Prediction of the energy required for extracorporeal shock wave lithotripsy of certain stones composition using simple radiology and computerized axial tomography

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Abstract

Objective: To demonstrate that urinary lithiasis have a specific susceptibility to fracture through extracorporeal shock wave lithotripsy (ESWL), which is common for all calculi with the same composition and which can be estimated before treatment using CT or plain X-ray.

Material and method: We present an in vitro, prospective, randomized, blind and multi-center study involving 308 urinary calculi. 193 of these met the inclusion criteria: whole calculi composed purely of calcium oxalate monohydrate (COM), uric acid (UA) or carbonate apatite (CA), or a mix of oxalate (COMix) and of a size greater than 0.5 cm. The samples were broken using lithotripsy until reaching a pre-established level of comminution. The variables employed were energy dose (Edose) per cm³ of lithiasis and Edose adjusted to lithiasic surface (EdAJ) per cm³.

Results: COM was the hardest, requiring an Edose of 119,624 mJ/cm³ and an EdAJ of 36,983 mJ/cm³, followed by COMix (75,501/36,983), CA (22,734/21,186) and UA (22,580/6837) (p<0.05). Gmax and Gmda were correlated with Edose (r=0.434/r=0.420) and EdAJ (r=0.599/r=0.545) (p<0.01). UH were correlated, in bone window and soft tissue window, with Edose/cm³ (r=0.478/r=0.539) y EdAJ/cm³ (r=0.745/r=0.758) (p<0.01).

Conclusions: In our in vitro research lithiasis require, due to the specific nature of their composition, a given amount of energy in order to be broken by ESWL, which is inherent to all those sharing the same composition, and can be predicted using CT or plain X-ray.

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KEYWORDS

Lithiasis; Extracorporeal shock wave lithotripsy; Shock wave; Composition; Tomography; Radiology

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Predicción mediante radiología simple y tomografía axial computarizada de la energía necesaria para fragmentar litiasis de distinta composición empleando litotricia extracorpórea por ondas de choque

**Resumen**

Objetivo: Demostrar que las litiasis urinarias necesitan, según su composición, una determinada energía para ser fracturadas mediante litotricia extracorpórea por ondas de choque (LEOC), pudiendo ser estimada antes del tratamiento mediante radiografía simple y TAC.

Material y método: Estudio experimental, prospectivo y ciego, con 308 cálculos urinarios de 4 hospitales. No cumplieron criterios de inclusión 115: litiasis intactas, mayores de 0,5 cm y de composición pura (≥75%) de oxalato cálculo monohidrato (OCM), urico o carbonatoapatita, o mixta oxalocalcica mono y dihidratada (OCMix). Las 193 restantes fueron sometidas a radiografía simple y a tomografía (TAC), valorando digitalmente el griso máximo (Gmax) y el griso mediano (Gmda) presentado mediante Adobe Photoshop® CS5, y la atenuación en unidades Hounsfield (HU). Posteriormente se les administró LEOC a una frecuencia fija de 1 Hz hasta alcanzar una cominución preestablecida, registrándose así la dosis de energía (Edose) y la Edose ajustada a superficie litiasica (EdAJ).

Resultados: La composición OCM resultó la más dura, precisando una Edose de 119.624 mJ/cm² y una EdAJ de 36.983 mJ/cm², seguida de OCMix (75.501/36.983), carboapatita (22.734/21.186) y urico (22.580/6.837) (p < 0.05). Gmax y Gmda se correlacionaron con Edose (r = -0.434 y r = 0.420) y EdAJ (r = 0.599 y r = 0.545) (p < 0.01). Las HU se correlacionaron, tanto en ventana de tejido blando como óseo, con Edose/cm³ (r = 0.478 y r = 0.539) y EdAJ/cm³ (r = 0.745 y r = 0.758) (p < 0.01).

