Predicting stone composition before treatment – can it really drive clinical decisions?

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Introduction

Determination of stone composition is considered to be crucial for the choice of an optimal treatment algorithm. It is especially important for uric acid stones, which can be dissolved by oral chemoysis and for renal stones smaller than 2 cm, which can be treated with extracorporeal shockwave lithotripsy (ESWL).

Material and methods

This short review identifies the latest papers on radiological assessment of stone composition and presents a comprehensive evaluation of current scientific findings.

Results

Stone chemical composition is difficult to predict using standard CT imaging, however, attenuation index measured in Hounsfield units (HU) is related to ESWL outcome. Stone density >1000 HU can be considered predictive for ESWL failure. It seems that stone composition is meaningless in determining the outcome of ureterolithotripsy and percutaneous surgery. Alternative imaging techniques such as Dual-Energy CT or analysis of shape, density and homogeneity of stones on plain X-rays are used as promising methods of predicting stone composition and ESWL outcome.

Conclusions

New imaging techniques facilitate the identification of uric acid stones and ESWL-resistant stones. Therefore, they may help in selecting the best therapeutic option.

Key Words: urinary calculi ◀ chemical composition ◀ computed tomography ◀ ESWL ◀ percutaneous nephrolithotomy

INTRODUCTION

Preoperative determination of stone composition seems to be essential for optimal stone management. It is important for three reasons. Firstly, composition is related to hardness, which in turn affects the outcome of extracorporeal shockwave lithotripsy (ESWL); hard stones may be resistant to ESWL treatment. Secondly, stones related to various metabolic syndromes, such as cysteine stones or uric acid stones may require systemic medical treatment. Finally, knowing the stone composition enables some preventive efforts (drug treatment, dietary restrictions) [1]. This is not an easy task. For years there have been many attempts to predict stone composition by analyzing metabolic status, searching for microcrystals in urine sediment, and finally by means of radiological examinations [2, 3]. In most cases minerals found in crystals from urine sediment corresponded to those found in stones [4]. However, the accuracy of these methods is not sufficient enough to use them in clinical practice. Additionally, stones are usually not composed of monocrystals and even two stones made up of the same minerals may differ in fragility because of their structural variability [5].

There are about eight minerals or substances that are frequent components of urinary stones and even more which occur sporadically. Chemical analysis, which is used in laboratory evaluation of extracted stones, is a complex process of reactions and requires the use of sophisticated techniques, such as X-ray diffraction or different types of spectroscopy [6]. None of these methods are able to define chemical composition of a stone in vivo. There is no simple and single radiological variable, such as attenuation index (Hounsfield units; HU), which can differentiate all of these substances. Different imaging methods have been tested as predictors of stone composition, fragility, or treatment outcome. The question remains whether knowledge of chemical composition or fragility of stones can ac-
tually influence our treatment decisions? And if so, whether this can apply to all patients?

This short review identifies the latest papers on radiological assessment of stone composition and presents a comprehensive evaluation of current scientific findings. The possibilities of currently available radiological examinations are discussed.

**Attenuation index and stone composition**

CT remains the gold standard for diagnosis of urinary calculi. Stone density, which can be the indirect exponent of its chemical composition, is measured as CT stone attenuation value on non–contrast computed tomography (NCCT). So far, many studies focused on the predictive value of CT as a diagnostic tool for stone composition assessment [7, 8, 9]. However, this method is not helpful enough for certain differentiation of varying stone compositions. Moreover, in the study by Grosjean et al. the capability of four different computed tomography scanners to estimate urinary stone composition based on CT attenuation values was assessed. Direct comparison showed that there is a great variability between CT scanner models. The authors concluded that CT analysis and evaluation of Hounsfield units is not sufficient for the characterisation of renal stones [10].

Another issue is relatively high radiation dose associated with CT scanning. Therefore, low–dose stone protocols are used and are an excellent diagnostic tool. There are doubts whether the low–dose NCCT affects the evaluation of stone attenuation values. Alsyouf et al. analysed HU assessments in low– and conventional dose NCCT (from 5 to 140 mAs) on identical stones placed in various ureteral locations in cadavers. They have found that the reduced radiation dose is not associated with significant differences in stone HU values [11].

Dual–energy CT (DECT) is a newer technique, which can more accurately discriminate between different types of urinary calculi [12, 13]. Recently published studies have found that DECT can be used for in vivo characterisation of urinary calculi and sub–differentiation of calcium stones. It also enables the detection of lithotripsy–resistant calcium oxalate monohydrate stones [14]. DECT showed excellent accuracy in identification of stone chemical composition except for that of mixed stones [15].

