THE USEFULNESS OF DENSITOMETRY IN PREDICTING THE COMPOSITION AND FRAGILITY OF UROLITHIASIS

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Summary.- INTRODUCTION: The choice of ideal treatment for a given lithiasis is a crucial factor for its success, minimizing the number of interventions and complications. Previous determination of stone composition and its fragility is desirable, to predict its behavior during extracorporeal shock wave lithotripsy and for evaluation of its appropriateness, or to set the indication for other techniques.

OBJECTIVES: To determine the role of densitometry in the prediction of composition and fragility of urinary lithiasis undergoing SWL.

METHODS: Experimental prospective, blinded, in vitro study using 193 urinary calculi of known composition: monohydrated calcium oxalate, mixed calcium oxalate, uric acid, and calcium carbonate, obtained from spontaneous passage or surgery. Densitometry and SWL were performed on them.

We compare the mineral composition of the stone and mineral density of each composition group to check if they are characteristic of each type and correlate these parameters with the energy dose required to fragment them down to a given fragment size.

RESULTS: Only 53 out of 193 stones showed valuable data. Calcium carbonate was the composition showing greater mineral content and density (1,24 gr and 0,47 gr/cm²), followed by mixed oxalate (0,51/0,26) and uric acid ((0,52/ 0,15), finishing with the monohydrate calcium oxalate group (0,32/0,05). Only the comparison between calcium carbonate and monohydrated calcium oxalate showed statistically significant results (p<0,05). Correlation coefficients between mineral content (0,347) and density (0,424) and the energy used for stone fragmentation to a given fragment size were statistically significant (p<0,05).

CONCLUSIONS: In our study, the use of densitometry to determine stone composition and lithiasic fragility did not show conclusive results due to the limited number of calculi tested. Nevertheless, there are signs that, with a different study design, more practically useful results could be achieved.

Keywords: Extracorporeal lithotripsy. Densitometry. Composition.
INTRODUCCIÓN: La elección del tipo de tratamiento ideal para una determinada litiasis es un factor crucial para el éxito del mismo, minimizando el número de intervenciones y complicaciones. Es deseable la determinación a priori de la composición de la litiasis y de su fragilidad, para predecir su comportamiento durante el tratamiento con litotricia extracorpórea (LEOC) y valorar la idoneidad de este, o si se deben emplear otras técnicas.

OBJETIVO: Determinar el papel de la densitometría en la predicción de la composición y fragilidad de litiasis que van a ser tratadas con LEOC.

MÉTODOS: Estudio experimental, in vitro, prospectivo, y ciego, realizado empleando 193 cálculos urinarios de composición conocida: oxalato cálcico monohidratado (OCM), oxalato cálcico mixtos, ácido úrico y carbonato de apatita, obtenidos mediante expulsión espontánea o cirugía. Éstos son sometidos a densitometría y litotricia extracorpórea. Comparamos el contenido mineral de la litiasis y la densidad mineral de la litiasis de cada grupo de composición para comprobar si son características propias de cada tipo, y correlacionamos estos parámetros con la dosis de energía necesaria para la fragmentación hasta una conminución definida.

RESULTADOS: Sólo 53 de los 193 cálculos arrojaron datos que pudiesen ser valorados. Carbonato de apatita ha sido la composición que ha mostrado un mayor contenido y densidad mineral (1,24 gr y 0,47 gr/cm²), seguido de los mixtos de oxalato (0,51/0,26) y único (0,52/0,15), finalizando con el grupo OCM (0,32/0,05). Sólo la comparación carboapatita-OCM mostró resultados estadísticamente significativos (p<0,05). Los coeficientes de correlación entre contenido (0,347) y densidad mineral (0,424) y la energía empleada para la fragmentación litotítica hasta la conminución definida presentaron significación estadística (p<0,05).

CONCLUSIONES: En nuestro estudio el empleo de la densitometría para determinar la composición y fragilidad litotítica no ha mostrado resultados concluyentes dada la escasez de cálculos detectados. Se aprecian no obstante indicios de que, con un diseño diferente, podrían conseguirse resultados de mayor utilidad práctica.


INTRODUCTION

We currently have a varied therapeutic arsenal for the treatment of urinary lithiasis. The choice of the ideal treatment type for each case is a crucial factor in the success of the treatment, minimizing the number of interventions and complications [1,3]. The a priori determination of the composition and fragility of the lithiasis is preferable, in order to predict the behavior during the treatment with extracorporeal shock wave lithotripsy (ESWL) and to evaluate the suitability of this treatment and whether other techniques should be employed (percutaneous nephrolithotomy, surgery, flexible retrograde ureterorenoscopy).

