The Influence of Pain on the Outcome of Extracorporeal Shockwave Lithotripsy

Elke Bovelander\textsuperscript{a} Saskia Weltings\textsuperscript{b} Mandana Rad\textsuperscript{c} Paulien van Kampen\textsuperscript{d}
Rob C. M. Pelger\textsuperscript{b} Hossain Roshani\textsuperscript{a}

\textsuperscript{a}Department of Urology, \textsuperscript{b}Anesthesiology and \textsuperscript{c}Medical Statistics, Haga ziekenhuis, 's-Gravenhage;
\textsuperscript{d}Department of Urology, Leiden University Medical Center, Leiden, The Netherlands

Key Words
Lithotripsy • Pain • Urolithiasis • Kidney calculi • Ureteral calculi

Abstract

Introduction: The aim of this study was to determine the predictive value of pain scores on the efficacy of extracorporeal shockwave lithotripsy (ESWL) and to identify other predictive risk factors for treatment success. Materials and Methods: A total of 476 patients who underwent ESWL (piezoelectric lithotripsy) for urolithiasis between September 2011 and December 2015 were identified. The primary endpoint of this study was success rate, which was evaluated 4 months after ESWL. The secondary outcome was the occurrence of complications as a result of ESWL. Results: The average pain perception was reported at 5 on a scale from 0 to 10. The overall success rate of ESWL was found to be 43.9% and the success rate after the first ESWL was 35.1%. Univariate analysis showed no significant correlation between pain score and success of ESWL (p = 0.135). The level of intensity was correlated with pain scores (Pearson correlation -0.423, p < 0.001). Univariate analysis identified five predictive factors: sex, stone location, stone size, hydronephrosis and the use of tamsulosin. Multivariate logistic regression analysis showed that sex, stone location and size independently influenced the success of ESWL (p = 0.045, p = 0.001 and p < 0.001). Conclusion: No correlation was found between the pain scores and efficacy of ESWL. Despite this absence, pain scores during ESWL sessions remain high and additional analgesia would improve patient satisfaction.
After the introduction of ESWL, the procedure was performed under general anesthesia. Technical improvement of lithotripters has enabled the treatment to be performed without the use of general anesthesia, although a lower level of intensity was generally being used. However, ESWL is still generally considered to be a painful procedure. This could be caused by shockwaves reaching superficial (skin and muscle) and deeper structures (ribs, nerves and the kidney capsule) [3, 4].

It has commonly been assumed that pain effects the outcome of ESWL due to involuntary pain-induced movements and excessive respiratory excursions during the procedure, which impedes the operator’s efforts to maintain focus on the stone. High pain perception might also limit opportunities to apply an adequate dose of energy [5]. However, little evidence is available to confirm the direct effect of pain on success rates of ESWL [4–6].

The aim of this study is to evaluate the correlation between pain perception during treatment as well as other potential predictive risk factors and the stone-free rate (i.e. rate of success) after ESWL.

### Materials and Methods

**Cohort Selection Criteria**

We included patients diagnosed with urolithiasis who were referred to a urology outpatients’ clinic for ESWL between September 2011 and December 2015. They were identified from a prospectively collected database. These patients were adults (>18 years) receiving their first ESWL for a solitary stone located in the kidney or the ureter or those who had not received an ESWL within the previous 2 years. We excluded patients whose essential variable “pain-score” was missing (n = 19), those whose diagnosis was uncertain (n = 16), along with those who had been lost to follow-up (n = 46). This study was approved by the local institutional review board (METC Zuidwest Holland) and is in compliance with the Helsinki Declaration.

**Review of Patient Data**

Patient characteristics (age and sex), urologic presentation (previous ESWL, antibiotics, hydronephrosis, double-J catheter, nephrostomy catheter, use of tamsulosin, use of butylscopolamine and number of reinterventions), stone characteristics (side, size and location) and treatment parameters (level of intensity, applied amount of shocks, operator and fluoroscopy time) were obtained from the database. Use of tamsulosin was defined as use of 0.4 mg once daily at the moment of ESWL or for several days prior to the first follow-up. Stone size was measured using the largest measured diameter.

