

Pediatric extracorporeal shock wave lithotripsy: Predicting successful outcomes

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ABSTRACT

Extracorporeal shock wave lithotripsy (ESWL) is currently a first-line procedure of most upper urinary tract stones <2 cm of size because of established success rates, its minimal invasiveness and long-term safety with minimal complications. Given that alternative surgical and endourological options exist for the management of stone disease and that ESWL failure often results in the need for repeat ESWL or secondary procedures, it is highly desirable to identify variables predicting successful outcomes of ESWL in the pediatric population. Despite numerous reports and growing experience, few prospective studies and guidelines for pediatric ESWL have been completed. Variation in the methods by which study parameters are measured and reported can make it difficult to compare individual studies or make definitive recommendations. There is ongoing work and a need for continuing improvement of imaging protocols in children with renal colic, with a current focus on minimizing exposure to ionizing radiation, perhaps utilizing advancements in ultrasound and magnetic resonance imaging. This report provides a review of the current literature evaluating the patient attributes and stone factors that may be predictive of successful ESWL outcomes along with reviewing the role of pre-operative imaging and considerations for patient safety.

Key words: Attenuation value, pediatric kidney stone, safety, skin to stone distance, shockwave lithotripsy

INTRODUCTION

Extracorporeal shock wave lithotripsy (ESWL) was introduced as a minimally invasive treatment for nephrolithiasis in 1980, with the first successful use in the pediatric population by Newman in 1986.^[1] In ESWL, shock waves are generated by a source (lithotripter) external to the patient's body and are then propagated into the body and focused on a renal stone with the goal of fracturing the stone and allowing passage of the stone fragments via the urinary

tract. In the past two decades, lithotripters have become more widely available throughout the world, and ESWL is now considered a first-line treatment for minimally invasive management of pediatric stone disease of the upper urinary tract.^[2-5]

Efficacy of ESWL is best measured by the stone-free rate, typically within 3 months of ESWL therapy to allow time for passage of stone fragments. In a review of 22 pediatric ESWL series, D'Addessi found that the stone-free rates mostly exceed 70% at 3 months, although many of these series included results after multiple ESWL sessions that are known to improve the stone-free rate.^[2] Our group recently reviewed results of 149 pediatric patients treated with a single session of ESWL at multiple community and academic centers in the Midwestern US and found a 71% stone-free rate.^[6] In other pediatric series, ESWL has been demonstrated to be successful in treating large stones (20–30 mm), with a 95% stone-free rate,^[7] staghorn calculi with a 73% stone-free rate^[8] and lower-pole calculi with a stone-free rate between 61% and 92%.^[7,9] Thus, the efficacy of ESWL for renal stones in the pediatric population is well established.

Caution should be taken when comparing success rates

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of different series, primarily for two reasons. Firstly, it important to recognize that some series achieving high stone-free rates have defined ESWL monotherapy to include up to 6 ESWL sessions,^[10] while single-session stone-free rates may be as low as 44%.^[3] Because multiple sessions result in additional patient anesthesia, stress to patients and families and expenditure of hospital and physician resources, Hammad and other authors have called for measurement of the efficacy quotient (EQ) as an important measure of ESWL success, particularly in the pediatric population.^[11] EQs account for repeat ESWL sessions as well as secondary and ancillary procedures with respect to the stone-free rate.

Secondly, some series consider ESWL stone fragments <4 mm to be clinically insignificant residual fragments (CIRFs), and include patients with these fragments as having a successful outcome.^[3,9] The definition of CIRFs is extrapolated from the finding that the majority of stones <5 mm pass spontaneously in the adult population. However, Afschar demonstrated in a study of children that 69% of ESWL stone fragments <5 mm resulted in the adverse outcomes of either clinical symptoms or growth.^[12] In our practice, we do not consider any residual stone fragments insignificant and patients with residual fragments require close monitoring for stone growth, potential complications and the need for subsequent intervention.

This report will discuss patient attributes and stone factors that may be predictive of successful ESWL outcomes along with reviewing the role of pre-operative imaging and considerations for patient safety.