To this end, techniques have been developed to attempt to predict the lithiasic composition and its hardness, by analyzing the data provided using different diagnostic tests. In 1988, Dretler was the first to attempt to approximate a prediction of the lithiasic composition in an in vitro study by means of simple radiology and densitometry (4). In 1990, Pérez Castro et al. presented their preliminary results on the study of lithiasis using densitometry, highlighting the advantages presented by the low irradiation and ease of access to the equipment, compared with other techniques such as CT scans, the rapidity of exploration and the absence of the need for protective measures for the staff. Under the precaution that the results were preliminary, they did not find a relation between the densitometric value obtained and the fragility of the calculus to the shock waves (5). Recently, the use of the degree of attenuation in Hounsfield units (HU) in the computerized axial tomography (CT) appears to have established itself as the technique for predicting the lithiasic hardness and composition. However, this technology is not without drawbacks, such as the excess irradiation and the cost (6).

Our objective is to study the possibility that densitometry offers in evaluating the lithiasic composition and fragility, taking into account the possible added value of improvements in equipment and software. In order to do so, we will determine whether different lithiasis compositions show a characteristic mineral content and density and whether this correlates with the energy necessary to fragment the lithiasis in vitro using ESWL.

MATERIAL AND METHOD

We present an experimental, in vitro, prospective blind study involving 308 urinary calculi obtained between September 2009 and June 2010 in the healthcare areas: Hospitales Universitarios Virgen del Rocío (Sevilla), Hospital de Jerez de la Frontera (Cádiz), Hospital San Juan de Dios del Aljarafe and the Hospital Clínico Universitario Lozano Blesa (Zaragoza).

The inclusion criteria were: intact urinary calculi, obtained from spontaneous expulsion or surgery, diameter greater than 0.5cm and a pure
composition of calcium oxalate monohydrate, uric acid or carbonate apatite, defining as pure those calculi whose composition included a percentage of one of these materials greater than 75%. We also included a group of calculi whose composition was a mix of calcium oxalate monohydrate and dihydrate in similar proportions (a proportion of between 40% and 60% of each of these components).

In total, 115 calculi were excluded from the study: 11 for having undergone previous lithotripsy in any of its variations (extracorporeal, endoscopic, percutaneous) or being fragmented for other reasons, 51 for not having a diameter greater than 0.5cm and 53 because their composition did not meet the inclusion criteria. The remaining 193 were subjected to study: 31 of calcium oxalate monohydrate, 32 of mixed oxalate and calcium, 33 de carbonate apatite and 97 uric acid.

Each calculus sent by the various study centers was measured using a digital Vernier caliper at each of its three widest diameters, numbered, placed in an individual container and stored in a classification box. All this was done by a single urologist who was not informed of the composition of the stones. Afterwards, they were subjected to densitometry using the Hologic QDR 1000 densitometer in “ultrahigh” resolution mode and the “forearm” program, normally employed for conducting bone densitometry. The mineral density of the calculus was calculated, corresponding to the quotient of calcium content of the calculus between the areas of the lithiasis (g/cm²). For this, they were placed in groups of three, elevated on a 4cm thick cardboard box to simulate the location of the forearm and to render the technique compatible with the program employed (Figure 1).

For the fragmentation, a Dornier Lithotripter S was used, along with an in vitro lithotripsy simulator which supplied with the machine by the Dornier Company and is usually used with standardized plaster spheres for periodical mechanical checks and adjustments.

Shock waves were administered, maintaining the fixed frequency at 1 Hz and the coupling pressure constant, at level 6 of the Dornier Lithotripter S. The simulator has a 2 mm filter and so wave administration is halted when none of the fragments is over the aforementioned greatest diameter, for which reason the filter is empty (Figure 2). The entire procedure was carried out by a single researcher.

Having completed the lithotripsy as described, the lithiasic fragments were gathered and compacted into a pellet with a SPECAC press, then dried with potassium bromide. After this, they were subjected
administered by each wave to an area equivalent to that of each calculus (calculated using its two largest diameters). In this way, and unlike the Edose, EdAJ expresses exclusively the energy that reaches the lithiass and not an area of 12 mm in which the aforementioned lithiass is to be found. This adjustment is not necessary for lithiases larger than 12mm since, given the design of the funnel basket, the lithiastic mass that is initially found outside the 12mm defined zone, is situated inside as the central zone of the lithiass proceeds to fragment.

- Value of the “mineral content of the lithiass” and the “mineral density of the lithiass” by means densitometry, expressed in grams and g/cm² respectively.