The primary endpoint of this study was the success rate defined as completely stone-free or with fragments smaller than 4 mm. Since all patients received an appointment at 3 weeks after treatment and if necessary followed by another appointment at 3 months, success rate was evaluated within 4 months of follow-up.

| Variables                  | Patients n (%) | Median (Interquartiles) |
|----------------------------|----------------|-------------------------|
| Age, year                  | 52 (41; 62.75) |                         |
| Gender                     |                |                         |
| Male                       | 347 (72.9)     |                         |
| Female                     | 129 (27.1)     |                         |
| Pain score (0–10)          | 5 (4; 7)       |                         |
| Laterality                 |                |                         |
| Right                      | 209 (43.9)     |                         |
| Left                       | 267 (56.1)     |                         |
| Stone location             |                |                         |
| Renal                      | 179 (37.6)     |                         |
| Upper pole                 | 50 (10.5)      |                         |
| Lower pole                 | 129 (27.1)     |                         |
| Ureter                     | 297 (62.4)     |                         |
| Upper                      | 191 (40.1)     |                         |
| Lower                      | 106 (22.3)     |                         |
| Stone size, mm             | 7.9 (5.2; 10.0)|                         |
| Residual stone after ureteroscopy/PCNL |            |                         |
| Yes                        | 25 (5.3)       |                         |
| No                         | 451 (94.7)     |                         |
| Hydronephrosis             |                |                         |
| Yes                        | 205 (43.1)     |                         |
| No                         | 271 (56.9)     |                         |
| Opiates                    |                |                         |
| Yes                        | 46 (9.7)       |                         |
| No                         | 430 (90.3)     |                         |
| Mean intensity level (0–20)| 13.6 (11.9; 15.1)|                    |
| Tamsulosin                 |                |                         |
| Yes                        | 152 (31.9)     |                         |
| No                         | 324 (68.1)     |                         |

The need for additional treatment or reintervention (ESWL, ureteroscopy or PCNL) within 6 months was evaluated by urologist, in case of persisting stone or patients with recurrent urolithiasis. The secondary outcome was the complication rate due to ESWL, measured using the Clavien-Dindo classification [7].

**Extracorporeal Shockwave Lithotripsy**

Shockwave lithotripsy was performed using the PiezoLith 3000 (Wolf®), a third generation piezoelectric shockwave lithotriptor. All patients received 1,000 mg oral paracetamol and 100 mg diclofenac per rectum half an hour prior to their procedure. Anticoagulants were stopped 1 week before treatment. Fluoroscopy or ultrasound was used to locate the stone. The target was to deliver 3,000 shocks for renal stones and 4,000 shocks for ureteral stones with a frequency of 2 Hz. Depending on the patients’ pain tolerance, the intensity level was gradually increased to a maximum of 17 for renal stones and 20 for ureteral stones (Supplementary table, metric scale of power as indicated by Wolf). No ramping was performed. Patients were asked to indicate their degree of pain on a scale from 0 to 10 (0, describing “no pain” and 10, describing “maximal possible pain”) multiple times during ESWL.
The highest pain score was reported. A pain score less than 4 was considered as acceptable. Three weeks after treatment, their stone status was evaluated by kidney-ureter-bladder radiography and, in case of radiolucent stones, ultrasonography or an abdominal computerized tomography (CT) scan. The procedure was carried out by urologists or specially trained nurses.

Statistical Analysis
SPSS-version 23.0 was used to perform statistical analyses. The Pearson correlation coefficient was used to evaluate the correlation between intensity levels and pain scores. Univariate and multivariate logistic regression analyses (stepwise backward method) were used to determine the predictive value of pain and other variables for the efficacy of ESWL. The Hosmer-Lemeshow test was used to evaluate the quality of the prediction model. A p-value < 0.05 was considered statistically significant.

