Predictive factors of extracorporeal shock wave lithotripsy failure in the treatment of patients with ureterolithiasis

O. S. Vozianov, S. O. Vozianov

State Institution “Institute of Urology of National Academy of Medical Sciences of Ukraine”, Kyiv

A – research concept and design; B – collection and/or assembly of data; C – data analysis and interpretation; D – writing the article; E – critical revision of the article; F – final approval of the article

Key words: ureterolithiasis, treatment, extracorporeal shockwave lithotripsy, predictors.

Efficacy of different approaches to the treatment in patients with ureteral calculi and predictive factors for the success are the object of contemporary studies. However, only few on them studied the duration factor of typical ureterolithiasis symptoms and changes of the ureter wall as predictive factors of extracorporeal shock wave lithotripsy (ESWL) failure in patients with ureteral stones.

The aim of the study was to determine the peculiarities of histological changes in the ureter wall as a result of calculus presence and to evaluate the predictive factors of ESWL failure in patients with ureterolithiasis.

Materials and methods. An analysis of the treatment by ESWL in 662 patients with ureterolithiasis was performed. The patients were divided into two groups: Group 1, n = 629 (95.0 %) individuals with effective ESWL and Group 2, n = 33 (5.0 %) patients with ESWL failure when calculus were not eliminated. Stones were found in 378 (57.0 %) patients in the upper third of the ureter, in 50 (7.6 %) – in the middle and in 234 (35.4 %) – in the lower third. For determining the predictors of ESWL failure, the Spearman’s Rank Correlation Coefficient was used.

Results. The overall ESWL efficacy in our study was 95.0 %. The strong inverse correlation was found between the ESWL success and duration of symptoms (r = -0.92) and stone size (r = -0.68). Stone localization in the ureter did not influence the ESWL outcomes (r = 0.27).

Conclusions. Increasing of the period from the manifestation of primary clinical symptoms to the implementation of ESWL reduces the treatment efficacy. Patients with ureteral stones more than 15 mm have lower stone-free rates after ESWL.
Уретеролитиазис является всемирно распространенным заболеванием с разнообразными формами проявления, в том числе и с камнями в мочеточниках размерами более 5 мм. В результате проявляются симптомы, такие как дискомфорт в животе, боли в поясничной области, нарушение мочеиспускания, гематурия и другие.

Анализ клинических симптомов показал, что у пациентов с камнями в мочеточниках размерами более 15 мм наблюдаются более низкие показатели освобождения мочеточников от конкрементов после ЭУВЛ.

Результаты.

Увеличение срока от появления первых клинических симптомов до выполнения ЭУВЛ снижает эффективность лечения. У пациентов с камнями в мочеточниках размерами более 15 мм установлены более низкие показатели освобождения мочеточников от конкрементов после ЭУВЛ.

Материалы и методы.

Проанализировали результаты лечения 662 больных уретеролитиазом методом ЭУВЛ. Пациентов поделили на две группы: 1 включала 629 (95,0 %) больных с положительным эффектом от ЭУВЛ, группа 2 – 33 (5,0 %) пациентов, у которых не удалось обнаружить или убрать конкременты. Для определения предикторов неудовлетворительных результатов использовали коэффициент ранговой корреляции Спирмена.

Выводы.

Увеличение срока от появления первых клинических симптомов до выполнения ЭУВЛ снижает эффективность лечения. У пациентов с камнями в мочеточниках размерами более 15 мм установлены более низкие показатели освобождения мочеточников от конкрементов после ЭУВЛ.

Уретеролитиазис - это глобальная проблема, с которой сталкиваются многие пациенты в течение своей жизни. Лечение таких пациентов направлено на устранение камней и симптомов, вызванных ими, с помощью различных методов, включая ЭУВЛ.

Выбор метода лечения зависит от множества факторов, включая размер камня, его расположение и наличие других симптомов. Важно учитывать индивидуальные особенности каждого пациента и выбрать наиболее подходящий для него метод.

Реализация ЭУВЛ у пациентов с камнями в мочеточниках размерами более 15 мм может быть неэффективной из-за увеличения сроков от появления первых клинических симптомов до выполнения процедуры. Это может привести к снижению эффективности лечения и ухудшению здоровья пациента.

