

Impact of urinary stone volume on computed tomography stone attenuations measured in Hounsfield units in a large group of Austrian patients with urolithiasis

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Introduction To investigate retrospectively the impact of urinary stone volume on computed tomography stone attenuations measured in Hounsfield units in 253 patients with urolithiasis.

Material and methods CT scans were performed in 253 patients with suspected urinary stone disease from 2008 to 2010 using CT-Scanner Siemens, SOMATOM, Sensation 64. One experienced radiologist (A.L.) who was blinded to the chemical composition of the stones retrospectively reviewed images and analyzed data to determine the composition of the stones. The results were compared with the biochemical analysis results obtained by infrared spectroscopy (100 FTIR, PerkinElmer).

Results 253 consecutive patients from 2008 to 2010 were included into analysis: 189 males, and 64 females. Mean age was 51.2. According to stone volume, stones were divided into 2 groups: 126 stones with volume of 4.3 mm or more, 127 stones with volume less than 4.3 mm. There was a significant relationship between stone volume and its CT attenuation only in stones with a volume 4.3 mm or more ($p < 0.05$).

Conclusions We failed to show a significant relationship between stone volume and its attenuations in Hounsfield units. We could not distinguish uric acid stones from non uric acid stones.

Key Words: computed tomography ◊ uric acid stones ◊ Hounsfield units ◊ none uric acid stones ◊ regions of interest ◊ shock wave lithotripsy

INTRODUCTION

Current evidence suggests an increasing prevalence of urinary stone disease in Western countries [1]. Main determinants in the clinical care of patients with urolithiasis are the location, size, and chemical composition of the calculi, the latter being particularly important in the presence of uric acid (UA) stones, since UA stones may be dissolved by urinary alkalinization.

The imaging modality of choice for the detection of urinary stone disease is unenhanced computed tomography (CT), offering high specificity and sensitivity [2].

However, despite promising in vitro results, the transferability of results to an in vivo setting was hampered by misregistration problems [3].

Symptomatic urinary stone disease affects approximately 900,000 persons in the United States each year, resulting in annual medical costs of \$ 5.3 billion [4]. The lifetime prevalence of urinary stone disease was estimated to be 10–14% [5]. The morbidity associated with urolithiasis includes colic pain and kidney obstruction, which can lead to renal failure and severe urinary tract infections such as pyelonephrosis and septic shock. Moreover, the institution of further prophylactic measures to prevent recurrences is of utmost importance. This necessitates a thorough metabolic workup and an accurate quantitative stone analysis. Without an appropriate workup, stone analysis and proper follow up, the recurrence rates may be as high as 10–23%/year and may reach to 50% within 5 years [6]. Among all types of urinary

stones, the frequency of calcium stone is 70–80%, struvite stone 5–10%, uric acid stone 5–10%, and cystine stone 1% [7].

In general, stones composed of UA are broken up easily by shock waves, whereas stones of calcium oxalate monohydrate (COM), brushite, or cystine are difficult to break [8].

Previous attempts [9, 10, 11] to predict stone composition using spiral CT were based on the analysis of CT attenuations. They could discriminate UA from non-UA stones.

Zarse et al. [12] demonstrated that high-resolution spiral CT yields unique CT attenuations for common types of stones if proper window settings are used to localize homogeneous regions within the stones.

Currently, the following methods are available for stone analysis: (1) chemical analysis, (2) emission spectroscopy, (3) polarizing spectroscopy, (4) X-ray diffraction, (5) X-ray coherent scatter/crystallography, (6) thermogravimetry, (7) scanning electron microscopy, and (8) infrared spectroscopy [6, 2].

Chemical analysis was traditionally used most widely due to its ease and low cost. However, this is time consuming, necessitates large stone samples and cannot distinguish between the two commonly occurring calcium stones (monohydrate/dihydrate). With the exception of infrared spectroscopy, none of the above can provide a reliable quantitative stone analysis [6].

Contradictory findings were published in literature regarding the ability of helical CT to accurately assess the chemical composition of urinary stones. Two *in vivo* studies [9, 10], both conducted at 120 kV with 3–5 mm collimation, concluded that CT density (attenuation/stone size) was the best predictor of stone composition and could differentiate UA from calcium oxalate stones. Most *in vitro* studies [14, 15] placed human calculi in a water bath to evaluate CT-attenuation values as parameters predicting stone composition; they could distinguish UA stones from other stones. However, cystine and UA stones were identified in only one study [13].