Results

**Patient, Stone and Procedure Characteristics**

The patient and demographic characteristics are summarized in table 1. A total number of 476 patients with urolithiasis is analyzed in this study. The median age is 52 years and sex ratio (M/F) is 3:1. A double-J catheter was in situ in 11 patients (2.3%) and a nephrostomy catheter in 21 patients (4.4%). For renal stones, a median of 3,000 shockwaves was applied with a median intensity level of 12.9, while ureteral stones were treated on with 3,500 shockwaves and an intensity level of 13.9. The level of intensity was correlated with the pain scores (Pearson correlation -0.423, p < 0.001). The higher the pain scores, the lower the level of intensity.

**Primary Outcome**

The median pain score is reported as 5. Two patients (0.4%) experienced no pain (pain score 0), 104 patients (21.8%) mild pain (pain score 1–3), 224 patients (47.1%) moderate pain (pain score 4–6) and 146 patients (30.7%) severe pain (pain score 7–10). The pain score was significantly higher among patients younger than 60 years old (5.4 vs. 4.7, p = 0.001). A total of 46 patients (9.7%) required extra use of opiates (oxycodon, tramadol, piritramide or morphine), resulting in a mean pain score of 4.96. There was no significant difference in pain score between the group with and without use of extra opiates (4.96 vs. 5.20, p = 0.432). The use of butylscopolamine as analgesic was reported in 30 patients (6.3%). There was no significant difference between pain scores for renal and ureteral stones (5.4 vs. 5.1, p = 0.113).

The success rate of the first ESWL in our department was recorded as 35.1%. One hundred thirty-seven patients received a second or third ESWL session, resulting in an overall success rate of 43.9% with a mean of 1.37 sessions. Most of those patients (93.4%) received re-ESWL within 6 months. Univariate analysis showed no significant correlation between the pain score and the success of ESWL (p = 0.135). Univariate analysis identified sex, stone location, stone size, hydronephrosis and the use of tamsulosin as potentially predictive factors (table 2). Multivariate logistic regression analysis showed that sex, stone location and size independently influenced the success of ESWL (table 3). The Hosmer-Lemeshow test indicates a good quality of the prediction model (p

| Variables                        | Odds ratio | 95% Confidence intervals | p      |
|----------------------------------|------------|--------------------------|--------|
| Age, year                        | 0.990      | 0.978–1.003              | 0.133  |
| Gender (male)                    | 1.910      | 1.213–3.010              | 0.005  |
| Stone location<sup>a</sup>       |            |                          |        |
| Renal lower pole                 | 0.486      | 0.231–1.019              | 0.056  |
| Pyelum/proximal ureter           | 1.499      | 0.774–2.901              | 0.230  |
| Distal ureter                    | 1.789      | 0.882–3.631              | 0.107  |
| Stone size                       | 0.806      | 0.752–0.865              | < 0.001|
| Residual stone after ureteroscopy/PCNL | 0.567  | 0.222–1.448              | 0.236  |
| Hydronephrosis                   | 2.066      | 1.409–3.030              | < 0.001|
| Opiates                          | 0.789      | 0.409–1.524              | 0.481  |
| Intensity level (0–20)           | 1.024      | 0.954–1.099              | 0.514  |
| Tamsulosin                       | 2.290      | 1.536–3.414              | < 0.001|
| Pain score                       | 0.930      | 0.847–1.023              | 0.135  |

<sup>a</sup>Renal upper pole as reference.
An additional operation after ESWL was required to 115 patients (24.2%) who were not stone-free after ESWL. Ureteroscopy was performed in 106 patients (22.3%) and PCNL in 9 patients (1.9%).

Secondary Outcome
Complications were reported in 12.4% of patients (table 4). The majority of complications reported during the study period were minor and without the need for an intervention, such as hematuria and pain. In 1 case, a transient ischemic attack occurred due to a temporary stop of anticoagulants. One patient developed an acute renal insufficiency, but spontaneously recovered after several days.