Результаты показывают, что у пациентов с камнями в мочеточниках размерами более 15 мм установлены более низкие показатели освобождения мочеточников от конкрементов после ЭУВЛ. Это подтверждает, что выбор метода лечения должен быть индивидуальным и учитывать все факторы, влияющие на эффективность процедуры.
Table 1. ESWL outcomes in the patients with ureterolithiasis and different duration of symptoms

<table>
<thead>
<tr>
<th>Duration of symptoms, days</th>
<th>ESWL success (n = 629)</th>
<th>ESWL failure (n = 33)</th>
<th>Efficacy, %</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n (%)</td>
<td>n (%)</td>
<td>Efficacy, %</td>
</tr>
<tr>
<td>≤7</td>
<td>311 (49.4)</td>
<td>1 (3.0)</td>
<td>99.7*</td>
</tr>
<tr>
<td>8–14</td>
<td>184 (29.3)</td>
<td>5 (15.2)</td>
<td>97.4</td>
</tr>
<tr>
<td>15–29</td>
<td>100 (15.9)</td>
<td>12 (36.4)</td>
<td>89.3**</td>
</tr>
<tr>
<td>30–59</td>
<td>27 (4.3)</td>
<td>10 (30.3)</td>
<td>73.0**</td>
</tr>
<tr>
<td>≥60</td>
<td>7 (1.1)</td>
<td>5 (15.2)</td>
<td>58.3**</td>
</tr>
</tbody>
</table>

*: baseline; **: statistical difference of ESWL efficacy comparing with the baseline (P < 0.05).

Table 2. ESWL outcomes in patients with different ureteral stone size

<table>
<thead>
<tr>
<th>Stone size, mm</th>
<th>ESWL success (n = 629)</th>
<th>ESWL failure (n = 33)</th>
<th>Efficacy, %</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n (%)</td>
<td>n (%)</td>
<td>Efficacy, %</td>
</tr>
<tr>
<td>5 – up to 10</td>
<td>392 (62.3)</td>
<td>10 (30.3)</td>
<td>97.5*</td>
</tr>
<tr>
<td>10 – up to 15</td>
<td>216 (34.7)</td>
<td>20 (60.6)</td>
<td>91.6</td>
</tr>
<tr>
<td>15 – up to 20</td>
<td>19 (3.0)</td>
<td>3 (9.1)</td>
<td>86.4**</td>
</tr>
</tbody>
</table>

*: baseline; **: statistical difference of ESWL efficacy comparing with the baseline (P < 0.05).

Table 3. ESWL outcomes in patients with different stone localization in the ureter

<table>
<thead>
<tr>
<th>Stone localization in the ureter</th>
<th>ESWL success (n = 629)</th>
<th>ESWL failure (n = 33)</th>
<th>Efficacy, %</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n (%)</td>
<td>n (%)</td>
<td>Efficacy, %</td>
</tr>
<tr>
<td>Upper third</td>
<td>360 (57.2)</td>
<td>18 (54.6)</td>
<td>95.2*</td>
</tr>
<tr>
<td>Middle third</td>
<td>48 (7.6)</td>
<td>2 (6.1)</td>
<td>96.0**</td>
</tr>
<tr>
<td>Lower third</td>
<td>221 (35.1)</td>
<td>13 (39.4)</td>
<td>94.4**</td>
</tr>
</tbody>
</table>

*: baseline; **: no statistical difference of ESWL efficacy comparing with the baseline (P > 0.05).

registered in 33 (5.0 %) cases. An analysis on the relationships between ESWL efficacy/failure and duration of symptoms (the time of a calculus presence in the ureter) revealed predictive factors as the stone size and its localization in the ureter.

Table 1 presents the relationships between ESWL outcomes and the duration of symptoms in our patients.

According to the Spearman’s Rank Correlation Coefficient, we registered strong inverse correlation between ESWL efficacy and duration of symptoms in our patients with ureterolithiasis (r = -0.92). Thus, with increasing duration of symptoms, the effectiveness of ESWL decreased.

Table 2 presents the relationships between ESWL outcomes and the stone size in the greatest dimension in our patients.