Conclusions: Las litiasis precisan, por las características propias de su composición, una determinada cantidad de energía para su rotura con LEOC en fragmentos de diámetro menor de 2 mm, que es predecible empleando la atenuación en HU en TAC, o escala de grises en la radiología simple.

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**PALABRAS CLAVE**

Litiasis; Litotricia extracorpórea por ondas de choque; Ondas de choque; Composición; Tomografía; Radiología

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**Introduction**

Nowadays, a varied therapeutic repertoire is available for the treatment of urinary lithiasis. The choice of the ideal kind of treatment is a key factor for success, minimizing the number of surgeries and complications. Success depends, among other factors, on stone composition and hardness. Determining in advance renal stone fragility would be desirable to predict its behavior during treatment with extracorporeal shock wave lithotripsy (ESWL) and to assess its suitability, or to consider if other techniques such as percutaneous nephrolithotomy or retrograde flexible ureteroscopy should be used.

Since Dretler first introduced the concept of stone fragility, attempts have been made to determine the hardness of stones by simple radiology, densitometry, and computed axial tomography (CAT) scan, which seems to have become generally accepted as a standard. There have been promising but variable outcomes, with different results on the same page of a journal as seen in 3 recent publications on this topic. This suggests that, in addition to the interest in this problem, there is little homogeneity among the different studies published. Besides, improvements in digital imaging have raised again the possibility that simple radiology might be helpful for this purpose, thus avoiding the excess of radiation from CAT.

The aim of this study was to determine the energy dose which is needed, in order to achieve pre-determined comminution, in urinary calculi with different stone composition, and to check energy predictability with simple radiology and CAT.

**Materials and methods**

We present an experimental, prospective, single-blind study, which used 308 renal calculi obtained between September 2009 and June 2010 in the health areas of the Virgen del Rocio University Hospital (Seville), the hospital of Jerez de la Frontera (Cádiz), the San Juan de Dios Hospital in Aljarafe (Seville) and the Lozano Blesa Clinical University Hospital (Saragossa).

Inclusion criteria: intact renal stones obtained after spontaneous expulsion or by surgery, with a largest diameter greater than 0.5 cm and pure composition of calcium oxalate monohydrate (COM), uric acid (UA) or carbonate apatite (CA), with those calculi with a percentage of any of these materials higher than 75% in their composition being defined as pure ones. We also included a group of stones of mixed oxalate monohydrate and dihydrate composition, in similar proportions (proportion between 40 and 60% of each component).

115 calculi were excluded from the study: 11 of them because the patients had undergone lithotripsy in any of its forms or because they were fragmented for other reasons, 51 of them because they did not have a largest diameter greater than 0.5 cm and 53 of them because they did not show a composition consistent with the inclusion criteria.
Prediction of the energy required for extracorporeal shock wave lithotripsy

The 3 largest diameters of each stone were measured with a digital caliper. Each stone was numbered, introduced in a separate container, stored and classified in a box by a single urologist, who did not know the composition of the calculi. Once the sample was complete, the calculi were distributed in an orderly manner in 8 plastic cuvettes filled with ultrasound gel to prevent displacement, maintain the established order and so that the radiological images obtained from those trays would simulate the variety of densities in the human body (Fig. 1). Radiological tests were then performed.

Plain X-ray was taken at 40 kV for each tray in digital form. The image-processing software Adobe Photoshop® CS5 was used to measure, according to the grayscale included in the program, the maximum gray (Gmax) and the medium gray (Gmed) values of each stone. To that end, in grayscale mode and by zooming in to 200 for a better selection of the edges, we used the lasso tool. The area surrounding the stone, which was named 'medium gray surrounding lithiasis' (Gmsrndg), was subsequently selected and thus we created the unit called 'medium gray minus medium gray surrounding lithiasis' (Gmed–Gmsrndg) in an attempt to correct environmental influences on gray values expressed in the calcili. All of this was done by the same researcher, who did not know either the composition and the real dimensions of the stones or the tomographic data (Fig. 2).

