Comparison of YAG Laser Lithotripsy and Extracorporeal Shock Wave Lithotripsy in Treatment of Ureteral Calculi: A Meta-Analysis

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Key Words
Ureteroscopy lithotripsy with holmium laser · Extracorporeal shock wave lithotripsy · Ureteral calculi

Abstract
Objective: To evaluate the clinical efficiency and safety of ureteroscopy lithotripsy (URSL) with holmium laser technology and extracorporeal shock wave lithotripsy (ESWL) on ureteral calculi using systematic reviews. Methods: Randomized controlled trials and prospective controlled trials accorded with inclusion among PubMed Database, EmBase Database, Cochrane Library and China National Knowledge Infrastructure were collected. Review Manager 5.0 was adopted to estimate the effects of the results among selected articles. Forest plots, sensitivity analysis and bias analysis for the articles included were also conducted. Pooled estimate of risk ratios and standard mean difference (SMD) with 95% CIs were used as measures of effect sizes. Results: Finally 1,770 patients were included in the 14 studies, which eventually satisfied the eligibility criteria. The number of patients in URSL group and ESWL group were 885 and 885, respectively. The results of heterogeneity test suggested that complication events (RR 1.12 (95% CI 0.63–2.00), p = 0.70), hospital days (SMD = –0.08 (95% CI –1.14 to 0.98), p = 0.88) and efficiency quotient (RR 1.31 (95% CI 0.96–1.80), p = 0.09) were insignificantly different, while the stone-free rate (RR 1.15 (95% CI 1.06–1.26), p = 0.002) and operation time (SMD = –2.27 (95% CI –3.42 to –1.11), p = 0.0001) between ESWL and URSL were significantly different. Conclusion: Although both URSL and ESWL have its own advantages and drawbacks, URSL is relatively a more efficient and safe method to treat ureteric stones, since it has shorter operation time and a better stone-free rate.

Introduction

Ureteral calculi or stones are common occurrences and it can easily become surrounded by tissue around leading to stone formations in tissue. The incidence of this disease accounts for more than 65% and presents a tendency of increasing incidence in recent years. However, it has been found that methods of conservative treatment to remove stones from the ureter has little effect, while open surgical methods may lead to trauma and many complications [1–3].

Extracorporeal shock wave lithotripsy (ESWL) is a non-contact, noninvasive technique for the treatment of calculi. It is widely used in clinical treatment, and this method of removing stones has advantages such as simple operation, less pain and lower cost [4–7]. Although ESWL is one of the most commonly used methods in the treat-
ment of ureteral calculi, it was observed that some parts of gravel could not be ejected spontaneously after treatment, and this sets limits for the application of ESWL.

Meanwhile, open surgery has been gradually replaced by ureteroscopy lithotripsy (URSL), which uses the holmium laser technology. Holmium laser is a kind of new laser commonly used in urological surgery. It can crush all kinds stones with whatever composition and density and cause little ureteral mucosal damage [7–10].

Both ESWL and URSL are effective treatment modalities in the management of proximal ureteral stones, and both therapies have their own advantages and disadvantages [11, 12]. There are several researches that compare URSL and ESWL in ureteral calculi therapy, in which there exist various research designs, recruit and exclusion criteria, measurement methods and so on. Randomized controlled trails and clinical prospective studies on URSL and ESWL are collected. A meta-analysis is performed to evaluate the clinical efficacy and safety of these 2 treatments comprehensively.

Materials and Methods

Literature Search Strategy

A comprehensive electronic literature search of the PubMed Database, EmBase Database, Cochrane Library and China National Knowledge Infrastructure from January 1981 to April 2016 was conducted in June 2016. Two researchers carried out literature search independently. The search terms were as follows: (1) ‘ESWL’ OR ‘extracorporeal shock wave lithotripsy’ OR ‘URSL’ OR ‘YAG laser lithotripsy’; (2) ‘ureteral calculi’ OR ‘ureteral calculus’ OR ‘ureter stones’; (3) ‘treatment’ OR ‘therapy’. These keywords were combined to identify researches using the Boolean operator ‘AND’ without any restriction on languages. In addition, the reference catalogues of all retrieved papers were checked for qualified articles that were not included as mentioned above.

Study Selection

The inclusion criteria were as follows: (1) ESWL and URSL were used to treat ureteral calculi; (2) the stone-free rate was clearly noted; (3) the complications that happened during the course of the treatment were clearly declared; (4) at least 10 patients were included; (5) no lapping data were included.

Two authors individually assessed related articles that were found to comply to the inclusion and exclusion criteria. If there was disagreement between 2 researchers, a third author was involved to help solve it.

