Reduction of pre-procedural anxiety for repeat sessions in extracorporeal shockwave lithotripsy (ESWL) reduces pain intensity
A prospective observational study

Vethunan Tamalvanan, MSurg\(^a\), Retnagowri Rajandram, PhD\(^a,\)O, Shanggar Kuppusamy, PhD, FRCS\(^a,\)b,\(^*\)

Abstract
Pain control is a major determinant for successful stone clearance in extracorporeal shockwave lithotripsy (ESWL) for urolithiasis. Pain perception during ESWL may be influenced by patient factors like gender, age, body habitus and anxiety level, and stone related factors like size, laterality and location of stone. We investigated in general, the confounding patient and stone factors influencing pain perception during ESWL with importance given to procedural anxiety in first and the subsequent session of ESWL. This was a prospective observational study of all new consecutive patients who underwent ESWL for a period of 1 year at a tertiary Urological Centre. Demographic and stone anthropometry were analyzed. Pre-procedural anxiety was assessed prior to procedure using hospital anxiety and depression score (HADS) and pain was scored using numerical rating scale-11 at baseline, 30-minutes (i.e., during) and 24 hours after ESWL. Univariate and multivariate analysis for confounding factors included HADs were performed for pain perception. A \( P \) value < .05 was considered to be statistically significant. For the study duration, 119 patients were recruited and 72 of them returned for a second session. Procedural anxiety was the only independent factor affecting pain score in ESWL for the first session in multivariate analysis. A statistically significant reduction of mean procedural anxiety score from 6.7 ± 4.5 to 3.2 ± 2.7 (\( P < .05 \)) for the second ESWL session was observed (\( n = 72 \)). This was in conjunction with statistical reduction of mean pain score 30 minutes after ESWL from 5.2 ± 2.1 to 4.2 ± 2.1 (\( P < .05 \)). Patients with HADS ≥ 8 had statistically significant higher mean pain score at all 3 intervals in the first ESWL session. This study has shown that pre-procedural anxiety mainly anticipatory, reduces and shows reduction in pain intensity among patients undergoing repeat ESWL. Hence, anxiety reducing methods should be explored in patients undergoing ESWL to avoid unnecessary analgesic use.

Abbreviations: BMI = body mass index, ESWL = extracorporeal shockwave lithotripsy, HADS = hospital anxiety and depression score, UMMC = Universiti Malaya Medical Centre, URS = ureterorenoscopy.

Keywords: anxiety, extracorporeal shock wave lithotripsy, HADS, pain score, renal stone

1. Introduction

Urolithiasis is a global burden with a lifetime risk of about 10% to 15% in the West and 20% to 25% in the Middle-East and South Asia\(^1-3\) of developing urinary stone disease. The rising incidence of urolithiasis since 1980’s has encouraged improvements in principles and management of urolithiasis. Extracorporeal shockwave lithotripsy (ESWL) has revolutionized management of renal and ureteric calculi since its introduction.\(^4\) ESWL is popular with patients because it is non-invasive, and it is an “office” procedure. However, ESWL requires more sessions to achieve stone clearance and might have a higher overall cumulative cost of treatment when compared to other methods of treatment such as ureterorenoscopy (URS).\(^1,6\) Hence every effort should be made to improve and refine ESWL deliverance to get the best out of each session and for better stone clearance rate.

ESWL is an inherently painful procedure. Pain control is a major determinant for successful stone clearance in ESWL.\(^7\) Pain perception during ESWL may be influenced by patient factors like gender, age, body habitus and anxiety level, and stone related factors like size, laterality and location of stone.\(^8,9\)
Pre-procedural anxiety due to anticipation of the procedure and uncertainty of the outcome is common in patients undergoing ESWL. The association between pre-procedural anxiety and pain perception explored in studies conducted in patient undergoing first session of ESWL has been discordant. Furthermore, these studies have not established an association between procedural anxiety and pain perception intensity in subsequent sessions of ESWL due to increase familiarity of the procedure. Assessment of procedural anxiety during repeat ESWL sessions adds to the novelty of our study which may contribute significantly in modifying hospital protocol for measures taken to reduce anxiety and need for pain relief. We investigated in general, the confounding patient and stone factors influencing the relationship between these factors and pain perception. Specifically, the significance of procedural anxiety in determining patient’s pain perception in first and the subsequent session of ESWL were also investigated.