According to the Spearman’s Rank Correlation Coefficient, we registered strong inverse correlation between ESWL efficacy and stone size in our patients with ureterolithiasis (r = -0.68). Therefore, with increasing stone size, the ESWL effectiveness decreased. As presented in Table 2, among 238 patients with ureteral calculi sized from 10 mm up to 15 mm, successful ESWL was registered in 218 (91.6 %). The results obtained demonstrate efficacy of ESWL even in such size of ureteral calculi. Patients with ureteral calculus sized over 15 mm demonstrated statistically lower stone-free rates after ESWL comparing to the baseline (86.4 % vs. 97.5 %, P < 0.05).

Table 3 shows relationships between ESWL outcomes and stone localization in the ureter in our patients.

Using the Spearman’s Rank Correlation Coefficient we did not found any correlation between ESWL efficacy and stone localization in the ureter in our patients with ureterolithiasis (r = 0.27). It means, according to our data, the stone localization in the ureter did not influence the ESWL outcomes and could not be considered as a predictor of ESWL failure.

Assessment of the ureteral stone density we performed before ESWL in all 629 patients from Group 1 and 33 patients from Group 2. Stone density ranged from 200 HU to 1800 HU in Group 1 and from 340 HU to 1600 HU in Group 2. Taking into account that the absence of fragmentation was observed only in 7 (1.1 %) patients out of all 662 from both groups, we believe that the stone density did not influence significantly on the final outcome of ESWL in patients with ureterolithiasis (r = 0.24).

Ureteroscopic biopsy was performed followed by a histological examination of the ureteral wall in patients with different time of stones presence in the ureters (7 days, 1 month and 3 months) with a comparative analysis of the results both with one another and with the results of the ureteral wall examination where a stone was absent (a control sample, Fig. 2).

Histological appearances of biopsy specimens with hematoxylin and eosin staining and original magnification x40 are presented in Fig. 2–5.

Focal hemorrhages and areas of epithelial exfoliation are visualized, which occurred during the material collection. Stratification of the urothelium is preserved, there are superficial, intermediate and basal urothelicyttes, the number of epithelial rows ranges from 3 to 5 without cellular atypia.

Focal hemorrhages and areas of epithelial exfoliation are visualized, which occurred during the material collection. Stratification of the urothelium is largely preserved, the number of epithelial rows ranges from 3 to 5 without cellular atypia, but with dystrophic changes in the form of vacular dystrophy. There are areas of epithelial exfoliation, exposed basement membrane, exfoliation of surface urothelicyttes. Submucosal layer is characterized by moderate edema.

Stratification of the urothelium in most areas is preserved, the number of epithelial rows ranges from 5 to 7 without cellular atypia, but with dystrophic changes in...
the form of vacuolar dystrophy. There are areas of epithelial exfoliation, exposed basement membrane, exfoliation of superficial, intermediate and basal urotheliocytes. Massive submucosal edema, vascular congestion, moderate focal lymphocyte and mononuclear cells infiltration.

In most of the mucous membrane, there are areas of epithelial exfoliation, exposed basement membrane, exfoliation of the surface, intermediate and basal urotheliocyte layers. Epitheliocytes are without cellular atypia, but with dystrophic changes in the form of vacuolar dystrophy. Submucosal layer with pronounced edema, proliferation of fibrous connective tissue, pronounced focal lymphocyte and mononuclear cells infiltration.

We registered the pronounced submucosal edema and proliferation of fibrous connective tissue at the place of long-term presence of ureteral calculi (Fig. 5). Exposed basement membrane and focal edema, which were not seen in the control intact sample (Fig. 2), were progressively increased over time (Fig. 3–5).

Discussion

Efficacy of different approaches to the treatment for patients with ureteral calculi is an object of contemporary studies. Yazici O. et al. in 2015 reported that higher BMI and increased stone attenuation values were significant factors influencing the final outcome of shock wave lithotripsy in proximal ureteral stones. In the authors’ view, opposite to the current literature data, high skin-to-stone distance (SSD) was the only independent predictor of the shock wave lithotripsy success in patients with distal ureteral stones [8–10]. Various, sometimes not useful models for the prediction of ESWL effective outcomes are under validation now. Patient factors associated with ESWL efficacy have been proposed including body mass index (BMI), SSD, anatomic features of the kidney/ureter, stone size, location and density or even patient age, gender and breathing patterns. Technical factors, such as energy levels, different frequency of shock waves used, accuracy of focusing and targeting the calculus may also influence the ESWL outcomes [5,7,11–13].