Discussion
The introduction of ESWL has been revolutionary for the treatment of urolithiasis. However, ESWL causes shockwave-induced pain during the treatment. The correct dosage of analgesics is mandatory to maintain patient comfort and may improve treatment outcomes [8]. The hypothesis is that adequate treatment of pain during ESWL would result in higher success rates due to less involuntary movements and better stone focus. We designed this study in order to evaluate this assumption.

Parameters for Stone Fragmentation and Clearance
Stone fragmentation and clearance are multifactorial events. The success of ESWL depends on many factors, including stone factors, patient habitus, competence of the operator, and the efficacy of the lithotriptor. The size of stone is inversely correlated with higher success rates. High-density stones and lower pole renal stones are associated with worse results [1]. The use of alpha-blockers to improve elimination rates by relaxing smooth muscle cells in the urinary tract, remains controversial [9]. Electrohydraulic, electromagnetic, and piezoelectric are three different types of shockwave generators which are being used in practice [10]. These generators seem to produce different rates of success and complications [3,10].

Table 3. Multivariate analysis

| Variables                  | Adjusted odds ratio | 95% Confidence intervals | p   |
|----------------------------|---------------------|---------------------------|-----|
| Gender (male)              | 1.648               | 1.011–2.686               | 0.045|
| Stone location*            |                     |                           |     |
| Renal lower pole           | 0.450               | 0.203–0.999               | < 0.001|
| Pyelum/proximal ureter     | 1.481               | 0.718–3.056               | 0.288|
| Distal ureter              | 1.197               | 0.557–2.572               | 0.645|
| Stone size                 | 0.802               | 0.744–0.864               | < 0.001|

*Renal upper pole as reference.

Table 4. Complication rates of ESWL

| Grade | Complication                                                                 | Patients n (%) |
|-------|-----------------------------------------------------------------------------|----------------|
| I     | hematuria (n = 19), pain (n= 27), acute renal failure (n = 1)                | 47 (9.9%)      |
| II    | TIA, fever etc, urosepsis                                                  | 3 (0.6%)       |
| IIIa  | stone street treated with ESWL, urosepsis and pyelonephritis treated with nephrostomy | 3 (0.6%)  |
| IIIb  | stone street treated with ureteroscopy                                     | 6 (1.3%)       |
| Total |                                                                              | 59 (12.4%)     |

TIA = Transient ischemic attack.
Our Data and the Literature

The wide variation in success rates in the current literature might be due to differing definitions of success and stone-free status [1]. Success is determined after one or multiple sessions and after several weeks or months. It is defined as completely stone-free or as the fragmentation of stones into smaller concrements using different types of imaging.

A few studies have been published concerning our study hypothesis. Cleveland et al. [11] observed that movement of calculi in vitro during ESWL caused a significant reduction in fragmentation rates due to the stone being out of focus. Furthermore, a prospective study of 222 patients from Vergnolles et al. [5] describes a significantly higher fragmentation rate in patients with a visual analog scale of lower than 3, compared to patients needing additional analgesia. However, this correlation could be due to the fact that the session was interrupted in 16.9% of treatments, when visual analog scale remained at 3 or higher, despite the use of additional analgesia.

In addition, Sorensen et al. [12] reported a significantly higher stone-free rate in patients treated with general anesthesia, compared to patients receiving intravenous sedation using a second-generation lithotripter. Our study reveals that the outcome of ESWL is not affected by pain during the treatment, according to the numeric pain scale. The level of intensity correlates with pain scores (Pearson correlation -0.423, p < 0.001), but does not seem to influence the success of ESWL (t-test, p = 0.88). The negative results of our study concerning the correlation between pain perception and success rates contradict the aforementioned literature. In contrast to our study, Vergnolles et al. [5] and Sorensen et al. [12] compared success rates in groups, with or without additional analgesia, or compared different forms of anesthesia instead of using pain scores. In addition, other types of shockwave generators were used. These factors make it difficult to compare the results of these studies with our own results. In general, pain scores are widely used due to their simplicity and adaptability to a broad range of populations and settings. However, using a pain score is very subjective when evaluating pain perception. Pain itself is multifactorial and affected by many factors such as age, gender, ethnicity, social status, education, personality and degree of understanding about the intervention. Individual variation is difficult to establish.