2. Materials and Methods

2.1. Ethics
Ethics approval was obtained from UMMC Medical Research Ethics Committee (MREC ID NO: 2017227-4976) before study commenced. Informed written consent was obtained from all participants according to International Conference on Harmonization for Good Clinical Practice and Declaration of Helsinki guidelines.

2.2. Study setting and participants
This was a single center, prospective observational study conducted at University Malaya Medical Center, Kuala Lumpur, involving patients with urolithiasis undergoing ESWL for the first and subsequent sessions. Data collection was done by in-person and telephone interviews, and by review of electronic medical records. All patients recruited into this study were uniformly counselled verbally with regards to the study.

2.3. Study inclusion and exclusion criteria
Consenting patients undergoing ESWL for the first time, with calculi at either renal or ureter or both were recruited into this study. Patient who had undergone pre-stenting for indications such as large stones (potential to present with obstruction post-ESWL) and with hydronephrosis were included in this study. Patients with risk of urinary tract infection, psychiatric disorder, severe skeletal malformations, severe obesity, known case of arterial aneurysm near the stone and with anatomical obstruction distal to the stone were all excluded. Patients who had prior endoscopic intervention by either URS, retrograde intrarenal surgery or percutaneous nephrolithotomy were also excluded. This study excluded patients who were taking analgesics during or prior to the first and second procedure.

3. ESWL procedure
ESWL was carried out with standardized analgesia, that is, intramuscular diclofenac sodium 75 mg given 30 minutes before the procedure, with additional oral paracetamol to be taken as needed after the procedure. The Storz Modulith SLX, 4th generation was used in our center without voltage ramping during the procedure. All ESWL in our center were performed in supine position. Prone position for ESWL is not practiced. If pain is intolerable, the energy level was titrated down to a tolerable level or the procedure was stopped. The ESWL protocol in UMMC was delivered by targeting the shock wave at 4000 shocks at 1 to 1.5 hertz. The procedure takes around 60 minutes to complete.

3.1. Data collection
A case report form was used to record the demographic and anthropometric details of the participants. The patients’ symptoms and stone parameters like laterality, radio-opacity, location and size of stone were recorded. Patient who underwent pre-ESWL ureteral stenting was identified by reviewing electronic medical records and confirmed with available radiological imaging. The patients who were subjected to a second session of ESWL were based on clinical decision by attending Urologist after taking into consideration location of the stone, the patient’s preference not to undergo endoscopic intervention under anesthesia and the financial implication. The second ESWL sessions were scheduled within 2 to 3 weeks of the first session. All patients undergoing the second ESWL session were confirmed to have no obstruction secondary to migrated stones by symptoms assessment, renal function and imaging if necessary. Stone clearance rates were not investigated as part of the study.

3.2. Specific outcome measures
Pre-procedural anxiety score before each ESWL sessions was assessed with hospital anxiety and depression score (HADS) consisting of 14 components with 7 components each for anxiety and depression. This self-administered questionnaire has been validated in both English and Malay language for use in this population. HADS anxiety score ranges from 0 to 21. Patients who scored <8 were classified as normal (not anxious) and ≥8 as anxious. Anxious patients were further subclassified as mild (8–10), moderate (11–14), and severe (15–21) for analysis.

Pain intensity was scored using numerical rating scale-11 from 0 to 10. Pain score was reported by the participants before the ESWL sessions to obtain a baseline pain intensity. Pain score was again assessed immediately after ESWL to ascertain the pain experienced during ESWL. Patients were then telephoned 24 hours following the ESWL session to obtain the average pain score experienced during the post-ESWL period. Pain score >3 or a difference of >3 between groups were considered clinically significant.

3.3. Sample size estimation
Sample size was calculated using GPower 3.1.9.4 tool to determine whether the correlation coefficient between HADS and pain score are different between first and second session of ESWL. Estimated correlation coefficient between HADS and pain score is 0.6, and with an effect size of 0.5 for reduction in this coefficient in the second session, each session required a minimum sample size of 69 participants.

3.4. Statistical methods
Univariate analysis for confounding factors was done with independent t test, one-way analysis of variance or chi-square test and binary regression for confounding with P value < .05 in the univariate analysis were analyzed in the multivariate regression model. A P value < .05 was considered to be statistically significant. Statistical analyses were carried out using IBM SPSS Statistics version 20 (IBM, USA).