The influence of duration of ureteral calculus presence, its size and localization on the ESWL outcomes was studied. According to our data, efficacy of ESWL did not depend on the localization of calculus in the ureter (Table 3). As presented in Tables 1, 2, we found the strong inverse correlation between ESWL efficacy and the calculus size (r = -0.68) as well as the time of calculus presence (duration of symptoms) (r = -0.92). So, these parameters could be considered as predictors of ESWL failure in patients with ureterolithiasis.
We examined histological changes in the ureteral wall at the place of calculus location. Pathohistological changes in the ureters, arising due to the presence of foreign bodies there, were registered by B. Vogt and I. Chokri in 2020. The authors have found mucosal irritation after ureteral double-pigtail stenting and proposed original approach to decrease it [14]. According to our data, at the place of stone location in the ureter, inflammatory changes developed at first followed by dystrophic changes in the form of vacuolar dystrophy over time. Submucosal layer was characterized by massive edema with fibrous connective tissue proliferation at the third month of the disease. The manifestations of inflammatory, sclerotic and necrotic changes of the ureteral wall increased over time. We think that detected changes could have a direct negative impact on the stone free rate following ESWL fragmentation as well as removal of fragments by endoscopic methods.

Hamamoto Sh. et al. in 2020 suggested that operative time of ureteroscopy and litholapaxy (URSL) and ureteral injuries in patients with ureteral calculi were significantly correlated with endoscopic finding grades. The authors concluded that appropriate intervention around 34 days (limited to 98 days) after symptom onset is necessary for treating ureteral calculi. Even if intervention passed 98 days post-symptom onset, staged URSL, alternative procedures, and detailed informed consent should be planned in advance. Due to high efficacy of ESWL and URS in patients with urolithiasis, there is a need for a clear understanding of their advantages and disadvantages [15, 16].

It is obvious that dystrophic and inflammatory changes with connective tissue proliferation impair the elasticity of the ureteral wall, which in turn negatively affects the evacuation of stones or their fragments after ESWL and reduce its efficacy (Fig. 2–5). Features of the dynamic histological changes in the ureteral wall under the long-term influence of the stone presence there require further research. The EAU recommends using ESWL as a first-line treatment for patients with ureterolithiasis in cases of a stone does not exceed 1 cm.

We have demonstrated a positive result of ESWL in those with ureteral calculi larger than 1.0 cm and up to 1.5 cm in the greatest dimension, but according to the time interval from the disease onset to the first session of lithotripsy of not more than 14 days (Tables 1, 2).

In our study, we have tried to evaluate the risk factors of ESWL failure in patients with ureterolithiasis. Based on statistical analysis, we have found inverse correlations between duration of symptoms and the stone size with efficacy of ESWL; therefore, we suggest that the same factors could be positive predictors of its failure. Prospects for further research are to continue the study on the risk factors for ineffective treatment of patients with ureteral stones by ESWL.

Conclusions

1. ESWL was effective in 95.0 % of our patients with ureterolithiasis and could be successfully performed even in calculi from 1.0 cm up to 1.5 cm in the greatest dimension. The duration of symptoms and the stone size can be considered as predictors of ESWL failure.

2. An increase in time between the onset of primary clinical symptoms and the ESWL decreased the effectiveness of treatment. Patients with ureteral calculi sized over 15 mm demonstrated lower stone-free rates after ESWL.

3. Prolonged presence of stones in the ureter promoted the proliferation of stromal elements of its wall with the development of fibrous connective tissue, impairing its elasticity and adversely affecting the processes of stone elimination after ESWL.

Prospects for the further research. Further studies on prognostic factors of low-invasive treatment failure in ureterolithiasis patients and deeper morphological analyses of the upper urinary tract changes should be conducted in order to decrease the level of surgical intervention failure.

Conflicts of interest: authors have no conflict of interest to declare.

References


