Invited Review

How to maximize the efficacy of shockwave lithotripsy

Neophytos Petrides 🗅, Safiyah Ismail 🗅, Faqar Anjum 🗅, Seshadri Sriprasad 🗅

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ABSTRACT

Since its introduction in the early 1980s, extracorporeal shockwave lithotripsy (ESWL) has proven to be a minimally invasive and efficient procedure for the management of renal calculi. It is currently one of the most recommended treatments for small- and medium-sized stones (<20 mm) in most guidelines internationally. The recent coronavirus disease 2019 (COVID-19) outbreak could lead to a further increase in ESWL use as it avoids a general anesthetic and its potential complications in patients with COVID-19 infection. Most publications exhibit ESWL stone-free rates (SFRs) of 70%-80%; however, this is often not the case in many centers, with multiple factors affecting the efficacy of the intervention. Various stone and patient factors have been shown to influence the ESWL success. Stone position, density and size, skin-tostone distance, and body-mass index contribute to SFRs. Modifications in the lithotripter design and revisions in the technique have also improved the SFRs over the years, with slower shock rates, power-ramping protocols, combined real-time ultrasound, and fluoroscopy imaging technology, all enhancing the efficacy. The adjuvant use of pharmacological agents, such as alpha-blockers, potassium citrate, and the emerging microbubble technology, has also been investigated and shown promising results. Arguably, the most significant determinant of the success of ESWL in a particular unit is how the lithotripsy service is set up and monitored. Careful patient selection, dedicated personnel, and post-treatment imaging review are essential for the optimization of ESWL. Through an analysis of the published studies, this review aimed to explore the measures that contribute to an effectual lithotripsy service in depth.

Keywords: Complications; efficiency; extracorporeal shockwave lithotripsy; lithotripsy; shockwave.

Introduction

Extracorporeal shockwave lithotripsy (ESWL) has been one of the mainstays in the management of renal and ureteric calculi since its inception in 1984. It is currently one of the most recommended treatment options for small- and medium-sized stones in most guidelines and the preferred treatment modality in the United Kingdom's National Institute Clinical Excellence guidelines.^[1]

The use of ESWL picked up in 2006 but has been in decline because many urologists switched to endoscopic surgical treatments, especially ureteroscopy and laser fragmentation.^[2]

Nevertheless, ESWL has been shown to be more cost effective than endoscopic surgical treatments, which is the driving factor behind it being recommended as the preferred treatment for various types of stones in many countries.^[1] In addition, the recent coronavirus disease 2019 (COV-ID-19) outbreak may lead to a further increase in ESWL use as it avoids a general anesthetic (GA) and its potential complications in patients with COVID-19 infection,^[3] with many centers trying to avoid GA use for less urgent cases.

Most publications demonstrate a stone clearance rate of 70%-80%, but this is not often the case in many centers that offer ESWL.^[4-6]

This review aimed to explore the factors that contribute to a successful lithotripsy service.

Stone and patient factors

Multiple stone and patient factors have been shown to affect the efficacy of ESWL. These include stone position, anatomy of the collecting system, skin-to-stone distance (SSD), stone density measured in Hounsfield units (HU), stone size, habitus, body-mass index (BMI) of the patient, and the presence of a ureteric stent (Table 1).

ORCID iDs of the authors: N.P. 0000-0001-5034-0212; S.I. 0000-0001-8143-9151; F.A. 0000-0001-9301-138X; S.S. 0000-0002-7654-0092.

Department of Urology, Darent Valley Hospital, Dartford, UK

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Corresponding Author: Neophytos Petrides E-mail: np262@cantab.net

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Available online at www.turkishjournalofurology.com Larger stones require more energy to be broken up and leave behind larger fragments. Early studies demonstrated that stone size severely affected the stone-free rates (SFRs). Kanao et al.^[7] showed that SFRs ranged from 94% for calculi <5 mm to 11% for patients with a stone burden of 2 cm or higher. In most guidelines, stones are categorized into 3 groups on the basis of size (<10 mm, 10–20 mm, and >20 mm), with ESWL mainly recommended for the first 2 groups.