4. Results
4.1. Data acquisition
A total of 119 new patients underwent ESWL for the first time from Jun 2017 to December 2018, and 72 of them returned for the second session of ESWL. It was noted that 47 patients did not return for a second session of ESWL. Among the reasons
for not attending the second session were those who had stone cleared (n = 21) (confirmed by imaging to have no stones or residual stone <3 millimeter) by first ESWL session, due to unbearable pain (n = 3), due to financial limitations (n = 2) and the remaining for unknown reasons as they were not contactable (n = 21).

4.2. Baseline clinical characteristics

Relevant clinical patients’ characteristics of those who underwent ESWL in both first (n = 119) and second session (n = 72) did not differ significantly. Males and Malay ethnic group were the majority in both sessions. The mean age of patients attending first session and second session was 55.7 ± 14.1 and 56.6 ± 14.0, respectively. The mean body mass index (BMI), and all stone and other disease factors were comparable between participants when those returning for the second session were analyzed (Table 1).

Overall, the patients in the first session (n = 119) had mean anxiety score of 6.32 ± 4.5 with a mean pain score of 2.03 ± 1.7, 5.04 ± 2.0, and 2.39 ± 2.2 for the 3 respective points of assessment, that is, pre-procedure, post-procedure and 24 hours after procedure.

4.3. Factors associated with pain during ESWL

Univariate analysis of factors affecting pain score at 30 minutes after ESWL showed that pre-procedural anxiety was significant as well as an independent factor which predicted patients with pain score >3 in the first ESWL session. Patients with pain score >3, had a higher anxiety score of 7.2 ± 4.5 compared to 3.0 ± 2.7 for patients with pain score ≤3 (Table 2). Based on the logistic regression analysis, patients with higher anxiety score (HADS) were more likely to have a pain score of >3 with an odds ratio of 1.36 (95% confidence interval, 1.16–1.59; P < .001). Other factors analyzed such as age, race, BMI, presence of ureteric stent, stone location and radiological characteristics of the stone were not statistically significant (Table 2) between both sessions of ESWL.

4.4. Association between procedural anxiety and pain score during ESWL sessions

Comparative analysis of 72 patients who attended both sessions of ESWL showed a significant reduction in anxiety score and pain score, prior and 30 minutes after the procedure. The mean anxiety score dropped from 6.7 ± 4.5 to 3.2 ± 2.7 (P < .05), pain score prior to ESWL dropped from 2.1 ± 1.8 to 1.7 ± 1.2 (P < .05), and pain score 30 minutes after ESWL from 5.2 ± 2.1 to 4.2 ± 2.1 (P < .05). However, these scores were not significantly different when assessed 24 hours after the procedure (2.3 ± 2.1 vs 2.0 ± 1.9; P > .05) (Table 3).

5. Discussion

5.1. Contextual procedural anxiety and pain perception

Pain and anxiety are bothersome side effects for patients undergoing ESWL for treatment of urolithiasis. As an outpatient procedure, anxiety is inherent during ESWL and this may be contributed by lack of preparedness, anticipation of discomfort and fear of negative outcome. In repeated sessions, procedural anxiety can either increase or reduce based on prior experience. Pain is subject to individual variation and is influenced by multitude of biopsychological factors. Hence, procedural anxiety being a component of psychological factor has been postulated to have an effect on pain perception on subjects undergoing ESWL. But the clinical impact of this relationship is yet to be conclusively established.

### Table 1

Baseline demographics and disease characteristics.

