Assessment of stone composition in the management of urinary stones

Kittinut Kijvikai and J. J. M. de la Rosette

Abstract | Several explanations have been suggested to account for the failure of extracorporeal shockwave lithotripsy (ESWL) treatment in patients with urinary stones, including large stone volume, unfavorable stone location or composition and the type of lithotriptor used. Unfavorable stone composition is considered a major cause of failure of ESWL treatment, and consequently knowledge of the stone composition before treatment is initiated is desirable. Plain abdominal radiographs cannot accurately determine either stone composition or fragility, and although the CT attenuation value in Hounsfield units (HU) (that is, normalized to the attenuation characteristics of water) is useful, this parameter has limited value as a predictor of stone composition or the response to ESWL treatment. By contrast, stone morphology as visualized by CT correlates well with both fragility and susceptibility to fragmentation by ESWL. For patients prone to recurrent calculi, analyses of stone composition are especially important, as they may reveal an underlying metabolic abnormality. The development of advanced imaging technologies that can predict stone fragility is essential, as they could provide extra information for physicians, enabling them to select the most appropriate treatment option for patients with urinary stones.

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Introduction

The risk of genitourinary stone disease varies around the world. In the US, it is around 13%, compared to around 5–9% in Europe. In Asia, the risk of stone formation seems to be lower at 1–5%.[1] Currently, the majority of stone patients can be treated by minimally invasive procedures, such as extracorporeal shockwave lithotripsy (ESWL). Although the success rate of ESWL is up to 90% for upper urinary tract stones <2 cm in diameter, the stones cannot always be fragmented.[2] Several factors have been suggested to explain this treatment failure, including stone composition.[3] Knowledge of stone composition before treatment initiated is, therefore, important, so that the most appropriate stone treatment modality can be selected. For example, if the stone is a type that is not amenable to fragmentation by ESWL, other modalities of treatment should be considered. However, stone retrieval and chemical analysis may not always be possible before treatment begins. Moreover, even if the major components of a stone are known, the prediction of its fragility is still complicated.[4]

Ideally, assessments of stone composition should be performed by using a simple, noninvasive method such as plain abdominal radiography or ultrasonography. However, ultrasonography is operator dependent and it is not able to classify subtypes of calcium stones. Neither ultrasonography nor radiography are sensitive enough to predict stone fragility. At present, several techniques, in particular CT, are being studied and several investigators have tried to formulate a reproducible method to predict the outcome of ESWL treatment from imaging findings.

In this Review, we address the importance of stone composition assessment before initiation of treatment in stone diseases. We also review the capability of various imaging modalities to determine stone composition and assess stone fragility, as these variables can affect the outcome of treatments for stone diseases.

Stone composition and fragility

Chemical composition

The concept of stone fragility and its effect on fragmentation was first described in 1988 by Dretler *et al.*,[3] who found that the rate of re-treatment with ESWL varied with stone composition. Calcium oxalate monohydrate stones required subsequent treatment sessions more often than calcium oxalate dihydrate and struvite stones. Struvite, uric acid and calcium oxalate dihydrate stones have a tendency to break into small pieces that can be passed easily, whereas calcium oxalate monohydrate stones usually break into large pieces that are more difficult to pass.[5,6]

Stone composition varies in different regions; for example, the composition of stones in the Indian subcontinent is different from that of stones in western countries.[7] Ansari and colleagues[7] studied the effect of stone composition on the fragility and clearance of upper urinary tract stones following ESWL in 300 renal and ureteral units. The majority of stones (90%) in individuals from the Indian continent were composed of calcium

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Key points

- The risk of urinary stone disease varies between 1% and 13% around the world and calcium oxalate lithiasis is the most common pathology worldwide
- Knowledge of the stone composition can uncover underlying metabolic abnormalities and help urologists to provide optimal treatment and also prevent stone recurrence
- Stone composition influences fragility, and thus knowledge of composition could enable urologists to predict the stone's susceptibility to fragmentation using extracorporeal shockwave lithotripsy (ESWL)
- Plain abdominal radiography is incapable of determining stone composition, and the CT attenuation value in Hounsfield units (HU) has limited value for this purpose
- Visualization of stone morphology on CT correlates well with susceptibility to ESWL, and could be used to select patients for this treatment
- For patients prone to recurrent stones, chemical analysis of stones (either following spontaneous passage or after stone collection via ESWL or endoscopic procedures) is important