Stone density measurements on computerized tomography of the kidneys, ureters, and bladder (CT KUB) were also studied to assess for any correlation with SFRs. Harder stones (brushite, calcium oxalate monohydrate, cysteine, and so on) are more resistant to ESWL. Mean HU measurements on non-contrast CT are commonly used to estimate a stone's hardness and hence its susceptibility to treatment using shockwave lithotripsy. El-Assmy et al.^[8] considered HU and found that ESWL for stones with >900 HU on low-dose CT KUB was less successful. As the composition of renal calculi is heterogeneous, HU measurements using the mean value for the whole stone may be misleading. Lee et al.^[9] measured the stone heterogeneity index, calculated as the standard deviation of HU measurements on non-contrast CT, in an attempt to see if it is useful in predicting ESWL success rate in stones with similar mean HU. The authors demonstrated that radiological heterogeneity of stones is an independent predictor of ESWL success in patients with ureteral stones.

SSD was also found to influence SFRs. Several studies considered this and found that an SSD of <9 cm was associated with favorable ESWL outcomes.^[10,11] However, a study on 597 Japanese patients by Yoshioka et al.^[12] showed that being underweight (BMI<25) had a significant negative association with success of a single-session shockwave lithotripsy (Odds ratio [OR], 0.25; 95% confidence interval, 0.09–0.69) compared with

Main Points:

- An overview of patient-related factors affecting the extracorporeal shockwave lithotripsy (ESWL) success rate. These include stone position, anatomy of collecting system, skinto-stone distance, stone density measured in Hounsfield units (HU), stone size, habitus, body mass index of patients, and the presence of a ureteric stent.
- An overview of lithotripters and their evolution and mechanism of action, including modern machines.
- An overview of the pharmacological agents used as adjuncts to ESWL and their efficacy.
- A review of ESWL service setup and how that affects the ESWL success, including a flowchart of a suggested ESWL pathway.
- An overview of common complications of ESWL and how to manage them.

having normal weight. Overall, in the majority of studies, a longer SSD and higher BMI are associated with less successful ESWL outcomes.

In a study from 2008, Lin et al.^[13] looked into the relationship between the radiological anatomy of the lower calyx and stone clearance for lower pole calculi. The study used pre-ESWL intravenous urograms to measure the lower pole infundibular length, width, and the infundibulopelvic angle. They then proceeded with ESWL and measured SFRs at 3 months post-treatment, which showed that 44% of the patients were stone free. Stone size (<10 mm, p=0.005) and greater infundibular width (>4 mm, p=0.03) were the significant favorable predictors for stone clearance.

Several groups developed predictive scores incorporating the above patient factors to try and identify the most suitable patients for ESWL. Tran et al.^[14] developed the Triple D score looking at SSD, stone size, and stone density. A score of 3 was associated with 96% SFR compared with 21.4% for a score of 0. Yoshioka et al.^[15] developed the S₃HoCKwave score based on the initials of the predictors (sex, SSD, size, Hounsfield units, colic, and kidney or ureter). This score was shown to predict the ESWL failure after 3 sessions with reasonable accuracy.

For ureteric stones, the degree of stone impaction is also thought to be a predictor of ESWL success. Pre-treatment ultrasound scan for markers of severely impacted stones has been shown to be able to predict the success rate of ESWL. Useful markers of impaction include the presence or absence of ureteric jets, degree of hydronephrosis, restrictive index measurements, and ureteric wall thickness.^[16]

Yazisi et al.^[17] reported a beneficial effect of pre-treatment insertion of ureteric stents for treatment of larger renal pelvis calculi (15–25 mm) with ESWL. They demonstrated significantly improved stone clearance rates in the stented vs. the non-stented

Table 1. Patient-related factors and scoring systems					
Patient-related factors	Included in Triple D	Included in S3HoCKwave			
Stone position	No	Yes (renal/ureteric)			
Stone size	Yes	Yes			
Skin to stone distance	Yes	Yes			
Infundibular angle/length	No	No			
Patient habitus	No	No			
Stone density	Yes	Yes			
Presence of stent	No	No			
Sex	No	Yes			

Table 2. Common types of lithotripter					
	Generation	USS enabled	Dual focus	Shockwave generator	
Dornier HM-3	1st	No	No	Electrohydraulic	
LiteMed LM 9200	3rd	Yes	No	Electromagnetic	
Modulith SLX-F2	3rd	Yes	Yes	Electromagnetic	
Piezolith 3000 PLUS	3rd	Yes	Yes	Pierzoelectric	
Sonolith i-move/i-sys	3rd	Yes	No	Electroconductive	

Table 3. Pharmacological agents

Agent type	Improves SFRs	Reduces complications	Improves patient experience
Alpha-blockers	Yes	Yes	Yes
Diuretics	No	Yes	Yes
Analgesia	No	No	Yes
Potassium citrate	Yes	Yes	Yes
Microbubbles	Yes	Yes	No

