Original Article

Impact of Pediatric Urolithiasis and its management on renal growth

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Abstract

Background: There are marked variations in the incidence of urinary tract stones in children worldwide. Unlike other pathologies, the incidence and nature of pediatric urolithiasis differ significantly from country to country. While the disease has been reported to be rather rare in some areas, it is still an endemic problem in developing countries. There is evidence that the incidence of nephrolithiasis is growing with data suggesting that the overall prevalence reaching 8.8 of the population and this is higher than previous data which recorded 5.2 prevalence of kidney stones. The major metabolic abnormalities include: hypercalciuria, hyperoxaluria, hypocitraturia, cystinuria, and hyperuricosuria. Hypercalciuria or hypocitraturia are the most frequently reported abnormalities in children. The classic adult presentation of acute, severe flank pain, which radiates to the groin is uncommon in children, particularly in children younger than 5 years. Although adolescents present similarly to adult patients, younger children have varied presentations including nonspecific pain localized to the abdomen, flank, or pelvis. In infants, symptoms of stones may be confused with colic pain. Macroscopic or microscopic hematuria can occur in up to 90% of children with urolithiasis. Imaging techniques are used to exclude or substantiate the diagnosis and to determine the size and location of a stone including assessment of the consequences of obstruction to the urinary tract and renal function. Knowledge of these parameters is necessary to plan therapy adequately. Kidney-Ureter-Bladder (KUB) The KUB film can only reveal radio-opaque calculi. Diagnostic sensitivity, and specificity of KUB is 69%, 82% respectively (40) Examination of the skeleton can provide evidence of other causes of pain (for example the vertebrae). The first goal of medical management should be directed toward control of the acute complications. Pain associated with the passage of a stone is often severe and should be treated promptly with narcotic analgesics (morphine sulfate) and/or nonsteroidal ant-inflammatory drugs (Ketorolac). If the patient has vomiting or unable to drink, parenteral hydration should be used to maintain a high urine flow rate. In the absence of oligoanuric renal failure or a complete obstruction, an intravenous infusion rate of 1.5 to 2 times maintenance is recommended. Agents that may promote the passage of stones and reduce symptoms (medical expulsive therapy), such as alpha-adrenergic blockers (tamsulosin) and calcium-channel blockers (nifedipine), have shown promising results in adults with distal ureteral calculi. ESWL remains the first line of treatment of renal stones in children (75) However, its scope is now being challenged for the reasons that there have not been any major improvements in ESWL technology to improve the ESWL outcome of renal stone management, and it has largely failed to keep pace and compete with the better outcomes now being reported from the newer MIS developments such as mini/micro PCNL

Keywords: Urolithiasis

INTRODUCTION

The kidneys are parenchymatous organs which are essential for life. They are situated in the retroperitoneal space and are suspended by fat and fibrous tissue. The medial border of each kidney curves inwards to form the renal sinus while the lateral border is convex. Cranially and caudally the rounded ends of the kidney are known as the upper and lower renal poles.(1-4)

The weight of the normal kidney range from 110.-170gm in males and 200-225 in females that depending on amount of urine and blood within it . (4-9)

In children the size of the kidney tend up to make larger proportion of body weight than observed in adults , as it tend to decrease in size after age of 60 .

The dimensions are craniocaudally 8-13.5 cm mediolaterally 4.5-7.5 cm anterioposteriorly 3-4.5 cm , table (1) showed the renal measurements by cm found by (9-12) .

Multiple studies showed significant relation between renal size and age in pediatric age . Svein Haugstvedt in 1980 published a study on 46 patients evaluating the relation between kidney size and age , he found that there was a close correlation

between age and kidney length. The first 1; years of life were characterized by more rapid growth of the kidneys. There was no significant difference in kidney length between boys. (12-15)

Table1 . Relation between renal morphology and age

Age (years)				
	Less than 1 year	1-5 years	6-9 years	10-15 years
Kidney length	57±6.7	76±4.6	82±7.2	98±11.4
Kidney width	20±2.6	30±2.7	34±2.9	39±4.9
Thickness	26±3.8	36±3.3	42±3.6	48±6.7

A OTIV et ,al showed that renal length correlated best with body height and body surface area, the calculation of body surface area is cumbersome and requires multiple measurements. (15-22)

1. **Renal stones**

i. Incidence and prevalence

Renal stones are highly prevalent over world , it ranges from 7-10 % in North America , 1-5 % in Asia , and 5-9% in Europe. (23, 24)

There is evidence that the incidence of nephrolithiasis is growing with data suggesting that the overall prevalence reaching 8.8 of the population and this is higher than previous data which recorded 5.2 prevalence of kidney stones .(25, 26).

Also , Japanese study documented that first-episode upper urinary tract stones in 2005 was 134.0 per 100,000 (192.0 in men and 79.3 in women) compared with 54.2 per 100,000 in 1965 . (27)

Urolithiasis is observed less frequently in children than in adults; however, the pathology is associated with considerable morbidity, with recurrence rates of 6.5–44 %. Without follow-up and medical intervention, stone recurrence rates have been reported to be as high as 50% within 5 or 6 years. (3)

ii. Pathophysiology

Urolithiasis is associated with an identifiable metabolic abnormality in approximately 40% to 50% of children . (28-30).

The major metabolic abnormalities include: hypercalciuria, hyperoxaluria, hypocitraturia, cystinuria, and hyperuricosuria. Hypercalciuria or hypocitraturia are the most frequently reported abnormalities in children (31-33) .

In the United States approximately 40% to 65% of calculi comprises calcium oxalate, 14% to 30% of calcium phosphate, 10% to 20% of struvite, 5% to 10% of cystine, and 1% to 4% of uric acid. Rarely, stones may also comprise xanthine, or 2,8-dihydroxyadenine. The initiation and growth of calculi requires the supersaturation of certain ions in the urine.