The tomographic study was performed with a multidetector scanner Toshiba Aquilllon 64, with cuts of 0.5 mm, collimation of 1.25 at an energy level of 120 kV at constant 250 mA. The images were sent to a PACS (AGFA-Carestream®)

Figure 1 Tray with stones immersed in ultrasound gel.

Figure 2 Measurement of the gray values of the stones studied, by using the 'lasso' tool.

1. Delivered energy dose (Edose). It consists of the product of the number of waves and the effective energy (EE) provided by each wave within a 12-mm diameter area in the focal point. It is established by Dornier for the lithotripter used at 23 mJ for level 3 (12.5 kV), 42 mJ for level 6 (15 kV), and 71 mJ for level 10 (17.5 kV).

2. Delivered energy dose adjusted to lithiasic surface (EdAJ). Since many of our stones had a large-diameter surface of less than 12 mm for which EE was calculated, we adjusted the share of energy provided by each wave within an area equivalent to that of each stone (this was calculated by using its 2 largest diameters). Thus, and unlike Edose, EdAJ expresses the energy delivered to the stone and not to a 12-mm area where the stone is located. This adjustment is not necessary for calculi greater than 12 mm, because given the funnel design of the basket, the lithiasic mass, which initially was outside the 12-mm defined area, will be located within this area.
Figure 3  Accumulated energy (mJ) to fragment the different stone compositions, according to the different variables defined. If we use the correlation in terms of volume, we observe that the pure calcium oxalate is the hardest one. The difference in the energy required for uric acid and carbonate apatite stones can only be appreciated by using EdAJ/cm³ (p < 0.05), and not with Edose/cm³ (p = 0.8).

as the central part of the stone is fragmented. All the procedure was performed by a single researcher.

When these energy units are correlated to the CT-scan results, adjustment for volume is used (Edose/cm³ and EdAJ/cm³) since, unlike in the case of plain film radiography, scanning allows for 3-dimensional viewing. After lithotripsy was performed as described, the lithiasic fragments were collected and compressed to pills using a SPECAC press for renal stones, and then desiccated with potassium bromide. An infrared spectroscopy assay was subsequently conducted using a Nicolet IR 200 FT-IR spectrophotometer, and the Nicodom Kidney Stone Library 2005®.

Microsoft® Excel® software was used to develop a database, which was subsequently exported to the IBM SPSS Statistics® software, version 19.

The median and interquartile range were used to express the variables which did not show a normal distribution, and the median and the standard deviation for those variables which did show it. The Kolmogorov test and the Shapiro–Wilk test (n < 50) were used to assess this aspect.

We used the Kruskal–Wallis test for independent data samples in order to compare energies according to their composition, and the nonparametric Spearman’s rho correlation coefficient to measure the linear relation between quantitative variables which do not follow a normal distribution.

The level of significance was established at 5%.

Results

193 calculi were valid: 31 were COM stones, 32 were mixed oxalocalcic stones, 33 were CA stones, and 97 were UA stones, with a mean area of 0.39 (0.27–0.63) cm² and a mean volume of 0.12 (0.08–0.32) cm³, CA stones being the largest ones (mean area and volume 0.90 cm² and 0.47 cm³) and COM stones being the smallest ones (0.28 cm² and 0.06 cm³).

Fig. 3 shows the values of the variables Edose/cm³, EdAJ/cm³, and EdAJ for each lithiasic composition included in the study. We had greater difficulty with COM at the time of fragmentation, with an EdAJ/cm³ value of 60,320 (29,911–109,856) mJ/cm³, followed by COM-COD, with 36,983 (18,704–71,850) mJ/cm³, ending with CA 21,186 (13,458–32,570) mJ/cm³ and UA 6837 (5514–9103) mJ/cm³ (p < 0.05). Only EdAJ/cm³ allowed us to identify greater hardness in calcium carbonate calculi than in uric acid calculi, since Edose/cm³ showed no significant differences in this comparison (p = 0.8). For all the other comparisons, the energy required for fragmentation was different depending on lithiasic composition. When we used the EdAJ variable, and therefore there was only correlation with area measures and not with volume, carbonate apatite stones showed higher values, and no distinction was possible between the 2 oxalic groups (p = 0.062).