oxalate. Of these, 80% were monohydrate and 20% were dihydrate stones, whereas the incidence of calcium oxalate monohydrate stones in patients from western countries was only 60–65%. Despite this discrepancy, the stone fragmentation rate achieved by ESWL was almost the same in both regions.[7] Fragmentation was classified as excellent, good, fair or absent. Excellent fragmentation was achieved in up to 64%, 50% and 100% of calcium oxalate dihydrate, struvite and uric acid stones, respectively, compared to 45% and 44% for calcium oxalate monohydrate and apatite stones. Fair fragmentation was seen in up to 9% and 3% of calcium oxalate monohydrate and apatite stones, respectively, compared to 6% or less in calcium oxalate dihydrate, struvite and uric acid stones. These data support the hypothesis that stone composition affects ESWL outcomes. However, reasons for the differences in fragility among the different type of stones are not well understood.

Crystal structure and morphology

Many factors influence the structural characteristics of renal stones. The absence of crystallization inhibitors, such as Zn, Mg and Mn, may have a critical role in stone formation. However, the role of these chemical elements in stone fragility is not well established.[8] The effects of specific chemical element concentrations in calcium oxalate monohydrate stones has been studied with respect to ESWL fragility in a cohort of 740 patients with a solitary calcium oxalate monohydrate stone of 5–20 mm in diameter in the renal pelvis. Stones with a low concentration of Zn, Mg and Mn were resistant to ESWL treatment.[5] This phenomenon can be explained by the fact that Zn, Mg and Mn are deposited between the interfaces of crystals that have differing composition. This process creates laminations, which increase the brittleness of stones. A lack of these elements during stone formation can, therefore, lead to the formation of compact and homogeneous crystals that are hard to fragment. This study demonstrated the importance of minor constituents of stones on stone fragility and on the effectiveness of ESWL treatment.

Calculi usually contain an initial core calculus. In some cases, the stone bulk consists of the same chemical elements as the core, but in others, the composition of the central core differs.[9] This phenomenon could explain why some calculi respond well to the initial ESWL session, but become resistant to subsequent treatment.

The role of radiography

The assessment of stone composition before starting treatment will unquestionably help physicians to optimize the management of stone diseases. The use of plain abdominal radiography for this purpose is of interest, as the technique is simple and widely available. However, researchers have raised concerns as to whether this method is sensitive enough to predict stone composition accurately. One study compared the radiodensity of stones to that of the ipsilateral 12th rib, to predict the outcome of lithotripsy.[10] The study was performed in 211 patients with solitary renal pelvic stones of <2 cm diameter. Results showed that this parameter is a useful marker of treatment outcome for stones >1 cm in diameter. The stone-free rate, measured at 3 months after treatment, was 60% if the stone had a radiodensity greater than that of the 12th rib, compared to a stone-free rate of 71% if the stone radiodensity was less than that of the 12th rib, although these differences were not statistically significant. However, for renal pelvic stones <1 cm in diameter, stone radiodensity as determined by a plain film was not predictive of successful ESWL treatment, and stone radiodensity did not correlate with stone composition.[10]

As an alternative method for evaluating the chemical composition of renal stones using conventional plain radiography, Oehlschlager *et al.*[11] digitized plain radiographs from patients with stones. The stone area was scanned using a digital camera, and the data were evaluated with a commercial graphics program to compare the total gray-scale levels of the images of the stones, which were assessed by using the histogram of an automatically marked stone surface from the film. Different stones could then be compared by calculating the difference between the histograms of the stone and of the area surrounding the stone. Using this method, the authors correctly identified 100% of calcium oxalate versus struvite or calcium phosphate stones. In addition, calcium oxalate monohydrate and calcium oxalate dihydrate stones could be defined by their significantly different mean gray-scale levels. However, the technique could not differentiate struvite stones from calcium phosphate stones because their gray-scale values overlapped. This method could be useful for determining stone composition before treatment decisions in patients with stone diseases. However, it is not easy to use and it may not be practical in clinical practice.

The role of CT

To date, CT is the investigation of choice for the diagnosis of urinary calculi.[12] Several studies have demonstrated that the information provided by CT scans can be used to predict both stone composition and the effectiveness of ESWL treatment.[14–24]

Predictions of ESWL outcome

In general, for stones of between 1 cm and 2 cm in diameter, an attenuation value >1,000 HU suggests an unfavorable outcome of ESWL treatment.[13] A stone clearance rate of 55% following ESWL has been reported for stones with attenuation values >1,000 HU, compared with 86% for those with attenuation levels of 500–1,000 HU and 100% for those with attenuation levels <500 HU.[14] A similar study of 112 patients who had stones of 5–20 mm in size demonstrated a linear relationship between attenuation values in HU and the number of ESWL treatments required for stone clearance.[15] When 750 HU was used as a cutoff level, the stone-free rate at 3 months after treatment was 65% in patients who had stones with high attenuation levels, compared to 90% for those with low attenuation levels.[15] However, no consensus data exist regarding the use of CT attenuation values to assess stone fragility.