The most important determinants of urine solubility and the likelihood of ion supersaturation (crystallization) are the total urine volume, the concentration of the stone-forming ions, the concentration of inhibitors of crystallization, the concentration of promoters of crystallization, and the urine pH. All types of calculi are less likely to form in dilute urine. Citrate, magnesium, pyrophosphate, certain glycosaminoglycans, nephrocalcin, and phytates all act to inhibit crystallization of calcium oxalate and calcium phosphate. Citrate acts as an inhibitor for the formation of calcium stones that binds to urinary calcium, thereby forming a soluble complex, which decreases the availability of free ionic calcium necessary for calcium oxalate or calcium phosphate crystallization. Citrate also acts as a direct inhibitor of calcium crystal aggregation and growth. (34-36).

Genitourinary anomalies (hydronephrosis, duplex ureter, posterior urethral valves, and bladder exstrophy) are found in approximately 30% of children with urolithiasis . Functional or anatomic obstruction predisposes children to stone formation by promoting stasis of urine and infection. Only 1% to 5% of children with urologic abnormalities develop calculi (37) .

iii. CLINICAL PRESENTATION

The classic adult presentation of acute, severe flank pain, which radiates to the groin is uncommon in children, particularly in children younger than 5 years. Although adolescents present similarly to adult patients, younger children have varied presentations including nonspecific pain localized to the abdomen, flank, or pelvis. In infants, symptoms of stones may be confused with colic pain. Macroscopic or microscopic hematuria can occur in up to 90% of children with urolithiasis .

Renal stones may be found incidentally and remain silent for years without causing symptoms. Approximately 10% of calculi can present with dysuria and urinary frequency and are usually localized to the lower urinary tract. UTI may also complicate nephrolithiasis, although pyuria may also be present without bacteriuria or infection. Rarely, a urethral stone can present with acute urinary obstruction. (38)

iv. Evaluation

iv.i. Imaging

Imaging techniques are used to exclude or substantiate the diagnosis and to determine the size and location of a stone including assessment of the consequences of obstruction to the urinary tract and renal function. Knowledge of these parameters is necessary to plan therapy adequately.

Ultrasonography

Ultrasound has the advantages of being easily available, non-invasive and avoiding radiation. On the other hand, it is highly dependent on the skills of the doctor performing the examination.

B-mode ultrasonography can reveal stones in the kidney, in the proximal ureter at approximately the height of the lower renal pole and in the distal ureter. Generally, stones in the other ureter segments cannot be visualized due to intestinal gases.

Sensitivity and specificity of ultrasound diagnosis of renal stones are approximately 61-93% and 95-100% respectively (39) The

accuracy of ultrasound in pediatric urolithiasis is also quite variable. Stones could be detected in 33-100% The detection rate was much higher in the kidney when compared to the ureter (32)

Conventional radiology (KUB, intravenous urography)

Kidney-Ureter-Bladder (KUB) The KUB film can only reveal radio-opaque calculi. Diagnostic sensitivity, and specificity of KUB is 69%, 82% respectively (40) Examination of the skeleton can provide evidence of other causes of pain (for example the vertebrae).

Radiation dose of the x-ray is a debatable risk especially when used in pediatric population , on the other hand abdominal distention and gases highly limit its accuracy , also Recent barium X-rays of the abdomen . The radiation dose is about 0.5 mSv (41)

Intravenous urography

In general, films are taken at 7½ and 15 minutes following intravenous contrast medium infusion. Enhanced parenchymal contrast on early films (for example 3 minutes after contrast medium administration) can indicate obstruction on the affected side. However, early urogram films are generally not required as ultrasonography will have already been performed, thus, also reducing radiation dose.

To reduce exposure to radiation, further films should not be taken if the first film reveals all relative information. Often, it is adequate to concentrate radiography on the affected side. Delayed contrast medium excretion necessitates late films (for example after several hours).

The intravenous urogram is analyzed regarding renal function, dilatation of renal pelvi-calyceal system and ureter, location and area of the renal stone and radiological opacity. Non-opaque stones (generally uric acid stones) are noticed as contrast medium filling defects.

Sensitivity and specificity of intravenous urography in the diagnosis of ureteral stones is 92-98% and 59-100% respectively (42) The accuracy of intravenous pyelography can be maximized with proper bowel preparation, and the adverse renal effects of contrast media may be minimized by ensuring that the patient is well hydrated. Unfortunately, these preparatory steps require time and often cannot be accomplished when a patient presents in an emergency situation . (43)

The use of IVP in diagnosis of pediatric urolithiasis is rarely indicated because of hazards of radiation and complication of the contrast .

Non- contrast spiral CT (NCCT)

NCCT is the method with the highest sensitivity, and specificity for examining kidney and ureteral stones . A prerequisite is utilization of thin layers (<5 mm) to also detect small concretions. NCCT is superior to all other imaging techniques (42, 44) Additionally, NCCT addresses to some extent other differential diagnoses. Density measurement (Hounsfield units) also facilitates estimation of stone composition. This is important for therapeutic planning (45) However, NCCT overestimates stone size by 30-50% (46)

The radiation dose is approximately 2.8-5.0 mSv , therefore being significantly higher than conventional radiology. As children affected by urinary stones are at high risk for multiple recurrences during their lifetime, they probably will need multiple imaging for stones during their life. Therefore, radiation exposure is an important issue. Kuhns *et al*. calculated that the ratio of the risk for abdominal and pelvic cancer due to a single NCCT for stones to the risk of a naturally occurring cancer over the lifetime of a child is estimated to be 2/1,000 to 3/1,000 (47)

During the last decade, examination protocols with lower radiation doses have been developed (so called ultra low dose NCCT). This term, however, is not standardized. Using those protocols, the radiation dose can be reduced to approximately 1-2.2 mSv(48, 49)

However, resolution also suffers especially with respect to stone composition (measurement of Hounsfield units), thus compromising therapeutic planning.

Aspects of differential indication of imaging techniques

Sensitivity and specificity are of great importance when comparing imaging methods. In this respect, native computed tomography is superior to all other techniques.