The median value of Gmax was 242.5 (213–251); 198.37 (180–237.25) in the case of Gmed, and 81.5 (40–140) in the case of Gmed–Gmsrndg.

The median attenuation value of the CT scan, measured in HU, was 387.35 (296.69–834.61) in the bony window. In the soft-tissue window, the median value was slightly lower: 379.25 (288.88–665.7).

Table 1 shows the correlation indexes between gray levels and those variables which quantify lithiasic fragility. When making this comparison, a statistically significant correlation was observed for all the variables, with the exception of the correlation between Edose and Gmed–Gmsrndg.

We found statistically significant results in the correlation coefficients among the fragmentation parameters determined during the ESWL procedure and the attenuation in HU expressed in the samples, as an expression of the predictability of lithiasic fragility provided by tomography modalities. The attenuation in the bony window and EdAJ/cm³ showed the highest correlation (r = 0.758) (p < 0.01), while it was slightly lower in the soft-tissue window (r = 0.745) (p < 0.01). EdAJ also showed a correlation in the tissue window, which was statistically significant in both windows (bony r = 0.605, soft tissue r = 0.653) (p < 0.01), as well as Edose/cm³ (r = 0.539/f = 0.478) (p < 0.01).

Table 2 shows the correlation indexes found between the measurement of the different gray variables detected by simple radiographic examination and the attenuation in HU found in tomography scans, using both the bony and the soft-tissue windows for measuring it. It can be seen that we found statistically significant values in all the correlations, with correlation indexes ranging from 0.72 to 0.79.

Table 1  Correlation coefficients between gray levels and fragmentation parameters.

<table>
<thead>
<tr>
<th></th>
<th>Edose</th>
<th>EdAJ</th>
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<tbody>
<tr>
<td>Gmax</td>
<td>r = 0.434</td>
<td>r = 0.599</td>
</tr>
<tr>
<td></td>
<td>p &lt; 0.01</td>
<td>p &lt; 0.01</td>
</tr>
<tr>
<td>Gmed</td>
<td>r = 0.420</td>
<td>r = 0.564</td>
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<td></td>
<td>p &lt; 0.01</td>
<td>p &lt; 0.01</td>
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<tr>
<td>Gmed–Gmsrndg</td>
<td>p = 0.367</td>
<td>r = 0.425</td>
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<tr>
<td></td>
<td>p = 0.01</td>
<td>p &lt; 0.01</td>
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</tbody>
</table>

Gmax, maximum gray; Gmed, medium Gray; Gmed–Gmsrndg, medium gray on lithiasis minus medium gray surrounding lithiasis.

r values in each correlation.

Spearman’s Rho. Significance if p < 0.05.
Discussion

The lithiasic composition defines the fragility of the urinary stone and therefore its response to treatment. Thus, COM, brushite, and cystine calculi show outstanding resistance to disintegration, doubling that of calcium oxalate dihydrate (COD) stones, but lithotripsy is not contraindicated when the lithiasic mass is small and patients want a non-invasive form of therapy. However, those are not the only intervening factors. The hardness of stones of the same composition sometimes shows a marked variability, due to their secondary composition or their crystallographic patterns.

Delius et al. studied the disintegration of samples of 3 synthetic materials, and of human calculi with ESWL, calculating the acoustic energy required for it (mJ/cm²). They observed that in the case of calculi, and unlike synthetic materials, there were 2 behavioral tendencies among 2 lithiasic ‘families’. Their composition was not described since ‘the sample was very small’. In this study, they used a ‘basket’ model like ours, with the differences in behavior that it may entail when comparing it with a live treatment session, where fragments remain in the focal point. In our research, we sought to gain an insight into the different behavior of ‘lithiasic families’. To this end, we increased the sample size and the diversity of compositions.

