

# Long-term effects of pediatric extracorporeal shockwave lithotripsy on renal function

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**Introduction:** Extracorporeal shock wave lithotripsy (ESWL) is a well-known and successful treatment modality. In addition, it can be used in premature infants. ESWL is used to treat kidney and ureter stones in children. However, although it is a preferred noninvasive treatment in that setting, there is debate about its long-term effects on growing kidneys in children.

**Objectives:** To investigate the long-term effects of pediatric ESWL on renal function in light of updated literature.

**Methods:** PubMed and Medline were searched for studies on ESWL in a pediatric population with keywords including efficacy, child, kidney calculi, ureter calculi, lithotripsy, injury, vascular trauma, and shock waves. The research was limited to the English literature during a period from 1980 to 2014. In total, 3,000 articles were evaluated, but only 151 papers were considered. Only the manuscripts directly related to the reviewed subjects were included in the current study.

**Results:** However, the acute effects of ESWL in kidney are well-described. Although there are limited studies on the long-term effects of ESWL in children, there is a widespread opinion that ESWL is not affecting renal functions in the long-term.

**Conclusion:** ESWL is a safe, effective, and noninvasive treatment option in children. Although ESWL can cause some acute effects in the kidney, there is no long-term effect on the growing kidneys of children.

**Keywords:** child, lithotripsy, nephrolithiasis, renal injury, vascular trauma

## Introduction

Since extra corporeal shock wave lithotripsy (ESWL) was introduced, noninvasive treatment of urinary stone disease jumped an age.<sup>1</sup> After these developments, Newman et al reported successful results of ESWL in the pediatric population.<sup>2</sup> The incidence of urolithiasis in the pediatric age group is 2%–3% of all stone diseases.<sup>3</sup> However, pediatric stone disease is endemic in Turkey, Pakistan, and some South Asian, African, and South American countries.<sup>4</sup> Recently, ESWL has been used worldwide with well-known advantages such as its high efficiency and ease of use in children.<sup>5</sup>

Both of the mechanical and dynamic effects in ESWL consist of effective stone fragmentation. However, the cavitation effect is the most important effect of ESWL, with shear and spalling effects being the other parts of the mechanism. Cavitation bubble collapse is responsible for stone fragmentation, which can create destructive forces. There are published reports in the literature that these effects of ESWL also can harm thin-walled vessels and surrounding kidney tissues.<sup>6,7</sup> These acute effects cause hemorrhage, release some cytokines/inflammatory cellular mediators, and cause infiltration of

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tissues by inflammatory response cells, which result in well-defined short-term complications. Animal studies have proved these adverse effects of ESWL in kidneys.<sup>8,9</sup> In addition, these studies showed histological changes in glomerular epithelium and interstitial cells, as well as an apoptotic effect on renal tubular cells.<sup>8,9</sup> However, ESWL has not caused long-term renal lesions identifiable by a dimercaptosuccinic acid renal scan up to now.<sup>10</sup> Goel et al reported there was not significant functional differentiation measured by the glomerular filtration rate (GFR) of the growing kidney.<sup>11</sup> The ESWL treatment has well-defined acute effects in kidney, although published reports showed normal GFR and scintigraphy. On the basis of these conflicting reports in the literature, we performed the present study to introduce the accurate long-term effects of ESWL on renal function in the pediatric population.

## Study design

PubMed and Medline were searched for studies on ESWL in the pediatric population with keywords including efficacy, child, kidney calculi, ureter calculi, lithotripsy, injury, vascular trauma, and shock waves. The research was limited to English-language literature from 1980 to 2014. In total, 3,000 articles were evaluated but only 151 papers were considered. Only the manuscripts directly related to the reviewed subjects were included in the current study.

## Current indications for SWL and success rate

ESWL is the preferred treatment for small upper urinary tract calculi smaller than 20 mm in children because of its ease of application and efficacy.<sup>13,14</sup> More effective disintegration of even larger stones, together with swifter and uncomplicated discharge of larger fragments, can be achieved in children by ESWL. As a consequence, ESWL can be indicated in children with a larger stone volume, and the placement of a ureteral stent before or after ESWL is generally unnecessary.<sup>14</sup> The stone-free rate of ESWL in children is between 37% and 52% in the short-term.<sup>15</sup> In the long-term, these rates increase to 57% and 100%.<sup>16</sup> However, stone clearance rate by ESWL in children is easier than in adults, and clinicians should be aware of this on acute complications.<sup>17</sup>

## Technical aspects of ESWL in children

The patient should be evaluated, in detail, before treatment. Kidney ureter and bladder X-ray, intravenous pyelography, or computed tomography should be checked for targeted stones. Children must not have a urinary tract infection or coagulation defect before or during ESWL.