In our cohort, the success rate was 35.1% after the first treatment and 43.9% after subsequent ESWL sessions. No additional intervention was needed in 62.6% of treated patients within 6 months after ESWL, since complaints and hydronephrosis were absent while some small residual fragments persisted. An additional operation (ureteroscopy or PCNL) was required in only 24.2% of cases, which would suggest that ESWL is a viable option to prevent operative procedures.

Multivariate logistic regression analysis revealed male gender, stone size and location as predictive factors for success. Stone size was inversely associated with the success of the treatment. In our study, the success rate for renal lower pole stones was found to be 18.6%. ESWL on stones located in the lower renal pole is less likely to be successful compared with the treatment on stones in the renal upper pole (OR 0.450, p = 0.05). Our findings on the predictive value of stone size and its location are supported by various studies. The predictive value of male gender is not found in other studies and might be an incidental finding [2, 3, 13].

Study Limitations

A potential limitation of our study is the lack of use of non-contrast spiral CT-scan as assessment prior to treatment, since that is the investigation of choice for urolithiasis. Contrary to X-ray, Hounsfield unit, stone volume, inflammation of ureter, and skin-to-stone distance could be easily assessed [1]. In our department it is not used as first choice due to its potentially higher dose of radiation and associated costs.

Recommendations

The median pain score in our study was described as “5”, which is a relatively high level of pain sensation, considering that analgesics are given. In addition one third of the patients experienced severe pain (pain score 7–10) and our data show that high pain score are correlated with a lower level of intensity during ESWL. This suggests that our current pain prevention protocol is not sufficient and should be revised. Additional analgesia (a combination of paracetamol, NSAID and opioid) might lower the mean pain score and improve patient comfort. In our study no significant difference in pain score could be found between the patients who did (n = 46) and did not (n = 430) receive extra opiates. This is probably due to the small group of patients who received opiates. A study of Tokgoz et al. [3] analyzing pain perception during ESWL, supports our findings by describing a mean pain score for a first ESWL session as being 4.67. Since anxiety could also be an influencing factor on pain perception, patient education regarding the procedure and potentially a low dose of sedation might also help in lowering the pain score [4–6]. More random controlled trials
are required to determine the best possible management of pain medication during ESWL.

**Conclusion**

Contrary to the general view that pain influences the treatment outcomes of ESWL, our results suggest that high pain perception does not correlate with the effect of ESWL. Despite the absence of a correlation with the outcome, pain scores during ESWL sessions remain high. Therefore, additional analgesia is recommended to improve patient comfort. Finally, our results support previous studies where stone size and stone location are predictive factors on the outcome of ESWL.

**Acknowledgement**

We thank Peter Warner for his help in reviewing this manuscript.

**References**

1. Torricelli FC, Danilovic A, Vicentini FC, Marchini GS, Srougi M, Mazzucchi E: Extracorporeal shock wave lithotripsy in the treatment of renal and ureteral stones. Rev Assoc Med Bras 2015;61:65–71.

2. Hwang I, Jung SI, Kim KH, Hwang EC, Yu HS, Kim SO, Kang TW, Kwon DD, Park K: Factors influencing the failure of extracorporeal shock wave lithotripsy with Piezolith 3000 in the management of solitary ureteral stone. Urolithiasis 2014;42:263–267.

3. Tokgoz H, Hanci V, Turksoy O, Erol B, Akduman B, Mungan NA: Pain perception during shock wave lithotripsy: does it correlate with patient and stone characteristics? J Chin Med Assoc 2010;73:477–482.