- Lithiastic composition, with the four groups already defined in the inclusion criteria.

The continuous quantitative variables have been expressed using the median and the inter-quartile range, as they do not present a normal distribution (Kolmogorov, Saphiro-Wilk, if n< 50). The non-parametric Kruskal Wallis test was applied to samples of independent data and the Mann-Whitney U test to compare them two by two. The level of significance was set at 5%. For the multiple comparisons, we used the Bonferroni correction to determine p value, which will be 0.008333 (0.05/4) for the comparison between four groups. With this, we reduce the possibility of obtaining significance due to the effect of the multiple comparisons.

The non-parametric Spearman’s rank correlation coefficient is applied to measure the linear relationship between quantitative random variables that do not follow a normal distribution.

RESULTS

In the densitometric study, only 53 of the 193 calculi produced data that could be evaluated. The rest of them either were not detectable being radiotransparent, or presented dimensions that did not enable their mineral content and density to be measured and their automatic conversion into grams and g/cm². Hence, the group for which it was possible to analyze the most calculi was the carbonates, being larger in average size, followed by the mixed oxalates and ending with the COM group and the uric acids.

The results obtained are shown in Table I.

The only comparison in the composition prediction that demonstrates statistical significance
is that realized between the carboapatite and COM (p<0.008).

When calculating the correlation coefficient between g/cm² and grams, and the values related with the energy employed in the fragmentation (Edose, EdAJ), we only found statistical significance with respect to the EdAJ, with a correlation coefficient of 0.424 (p=0.02) and 0.347 (p=0.01) respectively.

## DISCUSSION

Currently, CT appears to have established itself as the most useful test when predicting the composition of a calculus and its fragility (7-9). Yet, in the majority of the studies conducted with this technology, the attenuation values in Hounsfield Units obtained by different compositions overlap in their range. In fact, the only practical conclusion reached

<p>| Table 1. Results from the densitometry study, subdivided into composition subgroups. |
|-------------------------------------|---------|------------------|---------|------------------|</p>
<table>
<thead>
<tr>
<th>Composition</th>
<th>gr/cm²</th>
<th>grams</th>
</tr>
</thead>
<tbody>
<tr>
<td>Carbonate apatite</td>
<td>0.47</td>
<td>1.24</td>
</tr>
<tr>
<td>(n=25)</td>
<td>(0.24-0.49)</td>
<td>(0.13-2.58)</td>
</tr>
<tr>
<td>(lost=8)</td>
<td>p&lt;0.001</td>
<td></td>
</tr>
<tr>
<td>MONOHYDRATE</td>
<td>0.05</td>
<td>0.01</td>
</tr>
<tr>
<td>(n=15)</td>
<td>(0.01-0.10)</td>
<td>(0.003-0.02)</td>
</tr>
<tr>
<td>(lost=16)</td>
<td>p=0.069</td>
<td>p=0.37</td>
</tr>
<tr>
<td>COD-COM</td>
<td>0.26</td>
<td>0.32</td>
</tr>
<tr>
<td>(n=9)</td>
<td>(0.09-0.39)</td>
<td>(0.06-1.31)</td>
</tr>
<tr>
<td>(lost=23)</td>
<td>p=0.53</td>
<td>p=0.75</td>
</tr>
<tr>
<td>URIC ACID</td>
<td>0.15</td>
<td>0.52</td>
</tr>
<tr>
<td>(n=4)</td>
<td>(0.01-0.33)</td>
<td>(0.006-1.37)</td>
</tr>
<tr>
<td>(lost=93)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

The losses expressed are due to the radiotransparency of the samples or that although they are radiopaque, the results provided by the software are uninterpretable when the zone of lithiasis is selected.
is that calculi presenting an attenuation greater than 1,000 cannot be adequately fragmented with ESWL (2,3). However, the scanner is not a harmless test which irradiates, in a non-negligible manner, patients who in many cases will be recurrent and require many radiological studies throughout their lives (10).

Over the years, the possibility of using other techniques to this end has been studied. In 1993, in a study of 36 lithiases, Herremans et al. determined that the lithiasic density values in g/cm\(^2\) overlapped between different compositions, with the exception of those found in the lithiasis of uric acid, which, due to its low calcium content, differed from the others. Nevertheless, in this study, practically half of the calculi had a mixed composition (47%) and brushite, apatite and calcium oxalate dihydrate lithiases were not included (11). This does not occur in our study, in which we include different compositions and in which the majority of lithiases are pure.

