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Invited review

Effects of extracorporeal shock wave lithotripsy (ESWL) on renal tissue

A review

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Introduction

Electrohydraulic shockwaves represent a highly effective way of desintegrating stones in the urinary and also in the biliary tract. ESWL may also result in adverse effects on soft tissues adjacent to the stone.

Shockwaves exert their effect at the border of materials of different densities. The great difference between the density of the kidney stone and the surrounding tissue is one of the factors that contribute to stone desintegration, the exact mechansim of which is yet unknown. But shockwaves also exert an effect on the surrounding tissue.

Side effects of ESWL for renal lithiasis include hemorrhage, edema, tubular necrosis and subsequent fibrosis in the kidney. This form of renal trauma is associated with a sometimes permanent decrease in renal functions of the treated kidney. ESWL is also associated with the onset of hypertension, which may occur immediately of be delayed be several weeks or months.

Chaussy et al. [5] reported a series of 206 cases of upper urinary tract calculi treated with a total of 221 shockwave applications. Renal function, as determined by 131-I hippuran clearance before and after external shockwave treatment showed no significant changes in renal function and no side effects other than pain were seen.

The author also reported [6] that the major renal complication was ureteral obstruction caused by the desintegrated stone fragments. Another important complication was subcapsular hematoma. Gross hematuria was observed in all cases. It was concluded that the renal pelvis and ureter might have been injured indirectly by the stone fragments or directly by shockwave exposure. It was also stated that kidney stones were desintegrated by ESWL without any pathological changes in the kidney or surrounding tissue. These conclusions are based on experiments in dogs [7].

Despite the low rate of side effects reported by Chaussy in his early reports, there is now growing awareness that ESWL can induce serious side effects. Several studies indicate that tissue damage occurs during ESWL. The most observable and constantly noted effect is gross hematuria [6, 13] during the treatment, that generally disappears within 12 h after treatment. This strongly suggests that damage occurs in the urinary tract during ESWL treatment.

Morphological changes (Table 1)

Several studies have estimated that 63% to 85% of patients suffer substantial renal injury during ESWL [2, 13, 23]. These traumata can be detected by means of magnetic resonance imaging (MRI) and quantitative radionuclide renography. The two most common side effects seen after ESWL are hemorrhage and edema within and around the kidney. Perirenal and subcapsular fluid collection (blood or urine) have been noticed in 24 to 32% of the treated patients. The subcapsular fluid accumulation is reabsorbed within 6 weeks, the perirenal fluid within a few days [13]. The changes in the perinephric tissue are due to an increase in the number of septal strands and a thickening of Gerota's fascia, reflecting edema outlining the perirenal tissues. Probably these changes can lead to compression of the kidney, resulting in an alteration in renal hemodynamics [23].

In a recent study [15] it was found that patients with pre-existing hypertension are more likely to develop perinephric hematomas. In particular, those patients having unsatisfactory control of their hypertension at the time of treatment had the highest incidence of hematomas. In this study there was also an evaluation of the number of shockwaves and applied energy (voltage) as potential risk factor, but no correlation was found with the incidence of hematomas.

Table 1. Morphological changes in the kidney after ESWL

	No. of references
• Hematuria	[6, 13]
• Perirenal and subcapsular hematomas	[2, 7, 12, 13, 15, 16, 23, 27]
• Hemorrhage and edema within and around the kidney	[2, 13, 23]
• Perirenal and subcapsular fluid collection	[13, 23]
• Kidney enlargement	[10, 13, 23]
• Loss of corticomedullary demarcation	[10, 13]
• Rupture and congestion of capillaries	[11]
• Patchy fibrosis in the submucosa, muscle layer and perinephric fat	[11]
• Chronic interstitial and tubular scarring (?)	[16]