The aim of the present study was to investigate retrospectively the impact of urinary stone volume on computed tomography stone attenuations measured in Hounsfield units in 253 patients with urolithiasis using postoperative *in vitro* infrared spectroscopy (100 FTIR, PerkinElmer).

MATERIAL AND METHODS

Patients and diagnosis

This retrospective study was approved by the institutional ethics board of our university. From 2008 to

2010, 253 consecutive patients (189 men, 64 women) with urolithiasis were included into our analysis. Children and pregnant women were excluded from the study.

In patients with acute flank pain, suspected of having urinary stones, we performed so called “stone CT”, which is an unenhanced low-dose-CT. Participants were scanned using a 64-slice computed tomography unit (Siemens AG, SOMATOM, Sensation 64, Erlangen, Germany).

One unenhanced scan (Acquisition: 64x0.6 mm, 120 kV, 150 mAs) of the abdomen and the pelvis with a slice thickness of 3 mm was made. This protocol is routinely used at our institution to evaluate patients with acute flank pain suspected to have renal colic. No oral or intravenous contrast material was administered. A region of interest (ROI) was drawn on each stone, and the attenuation was measured. Regions of interest were defined according to the largest possible area for each stone. Analysis was performed at a workstation. The sizes and positions of the regions of interest were validated by an experienced abdominal radiologist (A.L) by using a conventional soft-tissue window and narrow bone windows. When the calculi had irregular contours, special attention was given not to include any surrounding soft tissue, which has much lower CT-attenuation values than calculi. The average, highest, and lowest CT-attenuation values in Hounsfield units were calculated. Our abdominal radiologist, who was blinded to the chemical composition of the stones, retrospectively reviewed the imaged and analyzed data to determine the HU of the calculi. The results were compared with the biochemical analysis results obtained by infrared spectroscopy.

Data and statistical analysis

SPSS software package version 13 (SPSS, IBM, Chicago, Illinois) was used. Variables were compared by ANOVA. Hereby, the *p* values were based on Levene’s test of equality of means. The Tukey’s test was used for post-hoc comparisons. A probability *p* level of less than 0.05 was considered statistically significant. All statistical tests were two-sided.

According to the European Association of Urology [2] the size of a concrement (stone burden) can be expressed in different ways.

The most common way of expressing size in the literature is to use the largest diameter, i.e. the length of the stone as measured on a plain film. The stone surface area (SA) can be estimated for most stones from the length (*l*) and width (*w*) of the stone using the following formula $SA = l \cdot w \cdot \pi \cdot 0.25$ ($\pi=3.14159$)

With the more common use of CT examinations, it is possible to get an even better estimate of the stone volume (SV) by combining measures of length (l), width (w) and depth (d) using the formula:
 $SV = l \cdot w \cdot d \cdot \pi \cdot 0.167$ ($\pi = 3.14159$).

Stone analysis

The biochemical composition of the stone was established after spontaneous passage, operation or shock wave lithotripsy. Stone analysis was based on infrared spectroscopy, which determines the molecular and crystalline composition of the stone. Infrared spectroscopy [15] is the spectroscopy that deals with the infrared region of the electromagnetic spectrum, that is light with a longer wavelength and lower frequency than visible light. It covers a range of techniques, mostly based on absorption spectroscopy. As with all spectroscopic techniques, it can be used to identify and study chemicals. A common laboratory instrument that uses this technique is a Fourier transform infrared (FTIR) spectrometer. We used PerkinElmer Spectrum 100 FTIR Spectrometer (PerkinElmer, Shelton, USA) to analyse urinary stones after passage or operation. -

RESULTS

We included 253 patients from 2008 to 2010 into our analysis (189 men and 64 women) with the mean age being 51.2 years and the median age 49.6 years (see Table 1). According to urinary stone incidence in relation to gender, we found a male predominance (2.9 higher risk).

There were 134 pure calcium oxalate monohydrate (Whewellit, COM) calculi, 29 stones with 50% uric

acid and 50% whewellit, 29 stones with 80% whewellit and 20% cystine and 12 pure calcium oxalate dihydrate (Whedelit, COD).

There were 49 mixed calculi according to their chemical compositions: struvite, carbonate, and xanthine, as well as protein.

The calculi were divided into 4 groups according to their clinical relevance:

- 1 – calcium oxalate monohydrate and dihydrate,
- 2 – uric acid stones,
- 3 – struvite,
- 4 – cystine.

The overall differences between the densities of the stones was not statistically significant (Table 2) ($p = 0.05$) and there was a cross-over in densities among all studied stones; a sharp demarcation among different types could not be found.