In the same year, Burgos et al. published a study on 114 pure composition lithiases. They concluded that bone densitometry has limited value in determining the lithiasic composition, as it only differentiates the uric acid from the rest of the compositions. However, they observed that densitometry could provide data on the content and distribution of mineral and non-mineral phases that could be useful for predicting the lithiasic fragility. The values obtained in this study did not coincide with Dretler’s results, though we should consider that a different densitometer was employed (photonic versus X rays) and the sample size was very different (12).

In general, it appears that the conclusions we can draw from the lithiiasis study by means of densitometry are few. Two main factors are responsible for this poor success:

• The large proportion of uric acid lithiases in our sample, which made it difficult to detect them using this technology.

• The accumulated progressive simplification of the bone densitometry equipment has transformed them into a cheap, convenient and very useful technology. This means that it is difficult to use them for studies for which they were not designed, as occurs in our case. Thus, the use of “forearm” mode in the equipment used implied that although the calculus was detectable on the image obtained, by encircling it with the selector point, the record obtained was incongruent, possibly due to the scarce surface marked compared to that which the program expected to gather. For this reason, we also had to discard from the analysis a large number of the samples with small surfaces, as the results obtained did not make sense (negative values, null determination, etc).

Thus, in global terms, if this technology does not enable more than half of the sample to be processed, the analysis of the data does not appear pertinent. We are unaware whether changing the design or using different equipment could avoid these difficulties. The lack of literature on the subject is notable, in terms of what can be found from the 90s. It is possible that the peak of tomography during these years led to a disinterest in densitometry as a predictor of lithiasic composition and/or fragility. Perhaps obtaining similar results to ours discouraged the publication of works on the subject. However, it is evident that some data lead to the suspicion that with the aforementioned adjustments, we could find some utility in densitometry. Thus, in an in vivo study of 30 patients, Zanchetta et al. found a positive linear correlation between the mineral content of the lithiiasis (grams) and the number of waves required for the fragmentation, but not between the area and the lithiasic density (g/cm\(^2\)) (13). In a study of 12 patients, Sakamoto et al. also determined that the mineral content of the lithiiases of those in which the ESWL was successful was greater that that presented by those in which the treatment was not effective. In an in vitro study of 20 specimens, they also found that the density (g/cm\(^2\)) presented by the different compositions was concordant with the normal hardness presented by: COM 0.98, apatite 1.01, DCO 0.86, struvite 0.53 (14).

In our study, and with the reserves mentioned previously, we find results that lead us to believe that a better design could have resulted in more useful conclusions.

• Our results resemble those in the literature in terms of the infective lithiiases (0.47 vs. 0.38 Burgos and 0.44 Dretler) and more like those obtained by Burgos et al., with respect to the calcium oxalate dihydrate (mixed) (0.36 vs. 0.26). However, the mineral density of the uric acid lithiiasis more closely resembles that obtained by Dretler (0.22 vs. 0.15 in our work), although this author found values generally higher and in a different order. However, the small sample size should be highlighted as well as the use of a photonic densitometer in this work, unlike that used by Burgos et al. (4,12).

• The group with the largest average lithiastic size (calcium carbonate) presented the least losses in its analysis. Perhaps by limiting the use of this technology to large lithiases could be useful, such as in the case of coraliform lithiiases or of a size limit that leads to doubts over the use of ESWL or percutaneous surgery.
In short, this is the situation in which the study on prediction using image techniques is most useful.

- The EdAJ required for the comminution appears to correlate with the lithiasic weight in grams and the mineral density of the lithiasis (g/cm$^2$) in the lithiases that could be measured.

- Despite the disproportion of compositions in the sample, some appear to differ significantly when the mineral density is used (calcium carbonate vs. COM). In a study of 216 lithiases obtained from open surgery, although Demirbas et al. did not find that the chemical composition could be predicted by means of using the radiographic appearance, they did find a correlation between the lithiasic weight in grams and the number of waves required for the fragmentation (although they did not specify the intensity parameters of these waves, which are assumed to be constant, or the energy provided) [15]. In the regression analysis they carried out to see which of the variables was the most important, they coincided with Zanchetta in that it was the weight in grams [13]. They propose an equation that predicts the number of waves required for the fragmentation.

**CONCLUSIONS**

In our study, the use of densitometry to determine the lithiasic composition and fragility did not produce conclusive results. Nevertheless, there is evidence to suggest that with a different design, taking into account only calculi sizes we could treat either with ESWL or percutaneous nephrolithotomy, results of greater practical utility could be obtained.

**REFERENCES AND RECOMMENDED READINGS**

(*of special interest, **of outstanding interest)