Ng *et al.*[16] created a simple scoring system based on three stone characteristics derived from CT scans: stone volume <0.2 cm^3, mean attenuation value <593 HU, and skin to stone distance <9.2 cm. The stone-free rates for patients who had 0, 1, 2 or 3 of these factors were 18%, 48%, 73% and 100%, respectively ($P<0.001$). Similarly, Perks and colleagues[17] demonstrated that the stone-free rate after ESWL was 91% if the CT attenuation value was <900 HU and the skin to stone distance was <9 cm, but decreased to 41% for stones with an attenuation value ≥900 HU and skin to stone distance ≥9 cm.

By contrast, several studies have suggested that the HU attenuation value has limited utility for predicting the effectiveness of ESWL treatment. The limitation in accuracy is dependent on several factors, including X-ray energy level, slice thickness, volume artifacts and motion artifacts.[18,19]

Predicting stone composition

Although the attenuation value is related to the density of the material being imaged, this relationship is nonlinear—at extremely high HU values, the actual change in attenuation represented by 1 HU is smaller than that of values near the center of the scale. Most physicians accept that CT can differentiate uric acid stones from other types of calculi;[18,20] however, struvite, calcium oxalate, brushite and hydroxyapatite calculi typically have attenuation values >1,000 HU, which result in decreased sensitivity of this parameter to differentiate between these different types of stone.

With these clinical problems in mind, several investigators have sought improved methods by which CT could be used to predict the internal structure or composition of urinary calculi. Sheir *et al.*[21] scanned urinary stones *in vitro* at 1.25 mm collimation (slice thickness), and used attenuation values in HU (derived from nine regions of interest throughout the stones) and the stone density as estimated from these attenuation values to identify stone types. By this method, the authors uncovered significant differences among all pure and most mixed types of urinary calculi ($P<0.05$). They could distinguish pure uric acid stones from all mixed calculi (except mixed uric acid with <40% calcium oxalate monohydrate), pure calcium oxalate monohydrate from mixed uric acid with <40% calcium oxalate monohydrate, and pure struvite from all mixed stones except mixed struvite stones. Another group studied the internal structure of calcium oxalate monohydrate stones *in vitro*, using 1 mm slide width CT visualization.[22] The rationale for this study was the wide range of calcium stone fragility that could be successfully treated by ESWL. Fragility varies among calcium oxalate monohydrate, hydroxyapatite and brushite stones, even when accounting for stone size—even stones with the same chemical composition can have different fragility. Variation in morphology within a single compositional class of stone has been proposed as an explanation for the variation of stone fragility response to ESWL. The authors found that comminution of calcium oxalate monohydrate stones that have a homogeneous composition requires ESWL treatment for almost double the duration of that required for calcium oxalate monohydrate stones that demonstrate heterogeneous internal stone structure on CT scans.[22] This finding suggests that using CT to visualize any internal stone structure can enable physicians to predict calcium oxalate monohydrate stone fragility. However, this study was performed *in vitro* and it may transpire that this CT technique cannot be used to predict stone fragility in clinical practice.

Dual-energy CT with postacquisition image processing for determination of urinary stone composition has been investigated. In a study by Ferrandino *et al.*, data were acquired using 64-slice multidetector CT with a simultaneous dual energy source (peak tube voltages 80 kV and 140 kV) and dual detector design.[18] This study used the raw attenuation data from the dual energy CT rather than converting the values to HU.[18] The investigators were able to identify the main different chemical stone compositions of brushite, calcium oxalate–calcium phosphate, struvite, cysteine and uric acid. However, they could not distinguish calcium oxalate stones from those composed of calcium phosphate. Multivariate analysis suggested that this modality could not reliably distinguish between uric acid and cysteine stones, or between uric acid or cysteine and struvite stones. However, this limitation may not be important, as the conditions arising from these particular stone compositions can generally be distinguished clinically.