The conventional imaging modalities (ultrasound, X-ray), however, are not so bad. A large study, recently published, demonstrated that in case of clinical suspicion of urolithiasis there was no difference between patients primarily diagnosed by NCCT and those primarily examined by ultrasound with respect to diagnoses and therapy results (50). As shown by Johnson *et al*. (51) nearly 90% of children treated for urolithiasis could have completed their work-up and therapy without undergoing CT. On the other hand, almost 75% of children undergoing NCCT for suspected urolithiasis did not have a stone (52)

iv.ii Metabolic Investigations

When urinary calculi develop during childhood, the risk of life-long stone formation is significant, with approximately 16% to 20% having recurrences within 3 to 13 years. (53) Furthermore, children with an identifiable metabolic abnormality have an up to 5-fold increased risk of having a recurrence as compared with children with no identifiable metabolic disorder (30) .

As a result, all children should undergo a comprehensive initial evaluation. Whenever possible, analysis should begin with an infrared spectroscopy or radiograph diffraction analysis of a passed stone. If a cystine or struvite stone is found, the analysis will be diagnostic.

Serum and urine studies should be obtained in patients in whom stone analysis could not be performed or for those with either calcium or uric acid-based stones. A serum creatinine level is essential to evaluate for possible acute kidney injury or chronic

kidney disease. Serum calcium, phosphorous, bicarbonate, magnesium, and uric acid levels are effective in screening for hypercalcemia- and hypocalcemia-associated calculi , hyperuricemia.

Unlike in adults, primary hyperparathyroidism is rare in children and an intact parathyroid hormone level is not an essential part of the initial evaluation unless there is evidence of hypercalcemia and hypophosphatemia. A 25-hydroxyvitamin D level should be evaluated in all patients with hypercalcemia. A spot urine beta-2 microglobulin (low-molecular-weight protein) is a useful screening test for Dent disease and should be considered in men and possibly carrier women if there are recurrent calcium-based calculi in the setting of proteinuria or a family history of renal failure, focal segmental glomerulosclerosis, or recurrent calculi.

V.Management of pediatric urolithiasis

v.i. Acute Management

The first goal of medical management should be directed toward control of the acute complications. Pain associated with the passage of a stone is often severe and should be treated promptly with narcotic analgesics (morphine sulfate) and/or nonsteroidal ant-inflammatory drugs (Ketorolac). If the patient has vomiting or unable to drink, parenteral hydration should be used to maintain a high urine flow rate. In the absence of oligoanuric renal failure or a complete obstruction, an intravenous infusion rate of 1.5 to 2 times maintenance is recommended. Agents that may promote the passage of stones and reduce symptoms (medical expulsive therapy), such as alpha-adrenergic blockers (tamsulosin) and calcium-channel blockers (nifedipine), have shown promising results in adults with distal ureteral calculi. (54)

Although studies in children are limited, 1 prospective study showed that in children with distal ureteral calculi who were treated with tamsulosin, there was a greater stone expulsion rate and decreased time to stone expulsion when compared with controls.(55)

v.ii. Preventative Measures

- Fluid

Fluid intake is a critical component of stone prevention by effectively reducing the concentration of lithogenic factors, including calcium, oxalate, uric acid, and cystine. Although high daily fluid intake reduces the risk of recurrent stone formation,(56) the exact prescription is unknown. Most clinicians recommend intake at least equal to calculated maintenance rates in children and no less than 2 to 2.5 L in adolescents and adults. Even higher fluid intake levels (1.5–2 L/m2) may be recommended for children with cystinuria or PH. Increased intake requirements may be required during periods of increased insensible water loss. Regarding fluids other than water, reports suggest that fluids that increase urinary pH and citrate excretion such as orange juice, lemonade, and black currant juice, as well as those that increase urinary volume such as coffee, tea, beer, and wine, reduce the risk of calcium stone formation Conversely, grapefruit juices seem to increase the risk of calcium-based stones. Whether cola drinks increase lithogenic potential or not remains controversial.(57, 58) .

- Sodium

The association between sodium intake and calcium stone formation has been reported but has not been confirmed in all studies Increased sodium intake is known to promote calciuria by competing for reabsorption at the level of the renal tubules. A low salt diet corresponding to less than 2 to 3 mEq/kg/d in children or less than 2.4 g/d in adolescents or adults is generally recommended for patients with hypercalciuria or calcium-containing stones. A low salt diet may also reduce urinary cystine excretion in patients with cystinuria.(58)

- Calcium

Until recently, higher calcium intake was thought to increase the risk of stone formation; however, there is substantial evidence now that a higher calcium containing diet is associated with a reduced risk of stone formation.

A potential mechanism that might explain this paradox is that higher calcium intake effectively binds dietary oxalate in the gut, thereby reducing intestinal absorption and eventual urinary oxalate excretion. The current recommendation for stone formers is to curtail excess calcium intake, but calcium restriction is not recommended, in part, because of the long-term risk of osteoporosis. Excess consumption of vitamin D with or without calcium supplements can also induce excessive urinary calcium excretion.(59)

- Oxalate

The role of dietary oxalate in stone formation is controversial because only approximately 10% to 20% of urinary oxalate excretion is derived from the diet. As a precautionary measure, most clinicians recommend limiting dietary oxalate ingestion in calcium oxalate stone formers who demonstrate evidence of hyperoxaluria.

Vitamin C supplements have been associated with increased risk of calcium oxalate stone formation because oxalate is a byproduct of ascorbic acid metabolism and therefore, these supplements should be discontinued in calcium oxalate stone formers with hyperoxaluria. (60)

v.iii. Medications

- Diuretics

A thiazide diuretic is often required for children with hypercalciuria who do not respond to a restricted sodium diet. The usual recommendation is hydrochlorothiazide 1 to 2 mg/kg/d .

- Alkali agents

Treatment with either potassium citrate (2–4 mEq/kg/d, adults 30–90 mEq/d) or potassium-magnesium citrate has been shown to reduce the recurrence of calcium oxalate stone formation in patients with low or normal citrate excretion. (61)

- Thiol-containing agents

These agents are used exclusively for patients with cystinuria in whom fluid and dietary modifications as well as urinary alkalinization are ineffective in preventing stone recurrences or dissolving preexisting stones. The 2 most common agents are

D-penicillamine and a-mercaptopropionylglycine

- Allopurinol

The mainstay of therapy for most children with uric acid calculi is a combination of high urine flow rate and alkalinization of the urine. Allopurinol (4–10 mg/kg/d, adult maximum 300 mg/d) is indicated in conditions in which there is both hyperuricemia and hyperuricosuria (62)

V.iv. Surgical management of pediatric nephrolithiasis

Pediatric patients carry a high probability of recurrence (63) , and therefore, every effort should be made to prevent stone recurrence by ensuring complete stone clearance (64).