SFR: stone-free rate

group (71% vs. 39%, p=0.002). Stented patients also visited the emergency department less frequently and had lower pain scores post-ESWL. However, Shinde et al.^[18] demonstrated lower SFRs when a ureteric stent was present (OR, 6.35). Overall, ureteric stents do not seem to improve the SFRs or lower the number of treatments needed but may reduce the formation of steinstrasse. ^[19]

Lithotripter and stone fragmentation factors

Since the first ESWL machine (Dornier HM-3) was developed in 1984, multiple new lithotripters have been developed to improve the effectiveness of ESWL. Initially, the machines were large, so decreasing their size, improving the ease of transport, and making them less cumbersome were the focus of development. However, unfortunately, these measures lead to a reduction in SFRs. This phenomenon was thought to be because of a narrower focal zone used in the newer machines. Second- and third-generation machines tried to improve the SFRs without compromising on size and mobility, with moderate results. Through the use of wider acoustic lenses, the focal zone of some of the newest machines has widened without compromising the benefits of limited skin contact and reduced pain.^[20] The mode of ultrasound wave generation was also associated with improvement in the SFRs. Newer machines using piezoelectric or electromagnetic generators were shown to be more efficient than the older electrohydraulic machines.^[21,22] Sohail et al.^[23] compared the SFRs between newer and older machines used at their center and found a significant improvement of SFRs with the use of newer devices (Table 2).

Shockwave delivery rate and shockwave power modifications were also looked at as potential ways of improving the stone fragmentation and minimizing the surrounding tissue injury during ESWL.

Early on, a high rate of shocks was preferred as it allowed for shorter operating times, but as the science underpinning ESWL progressed, many centers tried slower shockwave delivery rates with some success. In a meta-analysis, Kang et al.^[24] showed favorable SFRs for low (60–70 shocks/min) and intermediate (80–90 shocks/min) shock rates compared with higher rates (120 shocks/min).

In addition to using a slower rate, power-ramping protocols were assessed to see if they improved the SFRs. Although most studies demonstrated similar SFRs to the traditional protocol, many showed that ramping protocols reduced pain, seemed to protect the surrounding tissue from injury, and reduced the perirenal hematoma rates.^[25]

Developments in imaging technology also contributed to improved SFRs with ESWL than the traditional fluoroscopy-only setups. Real-time ultrasound is commonly used in many centers. It allows identification of radiolucent calculi, real-time feedback on stone fragmentation, and better targeting accuracy for ureteric calculi. Many newer machines combine fluoroscopy and ultrasound to improve the accuracy of stone targeting during ESWL. Abid et al.^[26] compared fluoroscopy-only ESWL with a combination of ultrasound and fluoroscopy using visio-tracking and ultrasound-guided stone locking system, although success with the ultrasound systems was heavily influenced by the experience of the operator. They reported improved SFRs and lower radiation exposure with the combination system. Similar findings were reported in a study by Chen^[27] who used a fluoroscopy-guided lithotripter (LiteMed LM-9200) with real-time ultrasound capabilities to show 80% SFRs.

Another technological development in the field of ESWL was the advent of dual-head shockwave lithotripsy machines. The theory behind them was that by targeting the stone from 2 different angles (2 heads), higher shockwave rates, and thus higher energy, could be delivered to the area of interest, thereby improving the fragmentation while minimizing the surrounding tissue damage. Initial studies demonstrated improved SFRs with no increase in complications^[28,29]; however, the technology was not widely used and did not make the anticipated impact.

Mechanical percussion has also been studied as an adjunct to ESWL. It has been shown to facilitate stone fragment passage post-ESWL, improving SFRs and reducing complications. Jing et al.^[30] studied the effects of the VT300 Mechanical Percussion Lithecbole Couch, a novel device that applies vibrations to the urinary tract. They demonstrated accelerated passage of fragments post-ESWL with overall higher SFRs and lower need for additional interventions. Other ways to achieve a similar effect without the need for specialized equipment have also been explored. A study by Li et al.^[31] found sexual intercourse to be beneficial post-ESWL. They demonstrated that having sexual intercourse 3 times per week post-ESWL could effectively improve the SFR, reduce the formation of steinstrasse, and relieve renal colic. The effects of sexual intercourse were similar to using tamsulosin post-treatment.

