Study of non-contrast helical computed tomography in evaluating holmium laser lithotripsy for urinary calculus

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Received March 13, 2018; Accepted July 20, 2018

DOI: 10.3892/etm.2018.6765

Abstract. The present study aimed to investigate the correlation between the parameters of non-contrast helical computed tomography (NCHCT) and the total energy of holmium laser lithotripsy, and establish a correlative mathematical model. From March 2016 to February 2017, 120 patients with a single urinary calculus were examined by NCHCT prior to holmium laser lithotripsy. The calculus location was confirmed, the CT value was measured and the volume of the calculus in the established three-dimensional reconstruction model was calculated. The total energy of lithotripsy (TEL) was recorded post-operatively. A significant difference in the TEL between renal calculi and ureteral calculi was identified (P<0.001) and a high and significant correlation between the volume of the calculus and the TEL was determined (Spearman r=0.827, P<0.001). Multivariate linear correlation analysis revealed that the CT value of the calculus and the TEL (Spearman r=0.468, P<0.001). A moderate correlation was identified between the CT value of the calculus and the TEL (Spearman r=0.468, P<0.001). Multivariate linear regression analysis revealed that the location, the volume and the CT value of the calculus were independently associated with the TEL (F=288.858, adjusted R²=0.879, P<0.01). A mathematical model correlating the parameters of non-contrast helical computed tomography (NCHCT) with the TEL was established, which may provide a foundation to guide the use of energy in holmium laser lithotripsy. The calculus location was confirmed, the CT value was measured and the volume of the calculus in the established three-dimensional reconstruction model was calculated. The total energy of lithotripsy (TEL) was recorded post-operatively. A significant difference in the TEL between renal calculi and ureteral calculi was identified (P<0.001) and a high and significant correlation between the volume of the calculus and the TEL was determined (Spearman r=0.827, P<0.001). A moderate correlation was identified between the CT value of the calculus and the TEL (Spearman r=0.468, P<0.001). Multivariate linear regression analysis revealed that the location, the volume and the CT value of the calculus were independently associated with the TEL (F=288.858, adjusted R²=0.879, P<0.01). A mathematical model correlating the parameters of NCHCT with the TEL was established, which may provide a foundation to guide the use of energy in holmium laser lithotripsy, and it was possible to estimate the TEL by the location, the volume and the CT value of the calculus.

Introduction

Urinary calculus is commonly encountered in urinary surgery, and its worldwide incidence has been constantly increasing in recent years (1). The cause of urinary calculus is complex and the major influencing factors include individual and environmental factors. Urinary calculus is likely to cause urinary tract obstruction, accompanied by dull or colic pain in the waist, hematuria and fever, which severely affects the quality of life and the health of affected patients (2-4).

Non-contrast helical computed tomography (NCHCT) is the gold standard for the diagnosis of urinary calculus, and provides accurate information, including the size, location, shape and amount of calculi. NCHCT provides a preliminary estimation of the hardness and fragility of urinary calculi by measuring the computed tomography (CT) value, which is the X-ray absorption coefficient of a certain tissue/material, and the volume of the calculus may be accurately calculated through the establishment of a three-dimensional reconstruction model.

After the first successful application of holmium laser to the urinary calculus (5), this technique has received increasing attention. Due to its precise and powerful fragmenting function and high safety, holmium laser has become one of the most popular treatments for urinary lithotripsy. Holmium laser is able to fragment the calculus more effectively than extracorporeal shockwave and other lithotripsy, and achieve a high calculus-free rate of >90% (6,7). Compared to other fragmenting equipment, holmium laser generates smaller fragments of the calculus, which are easier to discharge (8). Holmium laser treatment causes minimal injury to the surrounding area and is safer than other fragmenting operations (9).

Certain studies have demonstrated that the mechanism of holmium laser lithotripsy maybe a photomechanical effect. When the laser fiber is exposed to the calculus, the large energy is immediately absorbed by the internal and external water of the calculus. Cavitation bubbles are produced at the water-calculus interface and the shock waves produced by continuous rebound and countless bursting of the bubbles are transferred to the calculus, resulting in its fragmentation (10,11). However, certain studies have refuted this view. Dushinski and Lingeman (12) proposed that the mechanism of fragmentation should be explained by the photothermal effect on urinary calculi. Chan et al (13) also reported that the major mechanism of holmium laser lithotripsy is the photothermal effect. The large energy of the holmium laser increases the temperature of the irradiated region and exceeds the threshold.
temperature. The heat causes a chemical breakdown of the calculus and weakens the structural integrity of the calculus, and it also contributes to the fragmentation of the interstitial water and vapor expansion.