This is a greater challenge with minimally invasive surgery (MIS) and limits the applicability of extracorporeal lithotripsy. Risk factors need to be identified, and these may be anatomical or metabolic, which require evaluation by dietary, urinary, and stone composition analyses (65-67)

Historically, all stones are treated by open surgery (68-70) Currently, with the advent of MIS, the majority of the stones are managed by MIS utilizing extracorporeal shockwave lithotripsy (ESWL), percutaneous nephrolithotomy (PCNL), and ureteroscopy/retrograde intrarenal surgery (URS/RIRS) (71, 72). Undertaking MIS in small children is challenging , which to a certain extent has been overcome by improvement in technology by the development of miniaturized instruments, which are referred to appropriately as Miniperc or Microperc (73, 74).

EXTRACORPOREAL SHOCKWAVE LITHOTRIPSY (ESWL)

Since 1986, when ESWL was first described, it remains the first line of treatment of renal stones in children (75) However, its scope is now being challenged for the reasons that there have not been any major improvements in ESWL technology to improve the ESWL outcome of renal stone management, and it has largely failed to keep pace and compete with the better outcomes now being reported from the newer MIS developments such as mini/micro PCNL.

There is wide disparity in the stone free rates documented in the literature for ESWL in children ranging from 33 to 95% with incomplete information about the number of sessions (retreatment rates), residual fragments, and JJ stent placements. The results are incomparable not just for lack of information but also because of variability of the confounding factors like age, gender, the stone burden, location, composition, the type of lithotripter used, and the number of shockwaves in each session. All these factors impact ESWL outcome especially in children (76-78)

Although staghorn stones (>3 cm) have been treated with ESWL, the retreatment rates are high, requiring up to five sessions (79)

The European Association of Urology (EAU)/European Society for Paediatric Urology (ESPU) and American Urological Association (AUA) guidelines continue to recommend ESWL as the first line of treatment for renal stones .(80) and nomograms reflecting this have been developed . (81)

Metanalyses by sultan et al reported that increase in the mean number of ESWL sessions associated with an increase in stone burden . In the single stone group of 158 renal units with a mean stone size of 10 ± 2.5 mm, 76% (121 renal units) were cleared in a single session, and 21 units were cleared in a second session, giving an overall clearance rate of 89% in a mean of 1.14 sessions. In the second group of 58 renal units comprising multiple stones having a mean size of 17 ± 5.3 mm, 46% (27 units) were cleared in a single session, 32% (19 units) were cleared in a second session, and 7% (4 units) cleared in a third session, giving an overall clearance rate of 86% in a mean of 1.54 sessions. (82)

Also , he recommended restrict the use of ESWL for renal stones up to 1.5 cm, except for lower calyceal stones when the upper limit should be 1 cm. (82)

In addition , Stone location was one of the important factors for stone clearance . The relationship between stone location and clearance showed that the best clearance rates following a single session of ESWL were for the upper calyx (87%) and pelvis (84%), and the poorest for the lower calyx (67%). The mean numbers of sessions required for clearance in the upper calyx, pelvis, and middle calyx were 1.1, 1.2, and 1.3, respectively, as compared to the figure for the lower calyx of 1.5(82)

Furthermore , lower HU is associated with better clearance for the same size of stone . (83)

Predicting success of treatment

Various investigators have tried to define those patients who are more likely to have an unsuccessful outcome with ESWL. Stone burden (size and number) is an important factor influencing the choice of treatment modality for renal calculi. ESWL is successful in up to 90% of stones 2 cm in size, PCNL is the preferred treatment option and the presence of multiple stones also reduces the stone-free rate.

Stones in the lower pole are traditionally associated with lower success rates compared with stones in the upper and mid-pole regions. A meta-analysis published by Lingeman et al (84) reported only 60% stone-free rate for lower pole stones with ESWL; this was dependent on stone size, with only 33% stone clearance for stones larger than 20 mm. Spatial anatomy of the lower renal pole, as defined by the infundibulopelvic angle, infundibular length and infundibular width, appears to play a significant role in the stone-free rate after ESWL (85)

An infundibulopelvic angle 3 cm, or an infundibular width 5 mm were found to be unfavourable and are associated with poor stone clearance. The first lower pole study (2001) compared ESWL with PCNL for symptomatic lower pole only renal calculi (86)

A subsequent prospective, randomized, multi-center study from this group compared ESWL and ureteroscopy for the treatment

of lower pole stones 1 cm in 67 patients (87). The primary outcome measure was stone-free rate on non-contrast computed tomography (NCCT) at 3 months. Although ESWL had a significantly shorter procedure time than ureteroscopy (66 min versus 90 min), the study failed to demonstrate a statistically significant difference in stone-free rates between ESWL (35%) and ureteroscopy (50%). Intraoperative complications occurred in one ESWL case (unable to target stone) and in seven ureteroscopy cases (failed access in five and perforation in two), whilst postoperative complications occurred in seven ESWL and seven ureteroscopy cases. ESWL was associated with greater patient acceptance and shorter convalescence.

Kanao et al. (88) performed a multivariate analysis and logistic regression to create a nomogram to predict 3-month stone-free outcomes after a single ESWL treatment, which can be useful for counselling patients with urolithiasis before ESWL. A total of 435 patients with 507 urinary stones were treated with ESWL with a Dornier Lithotripter D. Patient age, sex, body mass index (BMI), number of stone(s) in each treatment, stone size, side and location were evaluated before ESWL, and treatment efficacies were evaluated at 3 months after each session. Stone size, location and number were identified as significant variables on multivariate analysis. In these nomograms the stone-free probability was highest for solitary proximal ureteral stones 21 mm (10.5%).