AGE AND GENDER

It is generally accepted that pediatric patients have an increased clearance rate of stones when compared with adult patients possibly due to lesser length and greater distensibility of the pediatric ureter.^[9,13] Children may also have an infundibulopelvic angle that is more favorable to clearance of lower-pole stones.^[14] In a study of children aged 0–14 years, Aksoy *et al.* found that after ESWL, children aged 0–5 years had the greatest stone-free rate and that children aged 11–14 years had the poorest outcomes, although age was not a statistically significant predictor of ESWL success in this series or other series to date.^[6,15,16] The efficacy of ESWL has been demonstrated to be up to 100% in both children under 6 years of age^[10] and in low birth-weight infants.^[5] To our knowledge, no study has demonstrated a significant relationship between gender and ESWL outcomes in the pediatric population.

BODY HABITUS AND ANATOMY

The increasing rate of pediatric nephrolithiasis in the United States over the past 30 years^[17] parallels an increase in obesity, which has been attributable to increased incidence

of nephrolithiasis in adults. In a multivariate analysis of adult patients, Ackermann and coworkers found that body mass index (BMI) was a predictive factor in the results of ESWL, with greater BMI linked to decreased stone-free rates.^[18] Subsequent studies in the adult population have confirmed this relationship, although studies of BMI in the pediatric population have been lacking. At our institution, we found pediatric BMIs to range from 12 to 44 among 149 children aged 1–17 years, yet found no significant relationship of BMI to ESWL success in this cohort.^[6] Our results may be attributed to the smaller body size of pediatric patients and the fact that many overweight and obese children have a skin to stone distance (SSD) within the focal distance of the lithotripter. For this reason, it may be valuable to evaluate SSD as a predictor of ESWL success in this population. A relationship of increased SSD has been correlated with ESWL failure in the adult population^[19] and has been suggested to be more prognostic than BMI. SSD is best evaluated on non-contrast computed tomography (NCCT),^[19] which is likely why study of this parameter in children has been limited to date. Future studies in the pediatric population should evaluate both BMI and SSD to determine the effect of body habitus on ESWL outcomes.

Anatomic factors, congenital or acquired, that hinder stone clearance adversely affect the results of ESWL, and any obstruction distal to the stone remains a contraindication to ESWL. In patients with anatomic abnormalities, stone-free status may be as low as 12.5%.^[20] In the presence of obstruction and infection, ESWL may result in life-threatening urosepsis. Furthermore, stone fragments are unlikely to clear and a stone is likely to recur if the concomitant obstruction is not resolved. Clearance of residual fragments is also impaired when hydronephrosis is present. When considering lower pole stones, infundibular length >3cm and infundibulopelvic angle <45° are associated with poorer outcomes.^[21,14] Gurocak *et al.* have introduced a pediatric infundibulopelvic index (IPI) for lower calyceal stones, suggesting that a combination of infundibular length, width and infundibulopelvic angle may be a more beneficial predictor of ESWL success than evaluation of these parameters individually.^[22]

THE ROLE OF IMAGING

The clinical suspicion of nephrolithiasis must be confirmed by imaging in order to make a definitive diagnosis. Pre-operative imaging is essential for the determination of stone characterization and location when planning management and treatment options. Current imaging modalities include NCCT, ultrasound, kidney ureter bladder plain film and intravenous pyelography. Of these modalities, NCCT has been demonstrated to be the most sensitive and specific,^[23] and also offers the added potential of illustrating patient anatomy, identifying alternative pathology, determining stone density via attenuation value (Hounsfield units),

determining the skin-to-stone distance as well as for characterizing stone volume using multiple views. Despite being the gold standard for evaluation of renal colic in the adult population, use of NCCT for the evaluation of stones in children has been limited to date because of concerns for ionizing radiation and the potential of cancer. Sound evidence for this concern derives from studies of atomic bomb survivors in Japan, demonstrating a direct relationship of the amount of ionizing radiation to the development of cancer. Along with the additive risk of repeated exposures, children are felt to be inherently more susceptible to ionizing radiation than adults because they have a higher population of dividing cells and because they have more remaining years of life during which a latent radiation-induced cancer could develop.^[24] In what is now a commonly cited study, Rice speculated the incidence of fatal cancer in children to be as high as one per 1,000 CT scans.^[25] In our practice, the use of NCCT scanning is limited and not considered necessary for all children if a stone is clearly visible on ultrasound and/or kidney-ureter-bladder (KUB) X-ray. But, in older children, those who present with symptomatic renal colic, or patients with hydronephrosis without a visible renal stone, NCCT imaging is the preferred imaging modality in our practice. Similarly, while NCCT most accurately determines the stone-free status post-ESWL, detecting fragments as small as 1 mm, use in this population is reserved for the same concerns, and either ultrasound or KUB is typically utilized for radiolucent and radiopaque stones, respectively.