Rigden and Tiselius, in a retrospective study, calculated a ‘factor for hardness’ for the different compositions of 247 calculi, estimating the energy and the number of waves and re-treatments required for a disintegration into fragments larger than 4 mm. However, when they mentioned ‘total energy’, reference was actually made to power index, which is ultimately a measure of the kilovolts used for shock wave generation, and not of energy (J), which does not enable us to compare between different treatment strategies, or between the results of different lithotripters. They used a treatment frequency which was not fixed, but adjusted to heart rate, as opposed to the frequency used in our study.

We believe it necessary to express the hardness of stones with a more appropriate and comparable parameter: the energy dose required for fragmentation (Edose), or EdAJ, which allow for higher accuracy. It should be also mentioned that we used the considerations made in this research in order to define as pure ones those calculi with a composition greater than 75% in any of the substances, given the existing difficulties to find infective calculi, composed of carbonate apatite/struvite, with a proportion higher than this percentage in any of these components.

The results of hardness obtained in our study were similar and comparable to those of other articles: the hardest ones being COM stones, followed by mixed COM-COD stones, calcium carbonate, and uric acid stones. However, the difference in hardness between the latter 2 compositions is much better expressed when estimating EdAJ/cm² than when taking into consideration Edose/cm². In the intergroup comparison we noted that there are no difficulties to conclude that the studied compositions have an intrinsic value which is characteristic of EdAJ/cm².

Since Dretler observed in 1988 differences in the radiographic appearance of pure COM, COD, brushite, uric acid, and cystine calculi, by analyzing them in a descriptive way, several studies have focused on this aspect, and on the predictability of fragility with simple X-ray examinations. The methodology was initially quite unsophisticated, using the description of lithiastic edges and the comparison between the density of the stones and the bone, either a rib or spine transverse processes. El-Gamal and El-Badry used image digitization for plain film radiography and the establishment of a grayscale with a previous version of the software used by us (Adobe Photoshop). Instead of using the gray level obtained, they associated it with an aluminum strip which provided a progressive grayscale from 1 to 8, thus creating a variable called ‘equivalence in millimeters of aluminum’, which were correlated with the number of waves. They observed that the 12 patients with failure of treatment with lithotripsy showed density values which were significantly higher than those cases in which fragmentation had been completed. They also observed an interesting direct correlation between the equivalence in millimeters of aluminum and HU, in an equivalent manner to what we also found in our study with grayscale.

Some authors have suggested that lithiasic density, measured in grayscale units or HU, could be complemented with the morphology and heterogeneity of this density to increase the predictability of radiographs with respect to fragmentation with ESWL. Zarse et al. studied in depth the ideal technical parameters used in CT scans in order to enable an optimal differentiation of stone heterogeneity, thus suggesting the need to avoid the soft-tissue window to that end. Arshadi et al. classified patients with stones between 10 and 15 mm into 2 groups depending on the estimated probability of being successful in treating them with ESWL, and based on 3 variables: density (greater or lower than the bone), homogeneity, and smooth or rough edges. The patients who were a priori classified as ‘high probability of success in fragmentation’ by using these parameters showed good results in 92.4% of the treatments, versus 64.4% in those classified as ‘low probability of success’. Krishnamurthy et al. found no association between density and stone hardness in those calculi smaller than 1 cm, but they did find it in larger calculi, so they recommended other support variables to be used for predicting success with ESWL therapy in the case of stones smaller than 1 cm. This is therefore a topic for further research.