El-Assmy et al , (89) carried a study on 57 child (less than 16 years) to asses the relation between stone size , Hounsfield unit and eswl success , this study found that Stone attenuation ≤600 HU and stone length ≤12 mm were significant independent predictors of SWL success in children.

Wang et al. (90) subsequently studied the relationships between the characteristics of renal stones as determined by NCCT and their outcome after ESWL. Multivariate analysis demonstrated that a stone burden of more than 700 mm3 (P ¼ 0.0003), the presence of non-round /oval stones (P ¼ 0.0072), and a maximal stone density of more than 900 HU (P ¼ 0.0430) were statistically significant predictors of a failure of outcome for ESWL. In another CT study, Gupta et al. [24] reported the best outcome in those patients with a calculus diameter of 750 HU and diameters of >1.1 cm, where 23 (77%) needed three or more ESWL sessions and the clearance rate was only 60%. It was noted that the calculus density was a stronger predictor of outcome than size alone.

Patient's age was an important predictor for response after ESWL monotherapy: not only did children respond better than adults, but age was also an independent predictor within the pediatric group . (91)

Mechanism of action

All shock waves (acoustic pulses) have both a positive and a negative portion. The positive portion of the wave, also known as the compressive phase causes pressure gradients within stones leading to shear and tensile stress. This compressive phase produces pressures of about 20–100 MPa depending on the lithotripter.

The negative portion of the wave, which has a lower amplitude causes mainly tensile stress (−5 to −15 MPa) but also causes cavitation in the fluid surrounding the stone. Both these forces are believed to contribute to stone fragmentation.

In general, fragmentation of stones occurs due to cracks that occur secondary to stresses that are caused by applied shock waves. With repetitive stresses these cracks grow and lead to fragmentation. The initial cracking of stones
occurs secondary to different theorized shockwave mechanisms including tear/shear forces, spallation, quasi-static squeezing, cavitation, and dynamic squeezing.

Tear/Shear Forces

Shear stresses are generated by a combination of both shear waves and compressive waves. These waves develop as the shock wave travels through
the kidney stone.

As a result, the shear and compressive waves cause large shear stresses at the crystal interfaces, which contribute to the fracture of the kidney stones. Shock waves move at different speeds in solid versus liquid mediums. This mismatch of the compressive waves results in shear stress.

Spallation

This theory hypothesizes that once the acoustic pulse has traversed the stone, it is inverted and reflected back from the distal surface of the stone. This creates a tensile (negative wave) force that can fragment the stone.

Quasi-Static Squeezing

Quasi-static squeezing occurs when the focal zone is greater than the diameter of the stone itself. Fragmentation occurs due to the difference in sound speed between the stone and the surrounding fluid. The acoustic pulse traveling through the stone is faster than the pulse that is traveling in the fluid outside the stone. This pulse produces a circumferential force on the stone, which results in a tensile stress on the stone. The force is maximal at the proximal and distal ends of the stone.

Cavitation

Cavitation bubbles are generated from the negative pressure phase of shock waves that occurs in both the fluid surrounding the stone and within micro-cracks of the stone. As the cavitation bubble collapses near a solid surface (kidney stone) a microjet of fluid is formed that pierces the bubble and impacts the surface of the stone. The collapse of the cavitation bubble also results in the formation of secondary shock waves. These secondary shock waves have amplitudes comparable to the focused shock wave. (Nakada and Pearle, 2016)

Complications of ESWL :

1- Obstruction

The most frequent problem following ESWL is ureteric obstruction caused by impacted stone fragments. Its frequency increases with a large stone burden and when the stone is disintegrated into larger fragments. Steinstrasse is the commonest presentation where stone fragments accumulate in the distal ureter and cause severe obstruction. The reported incidence of steinstrasse is 6-

8.5% , This can be avoided by the placement of an internal stent preoperatively.(71, 76)
ESWL for larger stones is a potentially significant complication of SWL and is associated with significant morbidity. Ureteral stents decrease the acute presentations of patients with steinstrasse. (92)
Although ureteral stents are associated with more irritative symptoms, their use resulted in fewer hospital readmissions and emergency room visits compared to when no stent was used to treat solitary kidney stones of 10 to 20 mm. or solitary proximal ureteral stones less than 20 mm. (93)

2- Infection

Urinary tract infection is another common complication which can occur secondary to infected urine or stone. This can be avoided by the use of preoperative antibiotics according to the culture and sensitivity reports and being insistent that preoperative urine cultures are confirmed as sterile.(82)

3- Subcapsular Hematoma and Collateral Injury

One of the major causes of subcapsular hematoma in children is the use of an excessive number of shockwaves and/or unnecessarily high energy levels in order to try to fragment the stone in a single session. It is always better to stop and re-treat. Successive ESWL sessions should have an interval of at least 10–14 days. Calcium channel blockers, various antioxidants, and free-radical scavengers have been used to decrease these injuries especially in retreatment cases(94)
Gradual increasing of the pressure and slower rate of shocks are recommended to decrease the incidence of hematoma .

Results of ESWL in children

In general, the criteria for the treatment of urolithiasis in children are the same as those for adults. Today, extracorporeal shock wave lithotripsy (ESWL) is the method of choice in the treatment of most pediatric urinary stones. Stone-free rates between 67% and 93% at short-term follow-up, and 57% to 92% at long-term follow-up, have proven the efficacy of ESWL treatment in children.
Nevertheless, the demand for auxiliary measures still remains. In order to achieve the most beneficial success rates under low complications, it is advisable to perform this type of ESWL in centers that claim the experience necessary for ESWL and endourological measures in children.
(95)
in earlier days, the chief aim of stone surgery was to achieve a complete stone-free condition. Although this does not quite apply to ESWL, long-term success depends on the stone-free rate. Complete stone disintegration is achieved in 57% to 97% of cases , but this is still only a prerequisite for a stone-free condition. In contrast to adults, more effective disintegration by ESWL, and subsequent swifter and uncomplicated passage of larger fragments, has frequently been observed in children (96, 97).
The reasons for this could be that, in general, the dwelling time of stones in children is only short, the shock wave effect is stronger in children, and they also quickly recuperate (97) from this method of treatment. Thirty-seven to 52% of the children were stone free at discharge .(98-100) and the stone-free rate was between 57% and 97% 3 months after ESWL.