**Uric acid stones**

The main issue is identification of uric acid stones, because they can be dissolved by oral chemolysis. This is an argument for making efforts to determine this fact prior to any treatment. There is evidence that the combined use of CT attenuation index (<500 HU) and urine pH (<5.5) can result in high sensitivity and specificity in predicting stones composed of uric acid [16]. Another method is use of DECT. In contrast to other types of stones, uric acid stones are characterized by no change in attenuation when scanned with the two different X–ray energy spectra [17]. Thus, being radiolucent on plain X–ray and having specific properties under DECT, uric acid stones may be diagnosed in vivo and surgical treatment can be replaced by conservative measures. However, this does not apply in every case. Patients with ureteral and large renal uric acid stones are mostly candidates for interventional treatment because fragmentation resulting in increased stone surface area is essential for effective chemolysis. Therefore, in those cases oral chemolysis is used as an adjuvant to an ESWL or endourologic procedure and any actions taken to determine stone composition beforehand are pointless.

**Non–uric acid stones**

It remains uncertain whether the type of non–uric acid stones can determine a treatment algorithm. According to the European Association of Urology Guidelines, identification of stone composition should be considered before selection of the stone removal procedure. This is mostly important in case of renal stones because of multiple treatment options available (FURS vs. PNL vs. ESWL).

Studies assessing the utility of stone CT attenuation as a predictor of flexible ureteroscopy with holmium laser lithotripsy outcome are limited. Ito et al. found that attenuation coefficients on NCCT were significantly related to the fragmentation efficiency and operative time, but they did not predict stone–free status [18]. Authors of another study did not observe differences in the operating time among the apatite, brushite, cystine, calcium oxalate monohydrate, calcium oxalate dihydrate, and uric acid stones [19]. Similarly, percutaneous lithotripsy dedicated studies are scarcely available. It seems that stone chemical composition is meaningless for the outcome of PNL. In the study concerning factors that affect bleeding during PNL, stone composition was not found as a predictor of total blood loss in a multivariate analysis [20]. In another study only struvite composition was an independent predictor for the development of complications [21].

**Predicting ESWL outcome**

Contrary to invasive intracorporeal methods of lithotripsy, there is strong evidence that chemical stone composition is one of the factors determining ESWL
success. Unfavourable stone composition (calcium oxalate monohydrate, brushite and cystine) is considered a major cause of ESWL failure [22]. For that reason, evaluation of stone composition before ESWL is clinically important. As stated previously, no imaging study can accurately predict chemical composition, however, stone fragility is related to its structure and density, which can be assessed by NCCT and expressed as an X-ray attenuation value. The relationship between stone density and ESWL outcome was evaluated in a number of studies (Table 1). Ouzaid et al. have prospectively analysed 50 patients with 5–22 mm renal stones to find the stone attenuation threshold predictive for ESWL failure [23]. In patients successfully treated with ESWL (stone-free or with only residual insignificant fragments four months after single ESWL session) stone attenuation values were significantly lower than in patients with poor ESWL outcome (715 HU vs. 1196 HU, p <0.001). The threshold of 970 HU was proposed by the authors as most sensitive (100%) and specific (81%), based on receiver–operating characteristic curves. The stone–free rate for patients with stones <970 HU was 96% vs. 38% for patients with stones ≥970 HU (p <0.001). Other authors have obtained similar results with the threshold assessed from 612 to 1200 HU [24–31]. Therefore, based on results of those papers, stone density >1000 HU is commonly considered as strongly predictive for ESWL failure [33].

On the other hand, even a simpler method may be sufficient to predict the ESWL outcome. Some authors argue that plain radiography can predict renal stone fragmentation by ESWL [34]. Unlike CT–attenuations, the stone radiodensity is presented directly during ESWL. Hussein et al. found that nonhomogeneous stones with an irregular outline and density less than or equal to that of bone (for example the 12th rib) are easily fragmented by ESWL. Thus, CT would be necessary to predict success of ESWL only in cases of homogeneous and smooth stones with a density higher than bone [35].

CONCLUSIONS

Analysis of stone images is crucial in selected groups of patients. Imaging techniques enable identification of uric acid stones and ESWL–resistant stones and therefore may lead to the selection of the best therapeutic option. Composition of non–uric acid stones, which need to be treated with invasive techniques, is very difficult to predict and the clinical value of this additional information is limited.