Data Extraction and Quality Assessment

Two reviewers independently scanned the full text of the manuscripts and extracted the following data from each eligible research: first author’s name, country of origin, publication year, sampling size, study period, age and gender of the patients in each article. The methodological quality of the studies was evaluated by Quality Assessment Tool for Diagnostic Accuracy Studies version 2 (QUADAS-2), which is an improvement over the original one, since it considers a more transparent rating of bias and applicability of primary diagnostic accuracy studies.

Statistical Analysis

Review Manager (version 5.0, The Cochrane Collaboration, 2011) was adopted to estimate the effects of the outcomes among selected reports. For continuous outcomes, a mean difference was calculated using the mean difference. Heterogeneity across studies using the I^2 statistic is a quantitative measure of inconsistency across studies. Studies with an I^2 of 25–50% were considered to be with low heterogeneity, I^2 of 50–75% was considered to be with moderate heterogeneity, and I^2 >75% was considered to be with high heterogeneity. If I^2 >50%, potential sources of heterogeneity were tested by sensitivity analysis conducted by eliding one study in each turn and investigating the influence of a single study on the combined estimates. Furthermore, when heterogeneity was observed, a random-effect model was adopted; while it was absent, the fixed-effect model was utilized. Funnel plots were used to examine the potential publication bias.

Results

Search Process

The initial search found 591 related publications, in which 63 were excluded because they were mere duplicates. After the screening based on the titles and abstracts, 49 articles were identified. Then, 44 researches were excluded because of unsatisfactory article type and insufficient data. Finally, 14 articles were selected for this meta-analysis, in which 7 were published in English and 7 in Chinese. The study selection process is detailed in figure 1.

Characteristics of Included Studies

There were 14 articles comprising a total sampling size of 1,770 patients with ureteral calculi meeting all inclusion and exclusion criteria; they were then included in this meta-analysis. The sampling sizes of these studies varied from 30 to 300. These researches were performed in America, South America, Europe and Asia. The publication date of 14 trails ranged from 1999 to 2016. Most of the researches were published in English and some were in Chinese. All of the 14 studies were conducted in randomized controlled design or prospective controlled design. The scope of age among patients was from 35 to 61 and in all the trials, the number of male patients was more than that of female patients. Recruitment time varied from 1 to 4 years. The characteristics of the involved researches are shown in table 1.
Results of Quality Assessment

The QUADAS-2 tool was used to evaluate the risk of bias in the 14 trials in which none of the trials showed problems in patient selection, 3 showed problems in reference standard, 4 showed problems in study flow, and 5 trials showed problems in the index test. When applicability was taken into consideration, no trails experienced any performance problems. In general, 3 trials were at risk of bias and 11 were out of risk. All the trials had little trouble regarding applicability. The detailed results of the quality assessment are listed in table 2.

Results of Heterogeneity Test

All the 14 articles reported the differences of stone-free rate of patients receiving ESWL and URSL. Figure 2 shows that the heterogeneity among studies was large, that I^2 of stone free rate was 77% with p for heterogeneity <0.0001, which indicated that significant heterogeneities were present in the studies. So, the random effect model was used to evaluate the pooled estimates. The overall RR (95% CI) was 1.15 (1.06–1.26); p value of the test for overall effect was 0.002. This demonstrated that URSL had better results in terms of the stone-free rate than ESWL, and had a significant 15% decrease in the stone-free rate of patients treated with URSL.

Fourteen research studies were analyzed along with the complication events of the patients after being subjected to the 2 different therapeutic methods. The result of heterogeneities showed no significant difference between URSL and ESWL and it indicated that the random effect model should be adopted (p < 0.0001, I^2 = 69%, Z = 0.39, p of overall effect = 0.70). However, the result of the overall effect showed no significant difference between URSL and ESWL, which demonstrated that similar complication events happened in URSL and ESWL (fig. 3).

In the analysis of operation time in URSL and ESWL, 12 articles were included. The results of heterogeneity test showed that the random effect model was needed to analyze the data (p < 0.00001, I^2 = 99%, Z = 3.84, p of overall effect = 0.0001). The overall effect was significant and the overall standard mean difference was −2.27, which showed that URSL consumed less operation time than ESWL (fig. 4).

A total of 6 papers were used to analyze period of hospital stay. The results of heterogeneity showed that the random effect model should be used to analyze data since p < 0.00001 and I^2 = 98%. In the results related to the overall effect, there is no significant difference between URSL and ESWL regarding the hospital stay (Z = 0.15, p of overall effect = 0.88; fig. 5).

In the result of heterogeneity in EQ between URSL and ESWL, only 5 papers were included. EQ is a measure to comprehensively evaluate the effect of 2 different therapies. The results of heterogeneity indicated that the random effect model should be used since p < 0.00001
and $I^2 = 87\%$. The overall effect showed that there is no significant difference between the EQ values in URSL and ESWL ($Z = 0.15$, p of overall effect = 0.09; fig. 6).