Study	Number of patients	Stone free rate after 3 – 6 months	Auxiliary procedures
Nijman et al., 1989(101)	73	79	-
Vandeursen et al., 1992(102)	28	90.5	-
Moreno et al., 1992(103)	14	71.4	14.28
Zanetti et al., 1993(104)	14	92.8	-
Moazam et al., 1994(105)	83	82	-
Myers et al., 1995(106)	446	Kidney : 67 Ureter : 91	Kidney : 36.3 Ureter : 17.7
Oktay et al., 1998(107)	67	88.6	9

Only five reports (95, 99-101, 108) in a long-term follow-up, between 18 and 46 months after ESWL in children showed A general recurrence rate of 2% to 44% has been reported for children after ESWL (53). the residual fragment rate is between 23% and 33%(95, 100) In contrast, the recurrence rate in adults is only between 8% and 10%, and residual stone growth averages 22% .
Complex etiology, a high rate of metabolism disturbances, anatomical changes, and urinary tract infection, are given as reasons for the higher rate of residual stone growth in children (53, 108) . Seventy-two percent of our small patients were stone-free after an average of 46 months; 5/42 (13.7%) of these developed recurring stones. Residual stone growth progressed in all 9 children who were not stone-free after 3 months. Either urinary tract infection, metabolic disturbance or an anatomical change were detected in those children suffering from stone recurrence or residual stone growth . (95)

Percutaneous Nephrolithotomy (PCNL)

During the past 10 years, miniaturization of endoscopic equipment and refinements in technique have led to the adoption of ureteroscopic and percutaneous techniques for ureteral and upper tract calculi in children that previously had only been applied to adult populations (109) .
Initially urologists were reluctant to perform PCNL in children because of concerns regarding the use of large instruments in

pediatric kidneys, parenchymal damage and the associated effects on renal function, radiation exposure with fluoroscopy, and the risks of major complications, including sepsis and bleeding. With increasing experience, however, PCNL has replaced open surgical techniques for the management of large stone burdens >2 cm with efficacy and complication rates similar to those of the adult population.

The earliest pediatric PCNL series were performed using standard adult-sized instruments. In 1985, Woodside and associates (110) reported a series of seven patients (age range 5–18 years) who were rendered stone free without complications using adult percutaneous techniques and equipment. Mor and colleagues (111) described another series using adult size instruments for PCNL in 25 children, demonstrating the technical feasibility of PCNL in children. There was continued hesitation among urologists to use this technique, however, because of concerns for renal damage from the use of large instruments in relatively small kidneys.

Based on this concern, PCNL was initially avoided in children younger than 5 years of age. Later, multiple PCNL series in young children indicated that age is not necessarily the issue, because safety and efficacy of PCNL in children as young as 3 months was established (11, 112-114)

The mini-perc technique is believed to have several advantages, including decreased blood loss, increased maneuverability, and shorter hospital stay. The risk of bleeding complications has been shown to be related to the number and caliber of used tracts, and in the series by Jackman and associates (115) 3 no transfusions were needed.

There are limitations, however, to the mini-perc technique, and access to pediatric size instruments is mandatory. In addition, the stone must be fragmented into small enough pieces to fit through a small diameter sheath, which can lead to prolonged operative times. Therefore, this technique may not be indicated in cases with large stone burden, and its usefulness may be questionable in kidneys with thin parenchyma .

Investigations regarding the risk of renal damage in pediatric patients who were treated with PCNL have revealed that there is no significant risk of renal functional loss. Mor and coworkers (111) performed radioisotope scans on 10 children before and after PCNL and found no change in differential function and no evidence of significant scarring. In fact, Dwaba and associates (116) found that there was a significant increase in glomerular filtration rate after PCNL in 65 children with no renal scarring after long-term follow-up.

Technologic advancement and miniaturization of instruments have changed the management of pediatric stone disease. SWL has been the preferred method of management of most stones in children. Certain factors, however, limit the success of SWL, including large stones, complex or multiple stones, large lower pole stones, cystine stones, and anomalous kidneys (117) .

In these circumstances, multiple sessions may be needed, pre-SWL stent placement may be necessary, and the potential risk of renal damage from repeated sessions must be considered. Recent advancements in instrumentation, such as smaller nephroscopes (15F–18F), more efficient energy sources for intracorporeal lithotripsy, including holmium: yttrium-aluminum-garnet (YAG) laser, and smaller pneumatic lithoclast and ultrasound probes have greatly facilitated percutaneous treatment techniques (118)

In the past, PCNL was reserved only for cases of failed ESWL . More recently, it is also being used as primary treatment in patients with large upper tract stone burden (>1.5 cm), lower pole calculi >1 cm, concurrent anatomic abnormalities impairing urinary drainage, and stone clearance, including ureteropelvic junction obstruction, ureteroenteral anastomotic strictures, infundibular stenosis, or stones in a caliceal diverticulum, and in cases of known cystine or struvite composition. Despite widespread adoption, however, there is currently no international consensus on the indications for PCNL in children . (118)

Complications of PCNL

1- Bleeding hemorrhagic complications

The PCNL-related bleeding can be divided into perioperative, immediate postoperative, and delayed bleeding. Bleeding during PCNL is generally common but is rarely clinical significant requiring transfusion. Transfusion rates ranging between 0 and 20 % have been documented with an overall of 7 % calculated in a recent systematic review (119)

Perioperative bleeding is usually caused after rupture of parenchymal vessels upon track dilation or kidney tear during excessive nephrostomy sheath bending. Such hemorrhage should not be considered as a complication unless requiring transfusion or quitting the operation. Aborting PCNL due to excessive bleeding has been documented in only 0.2 % of cases since nephrostomy sheath tends to tamponade most of the track-related hemorrhages while moving sheath close to the wall of the system improves vision and allows the safe accomplishment of the procedure(120)

Traditionally, entering pelvicalyceal system through the tip of the calyx within Brodel's avascular plane is considered the route causing less bleeding. In addition, the use of a flexible nephroscope to access distant calyces avoiding overbending of the access sheath is advisable to avoid significant bleeding. Predicting factors for hemorrhagic complications are multiple punctures, dilation with a large access sheath, large stones (staghorn), and long operative time (12, 121)