An ESWL session take approximately half an hour and focuses on the stone in a supine position. The patient should not move during ESWL. When the child is not old enough to understand our instructions, general anesthesia is needed (1.5 mg/kg ketamine and 0.05 mg/kg midazolam are preferred).<sup>18</sup> Small children also may need some suspension under the body, and the water cushion also should be adjusted.

The power of the shock wave should be started from the lowest level (14 kV) and may be escalated to the maximum level (20 kV) until fragmentation is observed in fluoroscopy. The number of shock waves should be limited to either the fragmentation observed or a maximum of 1,000 waves per session for children younger than 5 years and to fragmentation or a maximum of 2,500 waves per session for older children. Pulse frequency may be 70 pulses per minute.

After the procedure, patients should be kept under observation until they awaken. Analgesics are usually prescribed when the patient is discharged. It is very important to inform parents about possible hematuria and stone fragments during micturition. In addition, parents should be alert to fever and colic pain.

After ESWL treatments, ultrasonography and/or kidney ureter and bladder X-ray can be used for follow-up. Retreatment by ESWL may be used in case the residual stone size was larger than 4 mm. A maximum of 3 sessions should be performed. When the stone is not fragmented, the other treatment modalities come into question, such as percutaneous nephrolithotomy.<sup>19</sup>

## Acute effects of ESWL

The acute effects of ESWL are well-defined in the literature.<sup>7</sup> The acute trauma is localized in the area of the stone. More injuries are inevitable inside than outside the kidney. It is expected that all children will have hematuria after ESWL. Detailed morphological studies in animals showed that ESWL can rupture blood vessels and can damage the surrounding renal tubules.<sup>20,21</sup> In these studies, the researchers found that there were torn vessels with platelet aggregation and from vacuolization to complete necrosis of the endothelium. Damaged renal corpuscles in the Bowman capsule and damage to mesangial cells also could be seen. Renal tubules contained blood cell casts, and tubular epithelial cells could show characteristics of ischemia. Kaude et al reported hematomas in 29% of the patients after ESWL in magnetic resonance imaging.<sup>22</sup> In addition, there have been some published reports on severe acute injury of ESWL in kidney, such as subcapsular or perineal bleeding.<sup>23,24</sup> However, these acute complications can be formed after

ESWL, and Krishnamurthi and Stroom reported that most hematomas can resolve within weeks without long-term effects.<sup>25</sup> Similarly, Aksoy et al reported spontaneous subcapsular hematoma after ESWL in children.<sup>26</sup> In a recent series, including 128 pediatric ESWL, we reported around 44% hematuria, with 17.8% complications.<sup>17</sup> However, hematuria disappeared up to 1 week after ESWL, and most serious complications were in children with metabolic disorders.

In contrast, when there is a problem focusing on the stone, there can be some adverse effects, such as colon perforation, rupture in hepatic artery, hepatic hematoma, pneumothorax, rupture of spleen, acute necrotizing pancreatitis, urinothorax, and rupture of abdominal aorta.<sup>27–35</sup>

In summary, ESWL may lead to some acute effects in and around the kidney, but these are usually temporary, without long-term effects. In addition, to avoid extreme adverse effects, clinicians should be alert to complications, and they should not miss the focused stones during ESWL. The acute adverse effects of ESWL are shown in Table 1.