To study the effect of stone volume on density, we divided the stones into 2 groups according to their median stone volume values:

Group 1. 126 stones with stone size $>37.78 \text{ mm}^3$ and volume $>4.3 \text{ mm}$

Group 2. 127 stones with stone size $<37.78 \text{ mm}^3$ and volume $<4.3 \text{ mm}$.

The smallest stone had a size of 0.5 mm^3 and a volume of 0.9 mm . The largest stone had a size of 3620 mm^3 and a volume of 19 mm .

When the calculi were compared with each other, Levene's test was used.

The Hounsfield unit values for different types of calculi are shown in Table 3.

We compared groups 1 and 2 with each other according to Levene's test. There was significant relationship between stone volume and CT attenuation only in stones with a volume 4.3 mm or more ($p < 0.05$)

Table 1. Patients and study objects

	Number	Age (mean)	Standard deviation	Age (median)	Minimum	Maximum
Male	189	51.5	14.9	49.6	20.6	86.0
Female	64	50.4	16.0	49.7	22.1	87.3
Total	253	51.2	15.2	49.6	20.6	87.3

Table 2. HU of calcium and uric acid as well as for cystine and struvite stones

Groups(volume)	Number	Mean value	Standard deviation	Median	Minimum	Maximum
Ca-Oxalat	165	624.4	309.2	588	64	1552
Uric acid	29	385.8	167.3	414	112	768
Struvite	30b	678.1	334.2	588.5	221	1443
Cystine	29	713.2	317.2	641	150	1358
Total	253	613.6	311.5	573	64	1552

Table 3. Groups of uric acid and non-ua according to stones volume

Groups	Groups volume	Number	Mean value	Standard deviation	Median	Min	Max	95% confidence range upper limit	95% confidence range lower limit
Uric acid	1	16	302.7	168.3	289.5	112	768	213	392.4
	2	13	488	96.9	492	302	644	429.5	546.6
	Total	29	385.8	167.3	414	112	768		
Non uric acid	1	111	444.1	218.6	430	64	1142	403	485.2
	2	113	838.5	267.4	836	235	1552	788.7	888.4
	Total	224	643.1	313.9	591	64	1552		
Total	1	127	426.3	217.5	402	64	1142	388.1	464.5
	2	126	802.4	276.4	792	235	1552	753.6	851.1
	Total	253	613.6	311.5	573	64	1552		

(Figures 1 and 2). In order to study this trend, we performed a logistic regression analysis for the prediction of the stone composition, which failed to show any significant differences between group 1 and 2. Figure 3 shows an example of FTIR–Spectrum 100% Whewellit.

DISCUSSION

Yagisawa [16] showed that male patients had a significantly higher number of metabolic abnormalities than female patients, which is in agreement with our results which showed that urinary stone incidence has a male predominance (2.9 higher risk).

The clinical management of urinary tract stones depends on the location, size, and number of calculi, as well as their chemical composition. The success rate with shock wave lithotripsy depends on these factors in addition to stones fragility. Cystine, brushite, and

calcium oxalate monohydrate stones are less fragile and may be better treated with shock wave lithotripsy. Patients with uric acid stones may be treated medically by means of urine alkalization with or without shock wave lithotripsy [5].

Since the early 1990s, the use of unenhanced CT has gained widespread acceptance in the evaluation of nephrolithiasis. Studies showed that helical CT can depict urinary stones more precisely than radiography, nephrotomography and excretory urography [8]. The ability to predict the stone composition before treatment by CT helps in triaging patients. It enables the selection of patients with small UA-containing stones who benefit from medical management rather than shock wave lithotripsy [1, 11].

The usefulness of CT in making treatment decisions depends on the size, burden and location of the stone, as well as the degree of obstruction [3]. Due to the fact that uric acid stones are composed of only

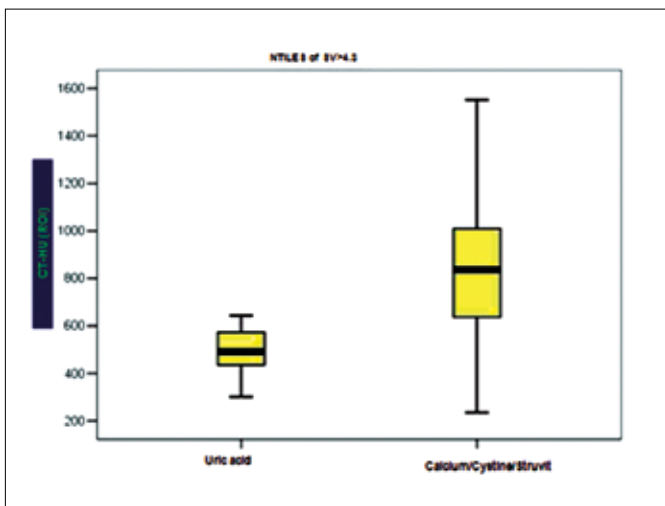


Figure 1. Group 1. CT stone Hounsfield units in stones with volume >4.3 mm. Group 1. stones with volume >4.3 mm on X axes and their Hounsfield units on y axes.