Clinical implications

Most renal and ureteral calculi are now treated using minimally invasive procedures, such as ESWL. However, the adverse effects of ESWL treatment include substantial renal injury, and this trauma can also result in subsequent development of other renal conditions, such as chronic kidney disease or renal hypertension.[23,24] The unnecessary or ineffective use of ESWL should, therefore, be avoided.

Diagnosis

Plain abdominal radiography is the simplest imaging method, and is used for initial stone detection. However,

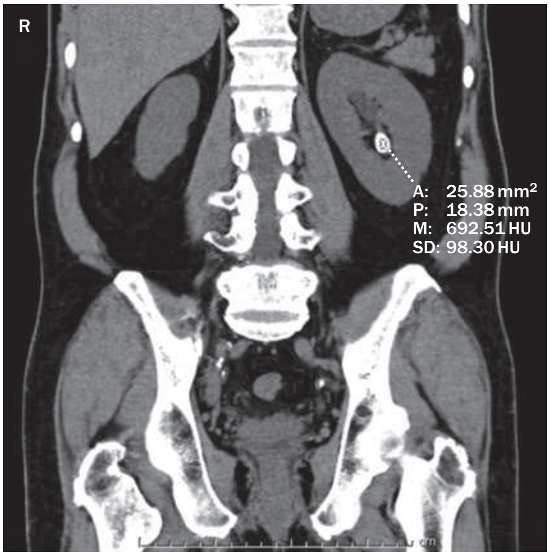

Figure 1 | CT scan from a patient with a 1.5 cm stone in the lower pole of the left kidney. The stone had a low attenuation value of 692 HU, suggesting that it would fragment easily. However, the stone could not be fragmented after two sessions of extracorporeal shockwave lithotripsy (ESWL). After endoscopic treatment, chemical analysis of the stone revealed that it was composed of calcium oxalate monohydrate, suggesting that the susceptibility of urinary stones to fragmentation by ESWL cannot be accurately determined by CT attenuation values alone.

this method is not sensitive enough to predict stone composition and stone fragility accurately. Currently, CT attenuation values in HU are the most efficacious imaging parameter for making these predictions. If a stone is not visualized by plain abdominal film and has a low attenuation value in HU on CT, it should be considered a uric acid stone, and alkalinizing urine should be considered the treatment of choice. However, the various types of calcium-based stones cannot be accurately distinguished by their CT attenuation values alone (Figure 1). The use of attenuation values in HU in conjunction with other CT imaging factors, including skin to stone distance and stone volume, can provide improved information regarding the probable response to ESWL treatment. However, visualization of internal stone structure using high-resolution CT with a 1 mm slide width or dual-energy CT currently provides the best images to identify the stone composition and enable physicians to predict the probable outcome of ESWL treatment, as it can identify stones with a homogeneous internal morphology, which are usually resistant to ESWL. However, these high-resolution CT scans are not often used in clinical practice, and no *in vivo* data exist to show that the technique is clinically viable.

Recurrence

Comprehensive stone treatment involves both stone removal and prevention of recurrence. In general, if a patient has had a calculus that comprised one main constituent, subsequent stones in the same patient are likely to be composed of the same material.[25] This observation has been confirmed by several studies, in which the reported stone recurrence rate ranged from 40–50% over 5–11 years.[26–28] Assessments of the chemical composition of calculi and metabolic evaluations are especially important for patients who are prone to recurrent stones. The stone should be collected for metabolic analysis following spontaneous passage or retrieved after ESWL or endoscopic procedures. The results of such analyses can then be used to select the most appropriate management strategy. If the stone is likely to be difficult to comminute, urologists should consider other treatment options such as endoscopic or percutaneous procedures instead of ESWL.

Conclusions

Information regarding stone composition or structure can offer useful guidance when planning treatment for patients with either initial or recurrent stones. Noninvasive assessment of stone composition before treatment can be performed using a standard CT scan. Although the CT attenuation values in HU are useful to predict stone composition, this parameter might be less accurate than using direct CT visualization of the internal stone structure. The development of advanced imaging technologies that can predict stone fragility accurately is essential, as these techniques can provide crucial information to enable physicians to select the most appropriate treatment for patients with stone diseases.

Review criteria

We searched the PubMed database using the search terms “urinary stones”, “stone composition”, “stone management” and “stone fragility”, for papers dating from 2000–2010, and selected only full-text articles published in English.

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K. Kijvikai researched data for the article. K. Kijvikai and J. J. M. de la Rosette were both involved in discussion regarding article content, writing of the article, and review and editing of the manuscript before submission.