Rupture of main renal vessels by accidental dilation is a very unusual complication (0.4 %) that can be life-threatening and can require emergency nephrectomy. To avoid such a mishap, aspiration of urine before track dilation should always be performed to verify correct positioning of the needle in the system. In case of blood aspiration, dilation should be aborted and the needle should be withdrawn and repositioned. Additionally, dilation should always be performed over a stiff guidewire coiled safely within the system or advanced down the ureter. The latter direct dilation forces away from the hilum in case of an abrupt insertion of a dilator. (122)

Bleeding in the immediate postoperative period is usually noted immediately after nephrostomy sheath removal and is caused by bleeding of either parenchymal renal vessels or by vessels located in the nehrpocutaneous track (i.e., subcostal vessels).

Parenchymal bleeding is evidenced by blood drain within the nephrostomy tube and can be managed by the elevation of

nephrostomy drain over patient's level or by clamping the tube for a few minutes to allow clot formation within the system. Minor bleeding at this point should not be considered as a complication unless it cannot be controlled easily and/or require transfusion. Track bleeding, evidenced by bleeding around the nephrostomy tube, can be easily managed by external pressure to the cutaneous orifice of the fistula. Use of additional hemostatic agents injected through the incision is seldom required. (122)

2 - fever/sepsis

Fever is a common postoperative complication of PCNL with an overall incidence of 10.8 % (119) Conservative management with a short course of intravenous antibiotics is usually effective in the majority of cases. Preoperative bacteriuria is a known cause of infectious complications in stone disease and should be preoperatively identified via urine cultures and treated accordingly (123)

In patients with preoperative sterile urine, duration of surgery and amount of irrigation fluid used have been identified as risk factors for postoperative fever (124)

In contrast to transient fever, urosepsis occurs rarely in modern series but can have deleterious effects for the patient (119, 124) Predisposing factors for postoperative sepsis include preoperative bacteriuria, neurogenic bladder dysfunction, renal anomalies, high intrarenal pressure during the procedure, and prolonged duration of surgery (125)

3 – Thoracic complications

The presence of pleura within the route of percutaneous puncture will most likely result in some kind of perioperative pleural complications including mild pneumothorax, hydrothorax, and rarely hemothorax or urinothorax.

Such complications are generally uncommon (<2 % of the reported cases) and as expected are more often in punctures above the 12th rib (126). Munver et al. (127) reported 8 intrathoracic complications after 240 PCNL of which seven developed after a supracostal puncture. Similarly, Lojanapiwat et al. (128) in a series of 464 patients documented the presence of hydrothorax in 15.3 % of patients treated with a supra-costal puncture as opposed to 1.4 % in cases operated via a subcostal access. Of notice, only 9 out of 26 patients required intercostals drainage. As a result, supra-costal accesses above 12th rib should not be preferred when other puncture options are available.(129)

4- Urine leak from nephrocutaneous fistula/peripheral obstruction

Normally, once nephrostomy drain is removed, nephrocutaneous fistula will drain some urine until the entrance to pelvicalyceal system heals. Urine leak from nephrocutaneous fistula is generally more prominent when large-bore nephrostomy catheters have been used , when catheterization time is long, and when no internal ureteral drainage (i.e., pigtail) has been used (130). An incidence between 1.5 and 3 % of persistent urine leak has been reported in the literature (120, 131)

In a study performed using the Clavien grading system, urine leakage from the flank for <12 h was considered a grade 2 complication, whereas implementation of a double-J-stent due to urine leakage lasting longer than 24 h was considered a grade 3a complication. Urine leakage that prolongs hospital stay is the most common type of group 3a complication (120) In another study, urine leakage lasting >1 week was detected in 1.5% of cases that underwent PCNL . prolonged complication duration leads to delayed discharge from hospital. In our study, we did not observe urinary leakage >1 week because persistent urine leakage after 48 h was managed with a double-J-stent.

In a study of post-PCNL complications, urine leakage lasting <24 h was detected in 15% of patients (132). However, it was concluded that ignorance and/or inadequate data records might have caused an underestimation of minor complications in that retrospective study

The majority of cases with persistent urine leak from nephrocutaneous fistula should be managed by the insertion of a double-J ureteral stent that resolves the symptom and radiologic assessment of obstruction.

5 - Rupture of the pelvicalyceal system

Literally, every PCNL puncture and access dilation is a form of rupture of the pelvicalyceal system. In addition, during wire and access sheath negotiation as well as lithotripsy maneuvers, a tear of the collecting system might be evident. Surgeon's aim was to access the system during lithotripsy in a controlled and safe way to avoid a major rupture that will lead to postoperative urinoma formation. According to our knowledge, in contrast to iatrogenic injuries of the ureter, currently there is no grading system for injuries of the kidney after PCNL.

Thus, such injuries are qualified as mild or severe by the need of postoperative drain or not. Still, the majority of pelvicalyceal tears will heal uneventfully if adequately drained postoperatively. Accordingly, although collecting system injury has been reported in up to 5.2 % of cases, urinoma formation is documented only in 0.2 % of cases(119, 133).

Based on the above, perioperative extravasation of contrast is not necessarily associated with any adverse outcome and only urinoma formation should be regarded as a complication.

6 - Organ injury

Puncture of irrelevant intra-abdominal organs such as bowel, spleen, and liver is a rare (<0.5 % of the reported cases) but significant complication of PCNL (122) Colonic perforation is more common in left-side procedures, in lower calyceal punctures, in elderly patients, and in patients with horseshoe kidneys or chronic colonic distension (134) .