Table 2. Functional changes of the kidney after ESWL

	No. of references
• Transient increase of cellular enzymes in blood and urine (N-acetyl glucosaminidase, beta-galactosidase)	[1, 14, 17, 24]
• Transient proteinuria	[9, 26]
• Enhanced excretion of kidney-derived antigens in the urine	[25]
• Transient changes in glomerular filtration rate	[9]
• Decrease in effective plasma flow in the treated kidney	[13, 28]
• New onset of hypertension	[13, 16, 20, 28]
• Worsening of hypertension	[15, 20]

In contrast Jocham [12] found that subcapsular bleeding was noted uniformly only after a large number of shocks. In these cases any diminished function of the treated kidney was found to be temporary and completely reversible. He also showed that using a higher shockwave energy subcapsular bleeding was noted and scintigraphic analysis of kidney function showed reduced function temporarily. Therefore the Munich group recommends using less that 2,000 shocks at 18 KV for treatment of stones in single kidneys.

Kidney enlargement and a loss of cortico medullary demarcation are other renal changes often seen after ESWL [10, 13, 23]. These changes suggest damage to either the nephron or the renal vasculature sufficient to cause extravasation of blood and urine into the extracellular space. Such edema could cause compression of structures within the kidney, resulting in chronic interstitial and tubular scarring [16].

Histopathological study of the perinephric fat early after ESWL by Hegazy [11] showed marked congestion and rupture of capillaries with small foci of hemorraghe. The pelvic and ureteric walls revealed focal disruption of the urothelium. The same histopathological study one month after ESWL therapy showed patchy fibrosis and organisation in the submucosa, the muscle layer and perinephric fat.

Functional changes (Table 2)

Several authors analysed the side effects of shockwave exposure by measuring chemical substances including cellular enzymes in blood and urine. Elevations in bilirubin, lactic dehydrogenase, creatine phophokinase, glutamic oxaloacetic transaminase, N-acetyl-beta-glucosaminidase, beta-galactosidase and gamma-glutamyl-transpeptidase were reported [1, 14, 17, 24]. This may indicate damage to the kidney and adjacent tissues (liver skeletal muscle) by shockwave exposure or local obstruction. Most of the elevated marker substances begin to fall within 3 to 7 days and are normal at 3 months.

Steinmann and associates [26] assessed renal damage after ESWL by measuring urinary proteins. They interpreted increase of large molecular urinary proteins (albumin and IgG) as alteration of glomerular permeability. Small molecule proteins (beta-2-microglobuline and Tamm-Horsfall-Protein) were thought not to be reabsorbed adequately by the tubular cells due to functional changes resulting from exposure to shockwaves. All these pathological protein elevations were limited in time and were normal again after 4 days.

In an attempt to study epithelial cell alteration or damage caused by shockwave treatment, Schultze [25]

examined the excretion of urinary antigens determined by tests using monoclonal antibodies specific for antigens in kidney epithelial cells. Increase of excretion of distal tubular antigens was first seen 12 to 24 h after ESWL and reached a four-fold pretreatment level on the fourth post ESWL day. This indicates that shock wave treatment causes alteration on the level of distal tubular epithelium.

The renal damage ranges from mild contusions localised in the parenchyma to large hematomas associated with severe bleeding, [2, 13, 23]. Gilbert [9] evaluated several basic physiological parameters: creatinine clearance, fractional sodium excretion, protein excretion and urine osmolality in an attempt to quantify changes in renal function. His data suggest that with ESWL treatment nephrotic range proteinuria occurs to a greater extent than can be accounted for by the hematuria, but returns to normal values within 3 to 6 months after treatment without a change in glomerular filtration rate. Glomerular filtration rate increases after ESWL in patients whose kidneys were obstructed before therapy. Treated kidneys appear to maintain the ability to dilute urine and to conserve sodium.