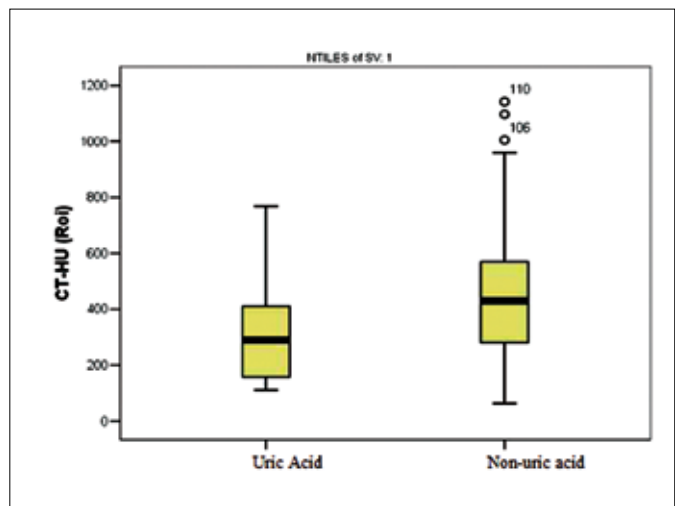


Figure 2. Group 2 CT stone Hounsfield units in stones with volume <4.3 mm. Group 2 Stones with volume <4.3 mm on x axes and their Hounsfield units on y annex.

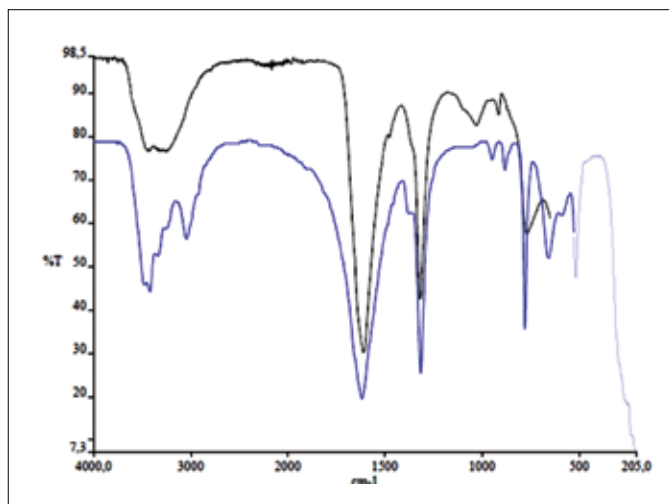


Figure 3. Example of FTIR-Spectrum for a 100% Whewellit stone.

light chemical elements (H, C, N, O), their x-ray attenuation properties are different compared to those characteristic of non-uric acid stone types such as calcium oxalate, and cystine. Non-uric acid stones include heavy elements (P, Ca, S). Consequently, uric acid stones have higher CT attenuations at higher kVp values than at lower kVp values, whereas non-uric acid stones have higher CT attenuations at lower kVp values than at higher kVp values [3, 4]. Since the early 1980s, several studies were conducted in an attempt to determine the chemical composition of stones on the basis of X-ray attenuation in vitro and in vivo. For our study, we used the largest number ($n = 253$) of stones so far described, to the best of our knowledge. The in vitro studies, however, did not reproduce normal abdominal wall and fat, perinephric fat or the spine, causing uncertainty about standardization of the values obtained. For example, Bellin [17] used excised pig kidney placed in water, Mostafavi [11] and Deveci [18] placed stones in air, Saw placed stones in water and Grosjean [3] used a jelly made of water, iodine and animal proteins surrounded with water. They did not study effect of stone size on its CT attenuation. Deveci [18] used an air-filled environment instead of phantoms containing water or fat. Thus, the density differences increased and overlap did not occur. Consequently, because the in vitro conditions were too far from the in vivo conditions, the results cannot be considered a reference for in vivo determination of chemical composition. Newhouse [13] failed to distinguish each type of stone from all other types at 120 kV. CT-attenuation values decline with smaller stones and wider collimation. Saw et al. [14] reported that a 1-mm collimation width allowed for better identification of stones than a 3-mm collimation. At a 10-mm

collimation, some uric acid stones with a diameter less than 4 mm could go undetected because of very low attenuation and partial volume effects.