Risks of radiation can be reduced with protocols that limit the area scanned to the region of necessity only and by proper radiation dosing tailored toward individual patient size and age. Lower radiation dose NCCT protocols can produce equivalent sensitivity and specificity for stone detection when compared with standard CT.^[23] However, it is not clear whether calculation of attenuation density in Hounsfield Units (HU) or post-processing algorithms designed to determine stone composition remain equally as accurate. We anticipate that advancements toward faster imaging, lower radiation dose and improved post-processing will allow more widespread use of NCCT for the detection of urolithiasis in the pediatric population without compromising patient safety.

STONE SIZE AND LOCATION

Stone size has frequently been cited as the most important predictor of ESWL success in the pediatric population,^[2,6] but variation in the methods by which stone size is measured and reported can make it difficult to compare individual studies and make recommendations for ESWL treatment. Stone size has been reported as a single diameter, a sum of diameters,^[3,11] an area^[9,10] and as total stone burden, which is the sum of the diameters or areas of treated stones in patients with multiple stones.^[6] With the use of CT, it is also possible to estimate the stone volume. Single transverse diameter

is the most commonly used measure of stone size in large retrospective ESWL studies to date.^[26] One could argue that future studies should move toward the use of stone area under the assumption that a 1 mm x 8 mm stone has a better likelihood of fracture and passage after ESWL than an 8 mm x 8 mm stone, despite having the same maximal transverse diameter. Regardless of the method of determining stone size, the vast majority of studies have demonstrated a direct relationship of worsening stone-free rate with increasing stone size. In studies that suggest that stone size does not significantly affect the stone-free rate, it is important to recognize that as the stone size increases, the number of sessions, number of shock waves and fluoroscopy time per session may have also increased.^[27] In the aforementioned multi-institutional study conducted by our group, stone burden, measured as the maximal transverse diameter, was the only independent predictor of single-session ESWL success on multivariate analysis.^[6] While multiple studies have demonstrated improved outcomes in stones <1 cm compared with larger stones,^[6,15,28,29] success has been seen in stones up to 25–30 mm in diameter with multiple ESWL sessions.^[27,30]

There is a general consensus in adult endourology that lower-pole stones tend to be more refractory to ESWL when compared with other stone locations. This same conclusion was met in a pediatric study by Ather *et al.* in 2003,^[30] but other series have shown no statistically significant relationship between stone-free rates and location when comparing lower-pole stones with other intrarenal stones or intrarenal to uretral stones.^[2,6,9,11,16] In our practice, ESWL is most commonly used for intrarenal stones of the lower pole that are <1 cm and for stones <2 cm in other locations. We typically avoid ESWL in the mid and distal ureter in children due to difficulties with localization over the sacroiliac joint and to avoid possible injury to the developing reproductive systems.

STONE COMPOSITION AND ATTENUATION DENSITY

The ease with which a stone is fragmented by ESWL varies among stones of different compositions. Data reported by Saw and coworkers showed that when adjusted for stone size, cystine and brushite stones are the least amenable to fracturing with ESWL, followed by calcium oxalate monohydrate stones. Hydroxyapatite, struvite, calcium oxalate dihydrate and uric acid stones are increasingly more amenable to fracturing with ESWL.^[31] A means to determine stone composition on initial presentation would be beneficial to planning surgical treatment or medical therapy. Different stone compositions have been demonstrated to have different radiodensities as well as different attenuation values measured in HU on NCCT. The HU is a measure of the radiodensity of a tissue or substance using an index based on the radiodensity of water.