Preoperative CT represents the only method to assure the absence of retroperitoneal colon within the route of desired puncture and avoid such a devastating complication. Intraoperatively, colonic injury can be detected by the opacification of the bowel with the injected contrast material through the nephrostomy tube . However, a delayed diagnosis after a CT performed due to postoperative fever or signs of peritonitis is also common. The majority of cases are successfully managed conservatively (134) The first step in the treatment of colon perforation should be based on conservative management. This includes separating the

nephrocolic communication, including double J stent insertion for adequate urinary drainage and retraction of the nephrostomy tube from the pelvicalicial system into the colon as a percutaneous colostomy tube. Other conservative strategies include broad spectrum antibiotics covering gram negative and anaerobic bacteria and parenteral nutrition. Occasionally, surgery is indicated in intraperitoneal perforation, peritonitis, sepsis and persistent nephrocutaneous fistula.(135, 136) In the recent years, some researchers have shown optimal primary results of fibrin glue application to correct persistent nephrocutaneous fistulas in some cases (137) .

In liver injuries that have occurred during percutaneous access, hemostasis and vascular sealing can be achieved using fibrin products if the patient is hemodynamically stable. Stepwise withdrawal of the nephrostomy tube is particularly important. Exploratory intervention is needed in rare circumstances, and the urologists should adopt a conservative approach (138)

The key points in the management of splenic injury are early diagnosis and determination of the most appropriate treatment strategy that will result in lower morbidity and mortality. The patients may need urgent laparotomy and splenectomy. Conservative methods, however, including close monitoring, use of coagulant agents, and delaying the withdrawal of the nephrostomy catheter, can be used in hemodynamically stable patients. The preparation of the patient for urgent splenectomy is of vital importance if conservative methods fail . (139)

7 - Neurologic complication

Neurologic complications after PCNL are rarely encountered, and the reported series are rather limited. (140).

8 – Pain

Postoperative pain is not and should not be regarded as a complication of PCNL but rather as an expected consequence of the approach. Still, significant variations in pain and analgesic requirements during immediate postoperative period among different PCNL techniques have been reported.

According to the recent studies, important role in reducing postoperative pain lies on the minimal use of nephrostomy tubes and ureteral stents in such situation tubeless PCNL are characterized by shorter hospitalization and lower analgesic consumption than the standard PCNL (141, 142)

9 – Death

Death as a direct consequence of PCNL is very rare complication. Unsal et al.(143) documented a 0.2 % mortality rate (three patients died) reviewing a cohort of 1,406 cases. Importantly, they revealed a direct association of life-threatening complication rates with Charlson Comorbidity Index (CCI). Life-threatening complications were developed in 2.9 % of patients with CCI 0, in 7.6 % of patients with CCI 1, and in 21.6 % of patients with CCI 2. Based on the above, it is evident that death is most likely a result in patients not fit to overcome potential PCNL complications such as bleeding or sepsis, and more conservative treatment options should be considered in very high risk patients.

Results of PCNL in children

In 56 children (mean age 9.1 years) with a mean stone burden of 337.5 mm2 ,Desai and coworkers reported a stone-free rate of 89.8% using electrohydaulic lithotripsy (EHL) through a 14F nephroscope and a 20–24 F sheath. Of these, 61% needed multiple tracts, and 45% were staged procedures. Findings demonstrated that the number and size of tracts were significantly associated with postoperative hemoglobin decrease (mean 1.9 g=dL) and overall transfusion rate (14%). (112)

In 52 children with a mean age of 7.9 years and a mean stone burden of 282 mm2 , Zeren and associates8 reported a 87% stone-free rate using ultrasound and EHL for fragmentation and tract dilation from 18F to 30F. Complications included postoperative fever (30%) and need for transfusion (24%). Transfusion was associated with operative time, sheath size, and stone burden. (11)

In 135 children who were aged 8.9 years with a mean stone burden of 507 mm2 , Salah and colleagues (144) reported a 98.5% stone-free rate using ultrasound through a 26F nephroscope. Complications were low (8% urine leak rate and 0.7% transfusion rate), with only one patient needing a second procedure. In a recent series of 46 children with a mean stone burden of 332 mm2 , Bilen and coworkers (145) reported an 88% stone-free rate using EHL, ultrasound, and the holmium laser .

In an effort to reduce the number of tracts and associated morbidity, some centers have chosen to follow primary PCNL with adjunctive SWL therapy to clear residual stone fragments. In a small series of 29 children with a mean age of 3.8 years and a mean stone burden of 2.4 cm, Mahmud and associates (146) reported a 60% stone-free rate after PCNL monotherapy using EHL through a 17F angled nephroscope. Only one tract was used in all patients, and after SWL sandwich therapy, the stone-free rate increased to 100%.

In a larger series of 169 children with a mean stone burden of 3.1 cm, Samad and colleagues reported a 59% monotherapy stone-free rate with 96% of cases performed through a single tract. Approximately one third (34.5%) of primary failures were treated with SWL; the cumulative stone-free rate in all patients was 93.8% with a 3.6% transfusion rate. When stratified by age, anatomy, bilaterality, and renal function, stone-free outcomes were equivalent in all groups. The decision to follow PCNL with SWL is related to operator experience with percutaneous technique and available technology. It is our preference to perform second-look nephroscopy through the original tract to ensure stone-free status during the initial hospital admission rather than progress to SWL sandwich therapy (147)

Between January 1997 and March 2003, 40 boys and 25 girls with renal calculi were treated with PCNL (116) documented stone-free rate in our series is within the previously reported range of 67% to 100% , Their findings confirm the observations of Goldwasser et al who showed that stone extent and size are major factors affecting the success rate (148) . success rate in children with single stones in the renal pelvis was as high as 100% after a single session of PCNL. In cases with a high stone burden PCNL can be integrated with SWL in a planned combined approach .

Some do not recommend PCNL in children younger than 8 years for fear of renal damage resulting from the relatively large

endourological equipment (149).
However, others reported that this treatment can be safely done in children older than 5 years.(150) Moreover, Callaway et al successfully performed PCNL in 8 patients 19 months to 5 years old with no increased complication rate.(114) In our series the youngest child treated with PCNL was 9 months-old and 27 children (41.5%) were younger than 5 years.
Most studies demonstrate minimal scar formation and insignificant loss of renal function (116, 149, 151) The latter observation is further confirmed by the present series as none of their patients studied with DMSA renal scan had renal scarring, and all except 1 experienced improvement or at least stabilization of renal function on DTPA scan after PCNL

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