Pharmacological interventions

The adjuvant use of multiple pharmacological agents to try and improve the SFRs post-ESWL has been studied in different centers (Table 3).

Analgesics are commonly used during ESWL because of lower pain scores and improved patient satisfaction with the procedure. It was thought that they would also result in improved SFRs owing to less patient movement during the procedure. However, no clear evidence exists linking lower pain scores with improved SFRs; moreover, Bovelander et al.^[32] reported that the degree of pain during ESWL did not correlate with higher SFRs. Furthermore, studies looking at the local anesthetic use, such as quadratus lumborum blocks, although demonstrating improved pain scores, did not show improved SFRs.^[33]

Many studies have reported the use of diuretics as an adjunct to ESWL to facilitate stone fragmentation and clearance. Diuresis is thought to cause the formation of a fluid film on the surface of stones assisting fragmentation. Findings regarding this were summarized in a systematic review by Wang et al.^[34] The authors found that diuretics seem to facilitate stone fragmentation but only had a small and statistically non-significant positive effect on stone clearance. Diuretics were also shown to reduce the number of ESWL shocks and the total number of sessions needed to achieve stone clearance.

The use of potassium citrate to facilitate SFRs post-ESWL has also been studied. The theory behind it was that potassium citrate prevented the growth of residual fragments and also prevented them from aggregating or forming a nucleus for new stones. Soygur et al.^[35] looked at the effect of potassium citrate on calcium oxalate lower pole calculi. They showed that in patients who were stone free after ESWL and were receiving medical treatment, the stone recurrence rate at 12 months was 0%; untreated patients showed a 28.5% stone recurrence rate (p<0.05). Similarly, in patients with residual fragments, the medically treated patients had a significantly greater remission rate than the untreated patients (44.5% vs. 12.5%; p<0.05).

The use of medical expulsive therapy in the form of alphablockers, especially tamsulosin, has been controversial with several studies showing conflicting results. The rationale behind the use of alpha-blockers post-ESWL is that it promotes the passage of residual fragments. Most of the randomized control trials and several meta-analyses support the use of tamsulosin after ESWL.^[36] They demonstrate that alpha-blockers seem to improve the SFRs and expedite the expulsion of fragments. Furthermore, they may have a role in reducing the need for analgesics post-treatment.

Microbubble technology is emerging as a potential adjunct to ESWL. In this approach, microbubbles can be modified with binding domains, which allow them to attach onto calcium stones. Experiments in animals^[20] used a 5-F ureteric catheter to introduce modified microbubbles every 90 seconds during ESWL treatment. Using the microbubble technology, stone fragmentation was faster at lower energy levels than without microbubbles. Furthermore, histological evaluation of the renal and ureteric parenchyma post-treatment showed no evidence of tissue injury. Therefore, microbubbles have the potential to improve the safety and efficacy of all ESWL devices by lowering the energy required to achieve fragmentation.

Service setup

Arguably, the most important factor determining the success rate of ESWL in a particular unit is how the ESWL service is set up and monitored.

We have already discussed multiple patient-related factors that need to be taken into account before committing a patient to ESWL. Therefore, patient selection is very important. Clinicians booking patients for ESWL must be experienced in the treatment and its limitations and consider all the factors mentioned previously, along with the wishes of the patient to optimize the treatment they receive.

Many centers do not have fixed personnel delivering ESWL but rely on rotating junior staff usually. As a result, treatment is delivered by an inexperienced team who also has fewer opportunities to improve as ESWL is not their main focus. This can result in lower SFRs, higher on-the-day cancellations, and treatment delivered to unsuitable candidates. Dedicated personnel are essential for a successful ESWL service. Stone fragmentation can take several treatment sessions, and successful units are able to distinguish between the cases that can achieve stone clearance with more sessions and ones that need to switch to a different treatment modality. Hence, review of the post-treatment images by experienced clinicians is essential in improving the overall quality of the service.