## Possible adverse effects of ESWL in long-term animal studies

To date, there has not been performed any study that can fully show the long-term effects of ESWL on kidney. Newman et al reported dose-dependent renal parenchymal fibrosis in dogs,<sup>20</sup> and this formation was also proven in rabbits by Morris et al.<sup>36</sup>

Lifshitz et al reported that alterations of growth rate in pediatric kidneys treated with ESWL were detected, but the real reasons for this were unknown,<sup>37</sup> and Claro et al reported that there was no long-term effect on renal function on growing kidneys of younger immature rats after ESWL.<sup>38</sup>

## Clinical observation

Despite there being some suspicious long-term clinical effects of ESWL in adults, Fayad et al reported that ESWL had no adverse effect on the kidney of growing children.<sup>18</sup> They

performed renal scintigraphy with dimercapto-succinic acid and GFR 6 months after ESWL. There were no significant differences in GFR and no renal scar in dimercapto-succinic acid. Vljaković et al also reported no significant changes in GFR in the kidneys of growing children.<sup>39</sup> Griffin et al reported their 20 years of experience on ESWL in pediatric stone disease and concluded that ESWL did not seem to cause long-term alterations in renal function or the development of permanent renal scars.<sup>40</sup>

In addition, McCullough et al reported that although microscopic hemorrhages were seen in the ovaries examined immediately after shock wave treatment, the number of follicles did not change in female young rats.<sup>41</sup>

In contrast, in the published literature, ESWL had some adverse effects in adults in the long-term. Krambeck et al reported an increased risk for diabetes mellitus and hypertension (HTN) after ESWL in the long-term,<sup>42</sup> but El-Nahas et al criticize them for performing their long-term follow-up by mailed questionnaire and because there was no comparison with a normal population to estimate the relative risks.<sup>43</sup> As El Nahas et al reported, the Mayo Clinic team found that ESWL was not associated with diabetes mellitus<sup>44</sup> and HTN<sup>45</sup> in the long-term.<sup>43</sup>

Frick et al reported HTN after ESWL in children with polycystic kidneys in the long-term.<sup>46</sup> This was in line with the results of Krambeck et al;<sup>42</sup> however, it was in contrast to El Nahas et al.<sup>45</sup> It seems there is need to perform multicenter, long follow-up studies to accurately investigate the long-term effects of EWSL for HTN in children.

In summary, it seems ESWL does not affect kidney functions in the growing kidneys of children in the long-term.

## Increasing the effectiveness of ESWL without adverse effects

Experimental studies showed that renal injury in ESWL is dependent on the number of shock waves, rate of shock delivery, and power setting of the lithotripter.<sup>47–50</sup> McAteer and Evan suggested that 30 shock waves in a minute had dramatic protective effects on kidney.<sup>7</sup>

In addition, some comorbidities may increase injury after ESWL, such as having a coagulation defect.<sup>51,52</sup>

Lithotripters come into question in the discussion of the effectiveness of devices. Pishchalnikov et al reported the assessments of renal injury by a LithoGold LG-380 (MTS Europe GmbH, Konstanz, Germany) lithotripter in an animal study, and they reported minimum acute injury.<sup>53</sup> Connors et al reported a low injury effect of MODULITH® SLX (Karl Storz Lithotripsy-America, Inc., Kennesaw, GA,

**Table 1** Acute effects of extracorporeal shock wave lithotripsy

Effect
Focal hemorrhage
Rupture of small veins
Extravasation and pooling of blood
Necrosis in vascular wall
Disintegration in podocytes and mesangial cells
Blood within Bowman's space and renal tubules
Ischemic changes
Infiltration by inflammatory cells

USA) in an experimental study.<sup>54</sup> These findings are important, particularly with regard to children. Thus, more studies for improving the less-acute effective ESWL devices have been needed.

Urinary stone management can be easily performed by ESWL; the indications were discussed earlier. The other treatment options for kidney stones are percutaneous removal and open surgery.<sup>13</sup> The complex stones and children who do not benefit from ESWL can undergo percutaneous endoscopic surgery. European guidelines on pediatrics suggested that young age with large stones and orthopedic deformities that limit positioning for endoscopic surgery are some of the indications for open surgery.<sup>13</sup> Nevertheless, most of the stones can be managed by ESWL in childhood.

## Conclusion

ESWL is safe and curative for urolithiasis in children, but there is no doubt that ESWL can lead to acute kidney injury. According to the literature, there is no proven truth about long-term adverse effects of ESWL in the growing kidneys of children. However, ESWL did not seem guilty of kidney damage in children in the long-term, and there is a need for more multicentered studies on this issue.

## Disclosure

The authors report no conflicts of interest in this work.

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