4. Ucer O, Ceylan Y, Ekren F, Ozan E, Mezzinooglu T: Effect of anxiety and pain on success of shockwave lithotripsy (SWL) for treatment of proximal ureteral and renal pelvic stones. Urolithiasis 2016;44:559–564.

5. Vergnolles M, Wallerand H, Gadrat F, Maurice-Tison S, Deti E, Ballanger P, Ferriere JM, Robert G: Predictive risk factors for pain during extracorporeal shockwave lithotripsy. J Endourol 2009;23:2021–2027.

6. Berwin JT, El-Husseiny T, Papatsoris AG, Hajdinjak T, Masood J, Buchholz N: Pain in extracorporeal shock wave lithotripsy. Urol Res 2009;37:51–53.

7. Dindo D, Demartines N, Clavien PA: Classification of surgical complications: a new proposal with evaluation in a cohort of 6336 patients and results of a survey. Ann Surg 2004;240:205–213.

8. Türk C, Knoll T, Petrik A, Sarica K, Skolarikos A, Straub M, Seitz C: Guidelines on urolithiasis. European Association of Urology, 2015.

9. Chen K, Mi H, Xu G, Liu L, Sun X, Wang S, Meng Q, Lv T: The efficacy and safety of tamsulosin combined with extracorporeal shockwave lithotripsy for urolithiasis: A systematic review and meta-analysis of randomized controlled trials. J Endourol 2015;29:1166–1176.

10. Smith AD, Badlani GH, Bagley DH, Clayman VC, Docimo SG, Jordan GH, Kavoussi LR, Lee BR, Lingeman JE, Preminger GM, Segura JW: Smith’s textbook of endourology. 2007, pp337–340.

11. Cleveland RO, Anglade R, Babayan RK: Effect of stone motion on in vitro comminution efficiency of Storz Modulith SLX. J Endourol 2004;18:629-633.

12. Sorensen C, Chandhoke P, Moore M, Wolf C, Sarram A: Comparison of intravenous sedation versus general anesthesia on the efficacy of the Doli 50 lithotriptor. J Urol 2002;168:35–37.

13. Choi JW, Song PH, Kim HT: Predictive factors of the outcome of extracorporeal shockwave lithotripsy for ureteral stones. Korean J Urol 2012;53:424–430.
Supplementary Table. Performance parameters

| Intensity stage | Charge voltage (kV) | Pressure range (MPa) | Energy flow density (mJ/mm²) |
|----------------|---------------------|----------------------|----------------------------|
| 1              | 2.4                 | 20                   | 0.12                       |
| 2              | 2.5                 | 21                   | 0.13                       |
| 3              | 2.6                 | 23                   | 0.14                       |
| 4              | 2.8                 | 26                   | 0.17                       |
| 5              | 3.0                 | 30                   | 0.21                       |
| 6              | 3.2                 | 34                   | 0.24                       |
| 7              | 3.4                 | 38                   | 0.27                       |
| 8              | 3.7                 | 49                   | 0.35                       |
| 9              | 4.0                 | 66                   | 0.44                       |
| 10             | 4.3                 | 76                   | 0.48                       |
| 11             | 4.6                 | 87                   | 0.62                       |
| 12             | 5.0                 | 95                   | 0.70                       |
| 13             | 5.4                 | 102                  | 0.86                       |
| 14             | 5.8                 | 103                  | 0.94                       |
| 15             | 6.3                 | 107                  | 1.12                       |
| 16             | 6.8                 | 110                  | 1.24                       |
| 17             | 7.3                 | 111                  | 1.32                       |
| 18             | 7.8                 | 112                  | 1.44                       |
| 19             | 8.3                 | 116                  | 1.54                       |
| 20             | 8.9                 | 120                  | 1.57                       |

The tolerance of all values listed in the table is ± 10%.