Several parameters affecting the effect of fragmentation of calculus by holmium laser lithotripsy have been evaluated. Sea et al (14) reported that with the increase of the frequency of constant pulse energy, the crushing rate was not increased. Chawla et al (15) have reported that the crushing rate rises accompanied by the increase of the pulse energy, but it does not increase with the pulse frequency. Kronenberg and Traxer (16) indicated that the setting of a low pulse repetition frequency and high pulse energy achieved a higher crushing rate. Bader et al (7) suggested that with the same power setting, there was no significant difference in the fragmentation rate between different pulse durations. Furthermore, Kronenberg and Traxer (16) observed that at the same power level, a setting with a low frequency and high pulse energy is more efficient than high a frequency and low pulse energy. They also identified a linear correlation of the pulse energy with the size of the fragment, as well as with the width and depth of the fissure.

Previous theoretical and clinical studies on holmium laser lithotripsy mainly focused on the mechanism, influencing factors, applied range and therapeutic efficacy of the operation. Only a few studies have assessed the correlation between the parameters of NCHCT and the total energy of holmium laser lithotripsy (17). Few studies investigated the guidance of the energy use in holmium laser lithotripsy (18). The purpose of the present study was to investigate the correlation between the parameters of NCHCT and the total energy of lithotripsy (TEL), and to establish a correlative mathematical model.

Materials and methods

Patients. A total of 125 patients with urinary calculi who presented at Shandong Provincial Third Hospital (Jinan, China) between March 2016 and February 2017, and who were scheduled for holmium laser lithotripsy, were enrolled in the present study. The present study was approved by the institutional review board of Shandong Provincial Third Hospital. All patients provided written informed consent prior to enrollment. Of all of the patients, 5 were excluded from the final analyses due to failure of their lithotripsy: In three cases, the necessary data were not obtained, and in two cases, the patients refused to participate. Of the 120 patients, 77 were female and 43 were male, the age range was 26-78 years and the average age was 47.9±12.7 years. Concerning the calculus location, 48 patients (40.0%) had renal calculus and 72 (60.0%) had ureteral calculus. In terms of the calculus volume, the largest calculus was 1,347 mm^3, the smallest was 254 mm^3 and the average volume of the calculus was 485.35±195.349 mm^3. The

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Fig. 1/2

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The highest CT value was 1,475 Hu and the lowest CT value was 374 Hu, and the average CT value of the calculi was 927.27±275.186 Hu. Among them, 5 calculi (4.2%) were grade 1, 32 (26.7%) were grade 2, 63 (52.5%) were grade 3 and 20 (16.6%) were grade 4 (Table I).

**TEL correlates with the calculus location, volume and CT value.** A strong negative correlation was identified between the TEL and calculus location ($r=-0.819$, $P<0.001$); the TEL for the renal calculus was higher compared with the TEL for the ureteral calculus. There was a strong positive correlation between the volume of the calculus and the TEL ($r=0.827$, $P<0.001$); larger calculus required higher TEL. A moderate correlation between the CT value of the calculus and the TEL was identified ($r=0.468$, $P<0.001$); a calculus with a higher CT value required higher TEL. Multivariate linear regression analysis revealed that the location, the volume and the CT value of the calculus were independently associated with the TEL ($P<0.01$; Table II).

**Establishment of the mathematical model.** To estimate the TEL of different calculi, a multivariate linear regression model was established with the following parameters: Calculus location, volume and CT value (Table III). After collinearity was eliminated and normality was tested (Figs. 3 and 4), the following multivariate linear regression equation was obtained: TEL (J) = 753.328 − 328.835x calculus location (0 = renal calculus; 1 = ureteral calculus) + 0.940x calculus volume (mm$^3$) + 0.421x CT value (Hu) ($F=288.858$, adjusted $R^2=0.879$, $P<0.01$). The adjusted $R^2$ indicated that the energy variation based on the location, the volume and the CT value of the calculus accounted for 87.9% of the samples. The equation indicated that more energy was required for lithotripsy in patients with a renal calculus, a calculus with a larger volume and a calculus with a higher CT value.

**Discussion**

The TEL required to fragment calculi varies depending on their specific features. Unguided use of energy in lithotripsy has certain disadvantages. Insufficient energy may not fragment the calculus effectively, while excessive energy may lead to a higher incidence of complications and adverse effects. If the TEL was to be estimated pre-operatively, the urologist would be able to predict the difficulty of the operation and arrange for a suitable type of anesthesia, operation monitoring and drug treatment, and the emergency program for high-risk patients may also be performed in advance. To facilitate the pre-operative estimation of the TEL, a mathematical model correlating the parameters...
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The present study indicated that the TEL required for renal calculi exhibited a significant difference from that required for ureteral calculi, with renal calculi requiring a higher TEL. A previous retrospective study by Molina et al (17) indicated that renal calculi required more energy than ureteral calculi, which was in agreement with the results of the present study. Although the exact reasons for this remain elusive, one conceivable explanation is that hydronephrosis or calyceal hydrocalycosis make the renal calculus more mobilized, while the location of ureteral calculus is relatively fixed. In the fragmentation of a renal calculus, the impact produced by holmium laser may cause the movement of the calculus, and the total impact of the laser fiber on the calculus is reduced. As a result, more pulses may be fired inefficiently and more energy is wasted.