Kaude et al. [13] observed different evidence of renal damage. They found a partial to total parenchymal obstruction not associated with ureteral blockage and a decrease in the percentage of effective plasma flow in the treated kidney. They observed some immediate decrease in effective plasma flow, measured by Hippuran renal scans, in 30% of the kidneys treated with ESWL. The authors consider retention of radioactivity and the morphological and functional changes seen, compatible with renal contusion resulting in edema and hemorrhage or both.

Williams [28] examined 21 patients 17 to 21 months after ESWL treatment for renal function changes. Quantitative radionuclide renography showed a statistically significant decrease in the percentage of effective renal plasma flow to the treated kidney.

Hypertension

Kaude [13] and Lingeman have independently noted a change in the systemic blood pressure of ESWL patients at 6 to 12 months. Lingeman [16] performed a retrospective study of 95 patients with at least one year follow up and found in 8% of cases a new onset of hypertension requiring drug therapy and in 15% an increase in diastolic bloodpressure not requiring further treatment. Recently this observation has been confirmed in a prospective study of R. C. Newman et al. [20]. 148 patients were evaluated to determine the incidence of high bloodpressure. 8% developed hypertension needing medical treatment or required an increase in previously prescribed drugs.

Williams [28] observed 91 patients for blood pressure changes 17 to 21 months after ESWL therapy and found that 8% had developed sufficiently severe hypertension to require treatment.

Knapp [15], as mentioned earlier, found that patients with pre existing hypertension and unsatisfactory control of their hypertension are at higher risk for developing hypertension. In an study of Waldthausen [27] on 1,311 ESWL treatments 19 (1.25%) hematomas were found: 9 intrarenal and 10 subcapsular. Ten patients were treated conservatively, two underwent a nephrectomy because of a rupture of the kidney and retroperitoneal hematoma. Six patients underwent a percutaneous puncture of the hematoma and one patient died from acute septicemia. Radionuclide examination showed in those six cases non significant alterations of the renal function on the treated side. It was concluded that when hematoma occurs, patients are usually without complaints three months after the initial treatment. A significant change in renal function was not observed.

Animal studies (Table 3)

There have been only a few animal studies documenting the effects of shockwaves during ESWL. All the published studies demonstrate morphological and functional changes after shockwave administration that correlate with the side effects observed in patients.

Applications of shockwaves of the kidney of normal dogs cause renal hemorrhages of various extent [4]. The larger hemorrhages extended into the subcapsular space and had a mushroomlike appearance with a thin layer of blood. Alternatively, these hematomas could drain to the renal pelvis, which would lead to transient hematuria.

The number of hemorrhages but not their size depended on the number of shockwaves applied. In addition to these subcapsular hematomas, confluent petechiae occured in the outer renal capsule but were never extensive. Interstitial edema could also be documented, it was distributed over the whole kidney. But the course of all these lesions was transient.

Light microscopic studies [21] have demonstrated that ESWL directed at the kidneys of dogs that did not have renal calculi produced intraparenchymal hemorrhages and disruption of some thin walled vessels. Perinephric hematomas also have been noted. This differs from the data of Chaussy that were derived from renal histological studies with dogs, in which no traumatic effect could be attributed to the shockwaves [5].

Table 3. ESWL side effects in the animal model

	No. of references
• Macroscopic changes	
hematuria	[4]
subcapsular, perirenal, intrarenal hematomas	[4, 8, 18, 22]
hemorrhages in various extent	[4, 8]
renal enlargement	[4]
fibrosis in the focal zone	[18]
shrinking of renal convexity	[22]
• Light microscopic changes	
intraparenchymal hemorrhages	[21]
disruption of thin walled vessels (Vv Arcuatae)	[21, 22]
venous trombosis	[8, 22]
tubular dilatation	[8]
partial glomerular hyalinization	[3, 22]
focal areas of calcification	[19]
diffuse interstitial and perivascular fibrosis	[3, 18, 19, 22]
• Electron microscopic changes	
loss of microvilli and ciliae	[22]
cell vacuolization and desquamation	[22]
rupture of glomerula	[22]

Scanning electron microscopy studies by Recker [22], showed in kidneys of rats after shockwave exposure diffuse loss of microvilli and ciliae on cell surfaces of tubuli, cell vacuolization and desquamation and sporadically rupture of glomerula.