In the last 2 decades, several studies were conducted to determine the chemical composition of stones using CT. Some authors reported promising results with the ability to identify all types of stones studied [11, 18]. Mostafavi [11] studied 102 pure stones with CT scanning at both 80 and 120 kV and was able to differentiate the most common stone types (struvite, cystine, and calcium oxalate) using single energy scanning at 120 kV. Dual energy scanning was used to differentiate the stones of similar densities. Deveci et al. [18] found that using an absolute CT value at 120 kV, all types of renal calculi could be differentiated from each other. The pure stones from the least to the most dense were as follows: UA, struvite, cystine, calcium phosphate, and calcium oxalate. Nakada et al. [9] analyzed 129 stones in an in vivo setting. In 99 patients, they identified 82 calculi predominantly composed of calcium oxalate and 17 calculi predominantly composed of UA. Motley [10] evaluated 100 pure human stones. All were visualized by CT before stone retrieval. When the HU values of calcium, UA, struvite, and cystine stones were compared, the overlap of ranges precluded accurate identification. By contrast, some authors reported limitations in identification of stone composition using CT. Saw [14] studied 127 stones at 1, 3 and 10 mm collimation and could differentiate the stone types studied except for brushite from hydroxyapatite at 1 mm collimation. Newhouse [13] could not distinguish calcium-based and struvite-based stones from each other. Grosjean [2] showed that an overlap between different types of stones prohibited a reliable determination of chemical composition by two subsequent scans and this was explained by the movement of the kidneys as a result of respiration. Hidas [5] could not distinguish struvite stones and the subtypes of calcium stones; this may be due to real chemical overlap between stone compositions and differences in absorption among patients of different sizes. Numerous factors influence the measured CT-attenuation values of a stone, mainly beam-collimation width, stone size and X-ray energy levels [15], CT-attenuation values decline with smaller stones and wider collimation. 1 mm collimation width allowed better identification of stones more than 3 mm collimation. We used 3 mm collimation. According to Saw et al. [15], this may be the cause of not differentiating among stone types of <4.3 mm. Nakada [9] reported that a more narrow collimation decreases the volume averaging artefact and improves the measurement of attenuation and size.

Our results are partially in agreement with the findings of Primak et al. [4] who could not identify small stones (<3 mm). Ascenti [19] et al. identified all stones with a diameter of >3 mm with a lower-dose single energy CT. According to Ascenti [19], characterization of stones <3 mm is often clinically less important because a high percentage of stone spontaneous passage. We failed to distinguish between UA and non UA stones because our analyzed stones were not pure stones, which are not uncommon in a clinical setting and most stones are not pure stones. Contradictory results were documented by Matlaga et al. [20] who found no significant differences in stones size among UA and calcium oxalate groups. Medical prophylaxis to prevent recurrence is still at the core of the treatment of urinary stone disease. Stone analysis complements, but does not replace, urine and serum studies to assess for metabolic stone disease. However, stone analysis can present useful information, as it represents a biochemical patient history, documenting the urinary environment over time through type and conformation of crystal deposition [21]. Quality control studies conducted in Europe from 1980 to 2001 [22] demonstrated that the overall accuracy of stone analysis was improving with time and experience. FT-IR and x-ray diffraction methods were most reliable for artificial stone substances, but wet chemical methods produced an

error rate from 6.5–94%. With existing technology, several steps could increase the reliability of stone analysis. Due to incomplete sampling leading to errors, all stones obtained by the patient or the surgeon should be submitted for analysis; this gives the analysis laboratory the best chance to detect all components that are present [21].

According to Singh [6], infrared spectroscopy is a sensitive, reliable, accurate, safe, and quick method of accurate stone analysis suitable for use in a clinical laboratory. The high degree of accuracy is possible due to the computerized area-measurements of specific absorption peaks of the spectrum of each sample, mean error rate being ± 2 –2.5%. The quantitative stone analysis by infrared spectroscopy allows accurate separate zone wise analysis of the stone nucleus, external and internal layers not possible by other methods.

Limitations of our study: results should be interpreted with caution because the retrospective design of our study.

CONCLUSIONS

We failed to show the effect of stone volume on its attenuations, and could not distinguish UA from non UA stones because most of our analyzed stones were not pure stones. More prospective studies are highly recommended.

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