|                  | Session 1 n = 119 | Session 2 n = 72 |
|------------------|-------------------|------------------|
| **Patient factors** |                   |                  |
| Age (yr) (mean ± SD) | 55.7 ± 14.1       | 56.6 ± 4.0       |
| Race; n (%)        |                   |                  |
| Malay             | 59 (49.6)         | 32 (44.4)        |
| Chinese           | 36 (30.3)         | 27 (37.5)        |
| Indian            | 24 (20.2)         | 13 (18.1)        |
| Sex; n (%)        |                   |                  |
| Male              | 84 (70.6)         | 51 (70.8)        |
| Female            | 35 (29.4)         | 21 (29.2)        |
| BMI (kg/m²) (mean ± SD) | 28.1 ± 6.1       | 28.2 ± 6.7       |
| **Disease factors** |                   |                  |
| Stone size (mm) (mean ± SD) | 9.7 ± 3.3        | 9.8 ± 3.2        |
| Symptoms experienced (%) |        |                  |
| Asymptomatic      | 37 (31.1)         | 22 (30.6)        |
| Symptomatic       | 82 (68.9)         | 50 (69.4)        |
| Lateralization of stone undergoing ESWL (%) |        |                  |
| Right             | 54 (45.4)         | 33 (45.8)        |
| Left              | 65 (54.6)         | 39 (54.2)        |
| Location of stone (%) |           |                  |
| Renal             | 82 (68.9)         | 51 (70.8)        |
| Ureter            | 37 (31.1)         | 21 (29.2)        |
| Radiological stone characteristic (%) |        |                  |
| Radiopaque        | 106 (89.1)        | 63 (87.5)        |
| Radiolucent       | 13 (10.9)         | 9 (12.5)         |
| Pre-procedural ureteral stenting done (%) |        |                  |
| Yes               | 32 (26.9)         | 26 (36.1)        |
| No                | 87 (73.1)         | 46 (63.9)        |

BMI = body mass index, ESWL = extra corporal shockwave lithotripsy, n = number, SD = standard deviation.
5.2. Pain perception and its confounding factors

In this study, analysis of pain score in relation to gender, ethnicity, age, BMI and stone characteristics were not significantly associated. Other studies have found that female patients and those aged <40-years-old experience more pain during ESWL.\[^{20-22}\] It is a common clinical observation that Indians have the lowest pain threshold as compared to Malays and Chinese in multi-ethnic Malaysian population.\[^{23}\] Regardless, this study did not show an association between ethnicity and pain intensity. Studies have shown that a BMI > 25 can be a predicting factor for higher pain score during ESWL.\[^{26}\] BMI was not associated with higher pain score in our cohort, probably due to the increased BMI in Malaysians caused by accumulation of subcutaneous fats and visceral fats rather than increased bulk of muscle mass which is common among westerners.\[^{22}\] Hence, as fats have few sensory endings, tissue damage due to passage of shockwave is less likely to produce more pain than muscular participants. Radiolucent stones were analyzed as they were hypothesized to predict higher pain scores due to difficulty to localize and focus the ESWL beam but there was no difference seen in this study between radiolucent and radiopaque stones. Patients who had pre-stenting due to presence of larger stones or potentially obstructing stones were also not significantly associated with higher pain score. Although literature have confirmed that presence of stents may contribute to stent symptoms,\[^{24}\] however this is not seen in this study probably due to the low numbers of patients with stents.

5.3. Pain perception in relation to ESWL

The mean pain score from this study during ESWL and 24 hours after ESWL was notably lower than other studies.\[^{12,27}\] Especially patients pain score 24 hours after ESWL in our study was almost negligible with a mean pain score of 2 and none reported pain score of >3. In comparison with reports of pain score after URS, the incidence of acute post-operative pain (score > 3) was 14% with the majority of patients reporting pain scores between 4 and 7.\[^{28}\] There are some common risk factors in determining the post-procedural pain for both ESWL and URS, such as anxiety or younger age. Factors which are specific for URS such as prolonged manipulation or ureteral dilatation may be the reason, patients undergoing URS have high incidence of significant post-operative pain. The difference in pain score among various reports during ESWL, could also be due to difference in premedication protocol. There are studies that did not use any analgesia as compared to our study which used intramuscular diclofenac sodium\[^{22,28}\] as a standard of care. Besides that, variation in the time of recording the pain score could account for some of the difference unlike prior studies. Previous studies with higher pain score were noted to have recorded the scores during the procedure rather than 30 minutes after the procedure.\[^{3,20}\] The measurement of pain score after the procedure may introduce some element of recall bias however, it must also be taken into consideration that the patient may not be in the right frame of mind to answer a pain score in the midst of the procedure.
5.4. Procedural anxiety related to ESWL