### Results of Sensitivity Analysis and Publication Bias

To examine the stability of the outcome, a sensitivity analysis was needed. A relative outlier was excluded, the result demonstrate that in heterogeneity part, $I^2$ value changed from 77 to 69%. It indicates that the heterogeneity is mainly due to the research by Paolo Verze et al. [26] in 2010. The forest plot without Paolo Verze’s article was shown in figure 7.

A funnel plot for the stone-free rate using URSL and ESWL was performed. All the studies were included in the plot. To some extent, the result indicated that there existed some publication bias since the symmetrical characteristic of the funnel plot is not good (fig. 8).

### Discussion

Ureteral calculi accounts for 65% on urinary stones, and the onset age is between 20 and 40 years. The incidence of Ureteral calculi in men is higher than that in women. To date, drugs, ESWL, ureteroscopy, percutaneous nephroscope lithotripsy and laparoscope are main therapies for ureteral stone [27–29]. However, the selection of treatment for ureteric stones remains a discussed

<table>
<thead>
<tr>
<th>Study</th>
<th>Nation</th>
<th>Recruitment time</th>
<th>Groups</th>
<th>Numbers</th>
<th>Age</th>
<th>Male/female</th>
<th>Course of disease</th>
</tr>
</thead>
</table>
Comparison of YAG Laser Lithotripsy and ESWL

Review

Topic in urology. This research is based on good quality researches to evaluate the effectiveness and efficiency of ESWL and URSL.

ESWL had been widely used in clinical treatment of urinary calculi since the 1980s, and it was one of the common minimally invasive ways, especially for ureteral stone less than 1 cm in diameter. But, the long-time existence of ureteral calculi would lead to obvious inflammation reactions, such as granulation hyperplasia, wall thickening, luminal stenosis and other pathological changes.

Table 2. Results of QUADAS-2 quality assessment for each trial

<table>
<thead>
<tr>
<th>Study or Subgroup</th>
<th>Events</th>
<th>Total</th>
<th>Events</th>
<th>Total</th>
<th>Weight</th>
<th>Risk ratio M-H, fixed, 95% CI</th>
<th>Risk ratio M-H, fixed, 95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bai Hong-qing (2015)</td>
<td>139</td>
<td>150</td>
<td>121</td>
<td>150</td>
<td>17.7%</td>
<td>1.15 [1.05, 1.26]</td>
<td>1.15 [1.10, 1.20]</td>
</tr>
<tr>
<td>Jia-rong Cai (2014)</td>
<td>47</td>
<td>50</td>
<td>40</td>
<td>50</td>
<td>5.9%</td>
<td>1.18 [1.01, 1.37]</td>
<td>1.17 [1.04, 1.31]</td>
</tr>
<tr>
<td>Min Fan (2007)</td>
<td>61</td>
<td>80</td>
<td>73</td>
<td>82</td>
<td>10.5%</td>
<td>0.86 [0.74, 0.99]</td>
<td>0.85 [0.73, 0.99]</td>
</tr>
<tr>
<td>Hendrikx (1999)</td>
<td>129</td>
<td>136</td>
<td>127</td>
<td>137</td>
<td>18.5%</td>
<td>1.02 [0.96, 1.09]</td>
<td>1.02 [0.96, 1.09]</td>
</tr>
<tr>
<td>Honeck (2006)</td>
<td>60</td>
<td>62</td>
<td>52</td>
<td>62</td>
<td>7.6%</td>
<td>1.15 [1.03, 1.30]</td>
<td>1.14 [1.02, 1.27]</td>
</tr>
<tr>
<td>John S. Lam (2002)</td>
<td>30</td>
<td>31</td>
<td>40</td>
<td>50</td>
<td>4.5%</td>
<td>1.21 [1.04, 1.41]</td>
<td>1.20 [1.03, 1.39]</td>
</tr>
<tr>
<td>Shuang-Quan Lin (2015)</td>
<td>73</td>
<td>80</td>
<td>53</td>
<td>80</td>
<td>7.8%</td>
<td>1.38 [1.16, 1.63]</td>
<td>1.37 [1.15, 1.62]</td>
</tr>
<tr>
<td>Mostafa Khalil (2012)</td>
<td>29</td>
<td>37</td>
<td>45</td>
<td>45</td>
<td>4.9%</td>
<td>0.95 [0.77, 1.18]</td>
<td>0.94 [0.76, 1.16]</td>
</tr>
<tr>
<td>Paolo Verze (2010)</td>
<td>79</td>
<td>87</td>
<td>35</td>
<td>69</td>
<td>5.7%</td>
<td>1.79 [1.41, 2.28]</td>
<td>1.78 [1.40, 2.26]</td>
</tr>
<tr>
<td>Cheng Peng (2016)</td>
<td>50</td>
<td>56</td>
<td>34</td>
<td>44</td>
<td>5.6%</td>
<td>1.16 [0.96, 1.39]</td>
<td>1.15 [0.95, 1.38]</td>
</tr>
<tr>
<td>Rodrigo Amarante (2012)</td>
<td>10</td>
<td>16</td>
<td>5</td>
<td>14</td>
<td>0.8%</td>
<td>1.75 [0.79, 3.89]</td>
<td>1.74 [0.78, 3.87]</td>
</tr>
<tr>
<td>Xiang Yan-qing (2013)</td>
<td>27</td>
<td>30</td>
<td>21</td>
<td>30</td>
<td>3.1%</td>
<td>1.29 [0.99, 1.67]</td>
<td>1.28 [0.98, 1.65]</td>
</tr>
<tr>
<td>Xiao-meng Yin (2014)</td>
<td>47</td>
<td>50</td>
<td>38</td>
<td>50</td>
<td>5.6%</td>
<td>1.24 [1.04, 1.47]</td>
<td>1.23 [1.03, 1.46]</td>
</tr>
<tr>
<td>Ying-Huei Lee (2005)</td>
<td>7</td>
<td>20</td>
<td>14</td>
<td>22</td>
<td>2.0%</td>
<td>0.55 [0.28, 1.08]</td>
<td>0.54 [0.27, 1.11]</td>
</tr>
</tbody>
</table>