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### Table 1. Prediction of successful ESWL based on stone density

| Study               | N    | Success definition | Results |
|---------------------|------|--------------------|---------|
| Foda K, et al. [27] | 368  | Stone fragments <3 mm | Best discrimination value in ROC analysis: ≤934 HUs (94.4% sensitivity and 66.7% specificity) |
| Panah A, et al. [28]| 97   | Clearing of ureteral stone | Mean HU values for success vs. failure: 480 vs. 612 (P=0.004) |
| Choi JW, et al. [29]| 153  | Stone fragments ≤4 mm | Mean HU values for success vs. failure: For stones ≤10 mm: 781 vs. 829 P=0.6 For stones >10 mm: 814 vs. 844 P=0.54 |
| Ouzaid I, et al. [23]| 50   | Stone fragments <4 mm | Best discrimination value in ROC analysis: 970 HU (100% sensitivity and 81% specificity) |
| El–Nahas AR, et al. [25]| 120 | Stone fragments ≤4 mm | Mean HU values for success vs. failure: 709 vs. 776 (P=0.2) |
| Weld KJ, et al. [30]| 200  | Stone fragments ≤4 mm | Mean HU values for success vs. failure in MVA: 638 vs. 801 (P=0.2) |
| Cheng G, et al. [31]| 52   | Stone fragments <3 mm | Mean HU values for success vs. failure: 579 vs. 1032 (P<0.01) |
| Gupta NP, et al. [24]| 112  | Stone fragments ≤5 mm | 72% of calculi >750 HU required three or more ESWL sessions |
| Pareek G, et al. [32]| 100  | Stone fragments ≤3 mm | Mean HU values for success vs. failure: 578 vs. 910 (P<0.05) |

N – number of patients in the study; ROC – receiver operating curve; MVA – multivariate analysis; HU – Hounsfield units
References

1. Eliahou R, Hidas G, Duvdevani M, Sosna J. Determination of renal stone composition with dual–energy computed tomography: an emerging application. Semin Ultrasound CT MR. 2010; 31: 315–320.

2. Marchini GS, Sarkissian C, Tian D, Gebreselasie S, Monga M. Gout, stone composition and urinary stone risk: a matched case comparative study. J Urol. 2013; 189: 1334–1339.

3. Moreira DM, Friedlander JI, Hartman C. Differences in 24–hour urine composition between apatite and brushite stone formers. Urology. 2013; 82: 768–772.

4. Kaid–Omar Z, Daudon M, Attar A, Semmoud A, Lacour B, Addou A. Correlations between crystalluria and composition of calculi. Prog Urol. 1999; 9: 633–641.

5. Williams JC Jr, Saw KC, Paterson RF, Hatt EK, McAteer JA, Lingeman JE. Variability of renal stone fragility in shock wave lithotripsy. Urology. 2003; 61: 1092–1096.

6. Miernik A, Eilers Y, Bolwien C, Lambrecht A, Miernik A, Eilers Y, Bolwien C, Lambrecht A. Automated analysis of urinary stone composition using Raman spectroscopy: pilot study for the development of a compact portable system for immediate postoperative ex vivo application. J Urol. 2013; 190: 1895–1900.

7. el–Assmy A, Abou–el–Gharem ME, el–Nahas AR, Refaie HF, Sheir KZ. Multidetector computed tomography: role in determination of urinary stone composition and disintegration with extracorporeal shock wave lithotripsy—an in vitro study. Urology. 2011; 77: 286–290.

8. García Marchiñena P, Billordo Peres N, Liyo J, Ocantos J, Gonzalez M, Jurado A, Daels F. CT SCAN as a predictor of composition and fragility of urinary lithiasis treated with extracorporeal shock wave lithotripsy in vitro. Arch Esp Urol. 2009; 62: 215–222.

9. Badereddin M, Patzak J, Lutfi A, Pummer K, Augustin H. Impact of urinary stone volume on computed tomography stone attenuations measured in Hounsfield units in a large group of Austrian patients with urolithiasis. Cent European J Urol. 2014; 67: 289–295.

10. Grosjean R, Daudon M, Chammas MF Jr, Claudon M, Eschwege P, Felblinger J, Hubert J. Pitfalls in urinary stone identification using CT attenuation values: are we getting the same information on different scanner models? Eur J Radiol. 2013; 82: 1201–1206.

11. Alsyouf M, Smith DL, Olgin G, Heldt JP, Lightfoot M, Li R, Baldwin DD. Comparing stone attenuation in low– and conventional–dose noncontrast computed tomography. J Endourol. 2014; 28: 704–707.

12. Fung GS, Kawamoto S, Matlaga BR, Taguchi K, Zhou X, Fishman EK, Tsui BM. Differentiation of kidney stones using dual–energy CT with and without a tin filter. Am J Roentgenol. 2012; 198: 1380–1386.

13. Jepperson MA, Cernigliaro JG, Sella D, Ibrahim E, Thiel DD, Leng S, Haley WE. Dual–energy CT for the evaluation of urinary calculi: image interpretation, pitfalls and stone mimics. Clin Radiol. 2013; 68: e707–e714.

14. Acharya S, Goyal A, Bhalla AS, Sharma R, Seth A, Gupta AK. In vivo characterization of urinary calculi on dual–energy CT: going a step ahead with sub–differentiation of calcium stones. Acta Radiol. 2014 Jun 17; pii: 0284185114538251 [Epub ahead of print].