It was noted that patients with an anxiety score of ≥8 had higher mean pain score at all 3 intervals measured in our report. However, this was not clinically significant as the difference in the mean pain score was <3 for each time interval. We found procedural anxiety was an independent factor in predicting an increased pain perception for first timers. Yilmaz et al. and Vergnolles et al also showed that patients with higher procedural anxiety score had higher pain score but was not clinically significant. Animal studies have proposed that anxiety influences pain perception via modulation of neurotransmitters at spinal and supraspinal level. Dysfunctional neurotransmitter system such as increased glutamate and N-methyl-D-aspartate in dorsal horn in spinal nerve, and modulation by descending pathway mainly alpha 2 sympathetic in affenter sensory fibers are probable explanation for physiological effect of anxiety on pain perception. In contrary, Salinas et al showed that in patients with high anxiety score during ESWL, the analgesia requirement is also increased which translates to clinical significance even though they did not assess pain score directly. This shows that procedural anxiety will increase the patient's pain perception either by means of increased in analgesia requirements and/or increased pain perception.

This study showed that both, procedural anxiety and pain score reduced during the second session for the same patient. We found that procedural anxiety was positively associated to pain scores in the first session but this positive association reduced in the second session. This study showed that the significant reduction of mean procedural anxiety score from first to second ESWL session was accompanied by a concordant reduction of respective clinical pain scores. Repetition of a similar procedure is known to alter anxiety level but evidence for such finding has not been confirmed for ESWL. Anxiety may reduce due to increase familiarity to the procedure or due to increased preparedness for it. To the best of our knowledge, there has not been any other prior study analyzing the effect of procedural anxiety on pain perception comparing the first and subsequent sessions of ESWL among the same cohort of patients. This is probably the first study to investigate the impact of procedural anxiety on pain perception during the second ESWL session. Evidence from this study strongly suggests that familiarity to the procedure have a significant impact in reduction of procedural anxiety in the second session. Nevertheless, this reduction was not enough to reduce pain scores to clinically significant level with a difference of pain score reduction of 3 or more.

5.5. Strengths and limitations

This study has several strengths and limitations. This is the first study to evaluate the pain perception and procedural anxiety in a repeat ESWL session among a multi-ethnic cohort with pain assessed at 3 different intervals. Pain experienced in ESWL is a continuum, as pain due to the shock wave is mostly experienced during ESWL, where else pain due to fragment movement extend beyond an ESWL session. There was limitation in assessing correlation between pain score and procedural anxiety in second session, as dynamic confounders which may have changed from the first to second session, such as stone size was not reassessed prior to second session. A larger cohort may have produced positive results for confounders such as age, sex or stone size and location. Another limitation of this study is possibly the lack of information with regards to the education and household income of participants which may have an impact on anxiety and pain perception.

5.6. Summary, recommendation, and future directions

We have found that by reducing procedural anxiety especially in the first session of ESWL, pain tolerance may be increased. This works by reducing anticipatory anxiety and increasing preparedness for ESWL as procedural anxiety and its relationship with pain score vanishes in the second ESWL session. Methods which may be introduced to increase preparedness include introducing patient information brochures to explain the procedure, clinical visits to urology day-care for exposure to the ESWL environment prior to appointment and patient support group where experiences can be shared by other patients who underwent ESWL. Institutional policy in developing protocol for managing patients during ESWL, targeting anxiety lowering measures in the first session of ESWL should be encouraged.

6. Conclusion

This study has shown that procedural anxiety was the only confounding factor that had a positive impact on pain intensity perception in first timers during ESWL. Procedural anxiety reduces on the second session of ESWL. This finding serves as a justification for introduction of anxiety relieving methods in multi-modality management of pain for ESWL which could be studied in the future with higher number of participants. This may contribute to avoidance of unnecessary use of analgesia.

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Author contributions

Conceptualization: Vethunan Tamalvanan,Retnagowri Rajandram,Shanggar Kuppusamy.
Data curation: Vethunan Tamalvanan.
Formal analysis: Vethunan Tamalvanan,Retnagowri Rajandram.
Investigation: Vethunan Tamalvanan.
Methodology: Vethunan Tamalvanan,Retnagowri Rajandram.
Resources: Shanggar Kuppusamy.
Supervision: Retnagowri Rajandram,Shanggar Kuppusamy.
Validation: Retnagowri Rajandram,Shanggar Kuppusamy.
Visualization: Retnagowri Rajandram.
Writing – original draft: Vethunan Tamalvanan,Retnagowri Rajandram.
Writing – review & editing: Vethunan Tamalvanan,Retnagowri Rajandram,Shanggar Kuppusamy.

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