Substances like bone have a higher density while air and fat have the lowest densities. Unfortunately, most stones are not pure in composition and attempts to correlate attenuation value with stone composition have demonstrated that it is possible to distinguish uric acid stones from calcium-based stones, but that it is not easy to discern between types of calcium-based stones (e.g., calcium oxalate monohydrate from hydroxyapatite),^[19,32] making it challenging to assess the usefulness of NCCT in predicting stone composition in the clinical setting. Newer dual-energy multi-detector CT protocols with advanced post-processing techniques appear to allow for improved discrimination among the main different subtypes of urinary calculi in both *in vitro* and *in vivo* when compared with single-energy multi-detector CT acquisitions with basic attenuation assessment.^[33] Despite advancements, these techniques require a near-perfect breath hold, which may be difficult to achieve in young children without the use of general anesthesia. Continued advancement in imaging modalities and post-processing of images may provide improved pre-operative characterization of stone composition and enhance surgical and medical management.

In addition to being used as an adjunct to predicting stone composition, CT attenuation value has been determined to be an independent predictor of stone-free rates after ESWL therapy in the adult population.^[34] Improved stone-free rates are seen for stones with lower attenuation values, with 1,000 HU being suggested as a significant cutoff for stones that are most amenable to ESWL. In a recent study that is pending publication, we retrospectively evaluated a cohort of 53 pediatric patients aged 1–18 years who underwent NCCT prior to single-session ESWL monotherapy and found that the stone attenuation value of the stone-free patients was 710 ± 294 HU vs. 994 ± 379 HU for those with treatment failure. When patients were stratified into two groups by attenuation value, $<1,000$ HU and $\geq 1,000$ HU, the ESWL success rates were 77% and 33%, respectively. As in adult studies, larger stone sizes tended to have higher attenuation values. Pre-operative knowledge of the stone attenuation value is beneficial when considering treatment modalities and discussing potential outcomes with patients and family members.

SAFETY

While the efficacy of ESWL is clearly established, there remains debate over the safety of this procedure, particularly in the very young patient with growing kidneys. Animal studies have demonstrated the appearance of histological changes when immature kidneys are subjected to shock waves, with parenchymal damage proportional to the number of shocks received.^[35] However, when children are evaluated clinically and with scintigraphy, parenchymal damage does not appear to persist on long-term follow-up,^[36,37] and renal growth and function do not appear

to be significantly altered.^[38] In 2006, Kramcheck *et al.* reported on a 19-year follow-up of adult patients treated with ESWL, raising concerns of long-term effects, namely an increased risk of developing hypertension and diabetes.^[39] The development of hypertension was associated with bilateral ESWL treatment. All patients in the Kramcheck study were treated with a first-generation lithotripter, which is known to have a greater focal diameter and likely causes more damage to the surrounding renal and pancreatic tissues than the second- and third-generation lithotripters more widely in use today. Furthermore, outcomes for patients with untreated stone disease are significantly worse than for those who undergo treatment, and multiple studies have shown ESWL to be a safe and effective procedure in children.^[1,29] Because the long-term safety of ESWL remains nebulous, we attempt a course of conservative follow-up in small children for as long as possible.

To optimize safety and efficacy, ESWL should only be performed if lithotripter focal size and treatment facilities are adapted to the size of the child. Modifications to ensure proper shielding, positioning of the child and appropriate dose of electrical discharge to the size of the patient are required to reduce the likelihood of complications such as hematomas or lung contusions. Specifically, polystyrene pads may be placed over the lung fields during an ESWL session to ensure pulmonary shielding. A traditional Dornier lithotripter may require modification of the gantry with wood slats or a car seat with an opening made on the rear. With regards to gating of shocks during ESWL, studies have demonstrated that ungated shocks are safe in the pediatric population, and that the arrhythmias seen in adults are not likely to occur in this population.^[40]

CONCLUSIONS

Despite numerous reports and growing experience, few prospective studies and guidelines for ESWL have been completed. Variation in the methods by which study parameters are measured and reported can make it difficult to compare individual studies or make definitive recommendations. Individual surgeon experience and availability of instrumentation remain the most important factors for counseling patients and determining the most appropriate treatment options for nephrolithiasis in children. At our institution, advancements in instrumentation for pediatric PCNL and ureteroscopy, for example, facilitate the application of similar protocols for surgical intervention in children and adults. ESWL remains the procedure of choice for most upper urinary tract stones <2 cm in size because of established success rates, its minimal invasiveness and long-term safety with minimal complications. Still, imaging protocols in children with renal colic must be improved to minimize exposure to ionizing radiation, perhaps utilizing advancements in ultrasound and magnetic resonance imaging.

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