi with Chinese minimally invasive percutaneous nephrolithotomy: A single-center experience with 12,482 consecutive patients over 20 years. *Urolithiasis* 2013;41:225–229.
- Knoll T, Schubert AB, Fahlenkamp D, et al. Urolithiasis through the ages: Data on more than 200,000 urinary stone analyses. *J Urol* 2011;185:1304–1311.
- Borghi L, Nouvenne A, Meschi T. Nephrolithiasis and urinary tract infections: ‘The chicken or the egg’ dilemma? *Nephrol Dial Transplant* 2012;27:3982–3984.
- Edvardsson VO, Indridason OS, Haraldsson G, Kjartansson O, Palsson R. Temporal trends in the incidence of kidney stone disease. *Kidney Int* 2013;83:146–152.
- Nadeem M, Ather MH, Jamshaid A, et al. Rationale use of unenhanced multi-detector CT (CT KUB) in evaluation of suspected renal colic. *Int J Surg* 2012;10:634–637.
- Kambadakone AR, Eisner BH, Catalano OA, Sahani DV. New and evolving concepts in the imaging and management of urolithiasis: Urologists’ perspective. *Radiographics* 2010;30:603–623.
- Viprakasit DP, Sawyer MD, Herrell SD, Miller NL. Limitations of ultrasonography in the evaluation of urolithiasis: A correlation with computed tomography. *J Endourol* 2012;26:209–213.
- Kaszniak-Brown J, Karnati G. Colicky patients: Is radiology necessary? *Br J Hosp Med (Lond)* 2011;72:M98–M103.
- Moore CL, Daniels B, Singh D, Luty S, Molinaro A. Prevalence and clinical importance of alternative causes of symptoms using a renal colic computed tomography protocol in patients with flank or back pain and absence of pyuria. *Acad Emerg Med* 2013;20:470–478.
- Thomas C, Heuschmid M, Schilling D, et al. Urinary calculi composed of uric acid, cystine, and mineral salts: Differentiation with dual-energy CT at a radiation dose comparable to that of intravenous pyelography. *Radiology* 2010;257:402–409.
- Ray AA, Ghiculete D, Pace KT, Honey RJ. Limitations to ultrasound in the detection and measurement of urinary tract calculi. *Urology* 2010;76:295–300.
- Pichler R, Skradski V, Aigner F, Leonhartsberger N, Steiner H. In young adults with a low body mass index ultrasonography is sufficient as a diagnostic tool for ureteric stones. *BJU Int* 2012;109:770–774.
- Oz U, Orhan K, Abe N. Comparison of linear and angular measurements using two-dimensional conventional methods and three-dimensional cone beam CT images reconstructed from a volumetric rendering program in vivo. *Dentomaxillofac Radiol* 2011;40:492–500.
- Li XH, Zhao R, Liu B, Yu YQ. Determination of urinary stone composition using dual-energy spectral CT: Initial in vitro analysis. *Clin Radiol* 2013;68:e370–e377.
- Kijviki K, de la Rosette JJ. Assessment of stone composition in the management of urinary stones. *Nat Rev Urol* 2011;8:81–85.
- Lopez M, Hoppe B. History, epidemiology and regional diversities of urolithiasis. *Pediatr Nephrol* 2010;25:49–59.
- Mahabadi AA, Achenbach S, Burgstahler C, et al. Safety, efficacy, and indications of beta-adrenergic receptor blockade to reduce heart rate prior to coronary CT angiography. *Radiology* 2010;257:614–623.
- Claves JL, Wise SW, Hopper KD, et al. Evaluation of contrast densities in the diagnosis of carotid stenosis by CT angiography. *AJR Am J Roentgenol* 1997;169:569–573.
- Smith RC, Rosenfield AT, Choe KA, et al. Acute flank pain: Comparison of non-contrast-enhanced CT and intravenous urography. *Radiology* 1995;194:789–794.
- Foell K, Ordon M, Ghiculete D, et al. Does a baseline KUB help facilitate stone management in patients presenting to the emergency department with renal colic? *J Endourol* 2013;1–18.
- Hidas G, Eliahou R, Duvdevani M, et al. Determination of renal stone composition with dual-energy CT: In vivo analysis and comparison with x-ray diffraction. *Radiology* 2010;257:394–401.
- el-Assmy A, Abou-el-Ghar ME, el-Nahas AR, Refaie HF, Sheir KZ. Multidetector computed tomography: Role in determination of urinary stones composition and disintegration with extracorporeal shock wave lithotripsy—An in vitro study. *Urology* 2011;77:286–290.
- Patel U, Walkden RM, Ghani KR, Anson K. Three-dimensional CT pyelography for planning of percutaneous nephrostolithotomy: Accuracy of stone measurement, stone depiction and pelvicalyceal reconstruction. *Eur Radiol* 2009;19:1280–1288.
- Sheir KZ, Mansour O, Madbouly K, Elsobky E, Abdel-Khalek M. Determination of the chemical composition of urinary calculi by noncontrast spiral computerized tomography. *Urol Res* 2005;33:99–104.
- Newhouse JH, Prien EL, Amis ES, Jr., Dretler SP, Pfister RC. Computed tomographic analysis of urinary calculi. *AJR Am J Roentgenol* 1984;142:545–548.
- Mostafavi MR, Ernst RD, Saltzman B. Accurate determination of chemical composition of urinary calculi by spiral computerized tomography. *J Urol* 1998;159:673–675.
- Motley G, Dalrymple N, Keesling C, Fischer J, Harmon W. Hounsfield unit density in the determination of urinary stone composition. *Urology* 2001;58:170–173.
- Nakada SY, Hoff DG, Attai S, et al. Determination of stone composition by noncontrast spiral computed tomography in the clinical setting. *Urology* 2000;55:816–819.
- Saw KC, McAteer JA, Monga AG, et al. Helical CT of urinary calculi: Effect of stone composition, stone size, and scan collimation. *AJR Am J Roentgenol* 2000;175:329–332.