Total (95% CI) 885 885 100.0% 1.15 [1.10, 1.20] 0.2 0.5 1 2 5 URSU ESWL

Fig. 2. Forest plots of the stone-free rate by URSL and ESWL for the treatment of ureteral calculi.

Yes = Low risk; No = high risk; ? = unclear risk.
changes. This kind of stone was even difficult for ESWL. ESWL had its own advantages and disadvantages. The advantages of the treatment were as follows: first, with the recovery of the patient’s back, hips, stomach and other soft tissue, the damage in breaking up stones was little, which might reduce the complications. Second, during the noninvasive treatment period, was unnecessary to be administered to the patients, and the operation was more convenient. Third, the success rate was higher. The following are the drawbacks of the treatment: first, there

**Fig. 3.** Forest plots of the complication events by URSL and ESWL for the treatment of ureteral calculi.

**Fig. 4.** Forest plots of the operation time by URSL and ESWL for the treatment of ureteral calculi.
were many factors, such as the power of eliminating stone, stone size, and the position of the stone, that influence the outcome of the treatment. Second, using ESWL, it was difficult to remove stones with diameter less than 1 cm and the lack of shock wave could not disintegrate the stones [30, 31].

Meanwhile, with the development of the technology of cavity mirrors, holmium laser lithotripsy became a safe and effective method for the treatment of ureteral calculi. It was reported by Wu and Geraghty that URSL achieved excellent results for upper ureteral calculi greater than 1 cm [32, 33]. Compared with the traditional cavity lithotripsy, holmium laser had the following advantages: first, in addition to the precise surgical incision and hemostasis, holmium laser could break up all kinds of stone and vaporize ureteral polyps. Second, holmium laser was effective and can crush stones to less than 3 mm. In the operation, the visual field was clear and therefore ureteral damage could be prevented. Third, it could release the stones embedded in polyps to enhance the efficiency of the discharge of stones. However, there was still a disadvantage: the shift of stone affected the success rate and effectiveness of stone cleaning [34, 35].

Since URSL and ESWL were good treatment choices for ureteral calculi, the comparison based on previous reports was required. Considering the results of heterogeneity analysis of the stone-free rate in URSL and ESWL, the stone-free rate of URSL was better than that of ESWL, in which the difference was significant. The overall risk ratio was 1.15, which demonstrated that the overall stone-free rate of URSL is 1.15 times as much as ESWL. This finding was consistent with the findings of many other reports. The operation time in URSL was shorter than that in ESWL, which reflected the efficiency in URSL.
But the difference of incidence of complication events in both 2 therapies was negligible. The hospital stay showed no difference between URSL and ESWL. These could be because the operation conditions in both treatments were similar. In the end, a comprehensive index to evaluate the effectiveness and efficiency was calculated. The index was based on the treatment rate and the auxiliary procedures used like hospital days. The results showed that the efficiency quotient of URSL was better than that of ESWL, in which the overall risk ratio was 1.31.

The conclusion was consistent with other researches [32, 35] that URSL is a relatively better way to cure ureteric stones than ESWL. The following are some limitations of this study: First, the comparison between upper and middle-lower ureteral calculi was not made, and this could be evaluated in the further research. Second, the details of complication in both methods were not analyzed, and it could be evaluated in the future.

**Disclosure Statement**

The authors declare that they have no conflict of interest related to the publication of this paper.

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