Unfortunately, in a modern busy healthcare environment, it is often very difficult for senior clinicians to be involved in ESWL treatment. Virtual stone clinics have been shown to be able to streamline many aspects of stone management by allowing input from senior clinicians at all points of care and by reducing the load on busy outpatient clinics.^[37] A commonly used model involves all new stone cases being discussed in a weekly or biweekly stone multidisciplinary meeting and, specifically for ESWL, all post-treatment imaging being reviewed and decisions taken about further treatment (Figure 1). This can be communicated to the patient remotely, streamlining the ESWL delivery. In an evaluation of such a model, using a virtual stone clinic (VSC) was found to reduce clinic appointments (237/300); in follow-up cases, a VSC review changed the treatment modality in 24/178 patients, mainly from ESWL to other modes of treatment.[37,38]

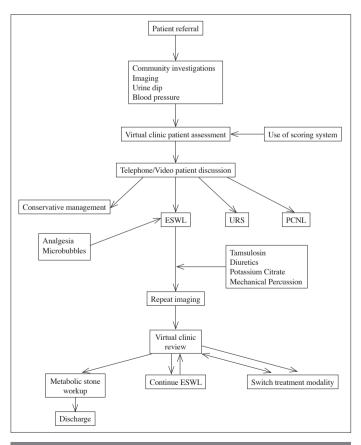


Figure 1. Proposed pathway for extracorporeal shockwave lithotripsy

Complications of ESWL

ESWL is broadly considered to be a very safe procedure. Nevertheless, complications (both short-and long-term) can occur after ESWL, and care needs to be taken to minimize them as much as possible.

Immediate complications are common, but are usually minor, after ESWL. Visible hematuria can occur in a third of cases.^[39] Usually, this is self-limiting and can stop within 48 hours but can occasionally require hospital admission for bladder irrigation.^[40] Renal colic has been reported in the literature in up to 40% of cases.^[41] Alpha-blockers have been shown to reduce the risk of ureteric obstruction from retained fragments post-ESWL. Many such cases are treated with medical expulsive therapy, but some may require ureteric stent placement, stone disimpaction using ureteroscopy, or further localized ESWL. Urinary tract infection can also occur in approximately 10% of cases post-ESWL. ^[42] In most cases, oral antibiotic therapy is the only treatment required, but occasionally, hospital admission for intravenous antibiotics and/or placement of a ureteric stent (in cases of associated obstruction) may be needed. Development of a perirenal hematoma is a rarer complication of ESWL (4.6% of cases).^[43] The treatment of choice is conservative management in almost all cases, with serial imaging, analgesia, and hemoglobin measurements. The risk factors for hematoma formation include the use of anticoagulant/antiplatelet agents and preoperative hypertension.^[44] Therefore, anticoagulants should be stopped before treatment as needed, and all patients should have their blood pressure measured pre- and post-treatment. Small, contracted kidneys are also associated with a higher risk of perirenal hematoma formation post-ESWL. Pre-treatment blood pressure measurements should always be taken, and the patient should be counseled about the increased risk of hematoma. The risk is higher in cases of untreated or poorly controlled hypertension.

Another rare immediate complication of ESWL is the formation of steinstrasse. This is essentially ureteric obstruction caused by a column of retained stone fragments. It occurs in approximately 3% of ESWL cases, and although most clear spontaneously, approximately 6% may require intervention.^[45] Common procedures for steinstrasse that do not resolve with conservative management (with or without use of alpha-blockers) include further ESWL, ureteroscopy±ureteric stenting, or percutaneous nephrolithotomy.^[45]

Delayed complications that are thought to be associated with ESWL are the development of hypertension and diabetes. Data from the literature are conflicting. Chew et al.^[46] looked at the incidence of hypertension and diabetes post-ESWL in a retrospective study of 127 patients and did not find any increase in the incidence of these diseases. Krambeck et al.^[47] in a study of 4,782 patients also demonstrated no association between ESWL

and hypertension. However, other studies have shown some association between ESWL and the development of hypertension. A study of 2,041 patients by Barbosa et al.^[48] found a statistically small but significant increase in the incidence of hypertension post-ESWL. With regard to diabetes, several large studies did not demonstrate any association between ESWL and developing diabetes.^[49] Finally, looking at the relationship between ESWL and the development of chronic kidney disease, a study of 156 patients by El-Asmmy et al.^[50] found no changes in the creatinine levels post-ESWL (average follow-up, 3.8 years).

In conclusion, shockwave lithotripsy will remain an important part of the urological armamentarium. Limits on the available operating theatre capacity and potential complications with GA owing to the recent pandemic, along with increased financial pressures, are bound to push many centers to utilize ESWL as much as possible. ESWL is operator dependent, and its success is determined by the dedicated operator and the passionate urologist experienced in the technique. Investment in newer shockwave technologies is always an attractive option; however, correct service setup, following international standards, and frequent auditing of the efficiency of the service are undoubtedly the most important factors to maximize and maintain the efficacy of lithotripsy.

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