15. Manglaviti G, Tresoldi S, Guerrer CS, Di leo G, Montanari E, Sardanelli F, Comalba G. In vivo evaluation of the chemical composition of urinary stones using dual–energy CT. AJR Am J Roentgenol. 2011; 197: W76–83.

16. Spettel S, Shah P, Sekhar K, Herr A, White MD. Using Hounsfield unit measurement and urine parameters to predict uric acid stones. Urology. 2013; 82: 22–26.

17. Wisenbaugh ES, Paden RG, Silva AC, Humphreys MR. Dual–energy vs. conventional computed tomography in determining stone composition. Urology. 2014; 83: 1243–1247.

18. Ito H, Kawahara T, Terao H, Ogawa T, Yao M, Kubota M, Matsuzaki J. Predictive value of attenuation coefficients measured as Hounsfield units on noncontrast computed tomography during flexible ureteroscopy with holmium laser lithotripsy: a single–center experience. J Endourol. 2012; 26: 1125–1130.

19. Wiener SV, Deters LA, 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.

20. Lee JK, Kim BS, Park YK. Predictive factors for bleeding during percutaneous nephrolithotomy. Korean J Urol. 2013; 54: 448–453.

21. Pérez–Fentes DA, Gude F, Blanco M, Novoa R, Freire CG. Predictive analysis of factors associated with percutaneous stone surgery outcomes. Can J Urol. 2013; 20: 7050–7059.

22. Kijvai K, de la Rosette JJ. Assessment of stone composition in the management of urinary stones. Nat Rev Urol. 2011; 8: 81–85.

23. Ouzaid I, Al–qahtani S, Dominique S, Hupertan V, Fernandez P, Hermieu JF, Delmas V, 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: E438–442.

24. Gupta NP, Ansari MS, Kesarvani P, Kapoor A, Mukhopadhyay S. Role of computed tomography with no contrast medium enhancement in predicting the outcome of extracorporeal shock wave lithotripsy for urinary calculi. BJU Int. 2005; 95: 1285–1288.

25. El–Nahas AR, El–Assmy AM, Mansour O, Sheir KZ. A prospective multivariate analysis of factors predicting stone disintegration by extracorporeal shock wave lithotripsy: the value of high–resolution noncontrast computed tomography. Urology. 2007; 51: 1688–1693.

26. Shah K, Kurien A, Mishra S, Ganpule A, Muthu V, Sabnis RB, Desai MJ. Predicting effectiveness of extracorporeal shockwave lithotripsy by stone attenuation value. Endourol. 2010; 24: 1169–1173.

27. Foda K, Abdelhafeim H, Youssif M, Assem A. Calculating the number of shock waves, expulsion time, and optimum stone parameters based on noncontrast computerized tomography characteristics. Urology. 2013; 82: 1026–1031.

28. Panah A, Patel S, Bourdoumis A, Kachrils S, Buchholz N, Masood J.
Factors predicting success of emergency extracorporeal shockwave lithotripsy (eESWL) in ureteric calculi – a single centre experience from the United Kingdom (UK). Urolithiasis. 2013; 41: 437–441.

29. Choi JW, Song PH, Kim HT. Predictive factors of the outcome of extracorporeal shockwave lithotripsy for ureteral stones. Korean J Urol. 2012; 53: 424–430.

30. Weld KJ, Montiglio C, Morris MS, Bush AC, Cespedes RD. Shock wave lithotripsy success for renal stones based on patient and stone computed tomography characteristics. Urology. 2007; 70: 1043–1046.

31. Cheng G, Xie LP, Li XY. Value of Hounsfield unit on CT in prediction of stone–free rate of upper urinary calculi after extracorporeal shockwave lithotripsy. Zhonghua Yi Xue Za Zhi. 2006; 86: 276–278.

32. Pareek G, Armenakas NA, Panagopoulos G, Bruno JJ, Fracchia JA. Extracorporeal shock wave lithotripsy success based on body mass index and Hounsfield units. Urology. 2005; 65: 33–36.

33. Türk C, Knoll T, Petrik A, Sarica K, Skolarikos A, Straube M, Seitz C. Guidelines on Urolithiasis. EAU Guidelines, edition presented at the 29th EAU Annual Congress, Stockholm 2014. ISBN 978–90–79754–65–6.

34. Kris hamurthy MS, Ferucci PG, Sankey N, Chandhoke PS. Is stone radiodensity a useful parameter for predicting outcome of extracorporeal shockwave lithotripsy for stones < or = 2 cm? Int Braz J Urol. 2005; 31: 3–8.

35. Hussein A, Anwar A, Abol–Nasr M, Ramadan E, Shaaban A. The Role of Plain Radiography in Predicting Renal Stone Fragmentation by Shockwave Lithotripsy in the Era of Noncontrast Multidetector Computed Tomography. J Endourol. 2014 Mar 31. doi:10.1089/end.2014.0034.