In the present study, a strong correlation between the calculus volume and the TEL was identified, with larger calculi requiring more energy for fragmentation. In their retrospective study, Molina et al (17) determined a significant correlation between the calculus volume and the cumulative holmium laser energy. Blomley et al (19) performed a systematic review of holmium laser lithotripsy and reported that the required cumulative energy of lithotripsy was increased with the increase of the calculus size and mass. These results are consistent with the conclusion of the present study and it was possible to evaluate the TEL preferably by the volume of the calculus, which may serve as an important index of the evaluation of the TEL.

The present study also determined a correlation between the CT value of the calculus and the TEL, with a calculus with a higher CT value requiring a higher TEL. Zhang et al (20) reported that the CT value was able to effectively predict the fragility of urinary calculi and the shocking times of extracorporeal shock wave lithotripsy. Gupta et al (21) came to the same conclusion that the fragility of a calculus may be estimated based on the CT value, with a lower CT value of the calculus being associated with an easier fragmentation. Wang et al (22) indicated that the CT value may be used to quantitatively analyze the hardness of urinary calculi. The study suggested a positive correlation between the CT value of urinary calculi and their hardness, with a higher CT value indicating a harder calculus and a more difficult fragmentation. The CT value is the X-ray absorption coefficient of a certain tissue/material, and it is an index providing information on the density, with a higher CT value indicating a larger density. However, the hardness and fragility of a urinary calculus mainly depends on other factors as well.

Table II. Results of Spearman's rank correlation analysis of the parameters of NCHCT and the total energy of holmium laser lithotripsy.

<table>
<thead>
<tr>
<th>Parameters</th>
<th>r</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Calculus location</td>
<td>-0.819</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Calculus volume</td>
<td>0.827</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>CT Value</td>
<td>0.468</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

CT, computed tomography.

Table III. Results of multivariate linear regression analysis of the variables estimating the total energy of holmium laser lithotripsy.

<table>
<thead>
<tr>
<th>Variables</th>
<th>B</th>
<th>SE</th>
<th>t</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Constant</td>
<td>753.328</td>
<td>67.941</td>
<td>11.088</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Calculus location</td>
<td>-328.835</td>
<td>32.965</td>
<td>-9.975</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Calculus volume</td>
<td>0.940</td>
<td>0.084</td>
<td>11.244</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>CT value</td>
<td>-0.421</td>
<td>0.045</td>
<td>9.373</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

CT, computed tomography; B, partial regression coefficient; SE, error of partial regression coefficient standard.

Figure 3. Normal P-P plot of regression-standardized residual. Cum prob, cumulative probability.

Figure 4. Histogram of regression standardized residual. Std. Dev., standard deviation.
on its chemical composition and inner structure, which has a high correlation with the CT value and may be used to estimate the major composition of calculus. Furthermore, the hardness and fragility of the calculus have a key role in the efficacy of lithotripsy, which exhibits marked differences for calculi with different hardness and fragility. Overall, calculi with different CT values have a different hardness and fragility, and the TEL is different.

In conclusion, the present study indicated a correlation between the parameters of NCHCT and the TEL. A mathematical model correlating the parameters of NCHCT with the TEL was established, which may provide a foundation to guide the use of energy in holmium laser lithotripsy. By providing a preliminary evaluation of the total energy required in holmium laser lithotripsy, NCHCT may be used to predict the difficulty of lithotripsy, and improve the safety and efficiency of lithotripsy.

Acknowledgements
The authors are particularly grateful to Professor Yuanyuan Liu (Statistics Department, Shandong Provincial Third Hospital, Jinan, China) for her assistance with the statistical analysis. The authors also thank Professor Mingjie Li and Professor Xiangtao Wang (both Department of Urinary Surgery, Shandong Provincial Third Hospital) for their technical advice on the holmium laser lithotripsy.

Funding
The present study was funded by the Science Foundation of Qilu Hospital of Shandong University and the Fundamental Research Funds of Shandong University (grant no. 2015QLMS39).

Availability of data and materials
The analyzed data sets generated during the present study are available from the corresponding author on reasonable request.

Authors’ contributions
JM, ZY, XZ, CW, XL, ZL, LYu and LYi were responsible for data collection. LC, JM, ZY, XJ and WH were responsible for statistical analysis. LC, JM, ZY, XZ and WH wrote the article. The final version of the manuscript has been read and approved by all authors, and each author believes that the manuscript represents honest work.

Ethical approval and consent to participate
The present study was approved by the institutional review board of Shandong Provincial Third Hospital (Jinan, China). All patients provided written informed consent prior to enrollment.

Patient consent for publication
Not applicable.

Competing interests
The authors declare that they have no competing interests.

References