<table>
<thead>
<tr>
<th>Table 2</th>
<th>Correlation indexes observed in the comparison between gray levels on simple X-ray and attenuation in HU.</th>
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<tr>
<td></td>
<td>Hounsfield Units (HU)</td>
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<tr>
<td></td>
<td>SW</td>
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<tr>
<td>Gmax</td>
<td>Cl: 0.727</td>
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<tr>
<td></td>
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<tr>
<td>Gmed</td>
<td>Cl: 0.731</td>
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<td></td>
<td>p &lt; 0.001</td>
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<tr>
<td>Gmed–Gmsrmdg</td>
<td>Cl: 0.798</td>
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<tr>
<td></td>
<td>p &lt; 0.001</td>
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</table>

Gmax, maximum gray; Gmed, medium Gray; Gmed–Gmsrmdg, medium gray on lithiasis minus medium gray surrounding lithiasis; SW, soft-tissue window; BW, bony window. Spearman’s Rho. Significance if p < 0.05.
In recent years, there has been a prolific scientific production on this topic regarding the identification of the composition and stone hardness with CT scans. However, the clinical benefit achieved so far has been limited. The 2013 European Guidelines on Urolithiasis only concludes that those calculi with attenuation higher than 1000 HU on a non-contrast CT scan are likely to be badly disintegrated during treatment with ESWL (level of evidence 2a, grade of recommendation B). This is due to the variability of values found by different authors, to the overlapping results observed in the different compositions, and to the lack of homogeneity in the tomographic parameters used for measurement (use of different windows, collimations, voltage, amperage, definition of stone purity, etc.). It seems that using dual-energy CT scans with image processing algorithms, a kind of technology which is still limited and quite expensive, or tomography at 2 intensity levels on the same patient could solve this problem. Nonetheless, it is essential to consider the performance of this technique with regard to increased radiation exposure and higher costs.21-23

Saw et al.,24 in an in vitro study at a fixed voltage, defined the concept of 'half attenuation rule': they observed that the quotient 'number of waves required for comminution' divided by attenuation in HU was never higher than 0.5 in the 6–13 mm stone size range. This rule does not seem especially useful for everyday use, due to the diameter range for which it was established and because it uses the number of waves and not energy in joules. Although this rule is fulfilled in our study, it cannot be applied to other equipments or to the strategies for voltage escalation which have led the way in the current development of lithotripsy sessions.

We encountered the limitations inherent to an experimental study, with the disadvantages of a basket design already mentioned. Besides, the high proportion of uric acid stones made it more difficult to assess the results of simple X-ray, since the radioluency of this composition complicates the translation to an in vivo model. However, and for this very reason, it is possible that we might get better results if predictability is only used for radiopaque calculi.

We should reflect on the real usefulness we want to achieve from using the predictive capability of radiology. When it comes to any decision-making about the preferable treatment modality for a given patient, the most important thing is not to determine the composition of the stone but the ease of fragmentation, irrespective of its main component.25 Once the stone is broken, the analysis of the fragments will become more important for establishing a preventive treatment. This was the practical aim of our study in its experimental phase: approaching the a priori determination of the energy required to treat stones with imaging tests. Once we know that, we can establish the number of sessions needed depending on the number of joulux administered per session. This has not been established in the literature, and it will depend on the equipment used, the patient’s tolerance, the availability of an anesthesiologist, the location of the stone, and the characteristics of the specific patient. In this regard, a recent study tried, by creating a coefficient named focal applied energy quotient (FAEQ) and by optimizing the number of joulux per session and the time of radiation exposure, to improve the results obtained using ESWL for the treatment of ureteral lithiasis, until they were equivalent to those obtained using the Holmium laser.26

Conclusions

In our in vitro model, stones required, due to the characteristics of their composition and crystal structure, a certain amount of energy for fragmentation with ESWL. Calcium oxalates, both in their pure or mixed composition, were more difficult to fragment, followed by carbonate apatite and uric acid stones.

Digital measurement of the gray levels expressed by stones and observed in simple X-ray and the determination of attenuation in HU on CT scan are correlated in vitro with the energy required for their fragmentation. It will be necessary to validate all the results in an in vivo model to check if they are affected by the constraints already referred to (use of a basket model, stone radioluency, attenuation caused by surrounding tissues, etc.).

Conflict of interest

The authors declare that they have no conflict of interest.

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