Shockwave effects on renal tissue were also studied in pigs [18]. Microscopic and gross tissue changes were found: perirenal and especially intrarenal hematoma, tissue damage and necrosis. The most damaged renal tissue was observed in the focal zone with a decrease to the peripheral zones. Six weeks after initial treatment regeneration started with persistant fibrotic tissue. There was a positive correlation between tissue damage and the number of impulses. Morphologic changes could not be observed with the normal clinical observation methods. The function of the treated kidney was not changed in comparison with the untreated side.

Delius et al. [8] examined the effect of shockwaves on normal canine kidneys which were exposed to 500, 1,500 or 3,000 shockwaves. Autopsy was performed 2 to 30 h later. They found that the number of hematomas was larger and diffuse hemorrhages were more extended after the application of 1,500 and 3,000 than after 500 shockwaves.

Tubular dilatation and venous trombosis occurred in association. No difference was seen between 500 and 3,000 shockwaves. They also stated that the increase in renal damage seen with up to 3,000 shockwaves was not severe enough to warn against the application of such high number of shockwaves.

R. Newman et al. [19] performed a pilot study where kidneys of female dogs were shocked in a range from 1,800 to 8,000 shocks at 18–24 KV. The first group of 3 kidneys were sacrificed after 48–72 h. The second group of two kidneys were examinded 28 to 32 days after treatment. Evidence of permanent change was noted in the second group and consisted of diffuse interstitial fibrosis, focal areas of calcification, nephron loss, dilated veins and hyalinized, acellular scars running from the cortex to medulla.

Begun [3] examined the kidney of 14 pigs 4 weeks after shockwave exposure. They found that the residual scar was surrounded by a marginally vascularized halo of injury. These areas were characterized by interstitial and perivascular fibrosis, partial glomerular hyalinization and tubular injury similar to the histopathology seen in end-stage renal disease.

In his study on kidneys of rats Recker [22] found that acute lesions especially were caused by thrombosis and ruptures of Vv arcuatae with intrarenal hematoma. Longterm lesions consisted in organisation of the intrarenal hematoma, interstitial fibrosis and shrinking of renal convexity. In these areas, glomerular and tubular atrophy and necrosis occurred.

ESWL has proven to be the treatment of choice for most urinary tract stones. This new medical technology has revolutionized the management of stone disease. Although more and more data become available on the pathological effect of shockwaves, the quick acceptance and proven effectiveness has derived our attention from the lack of randomized controlled trials on safety of this new form of therapy. The information we have is still inadequate to define the tissue damage caused by shockwaves. The studies do not provide objective criteria for safe treatment and have no explanation for the mechanism of this tissue damage. Furthermore, ESWL is a rapidly economically evolving technology and already other types of shockwave generators are available. This may lead to other, yet unknown side-effects. More studies are necessary to better understand and better define the risks of ESWL.

References

1. Assimos DG, Boyce WH, Furr EG, Espeland NA, Harrison LH, Kroovand RL, Salem W (1986) Urinary enzymes levels after extra corporeal shock wave lithotripy (ESWL). J Urol 137:143A
2. Baumgartner BR, Dickey KW, Ambrose SS, Walton KN, Nelson RC, Bernardino ME (1987) Kidney changes after extra corporeal shockwave lithotripsy: appearance on MR imaging. Radiology 163:531–534

3. Begun FP, Laswon RK (1988) Renal injury from focused electrohydraulic shockwaves. Sixth World Congress on Endourology and ESWL. Paris, France
4. Brendel W (1986) Effects of shockwaves in canine kidneys. In: Gravenstein JS, Peter K (eds) Extracorporeal shockwave lithotripsy for renal stone disease. Technical and clinical aspects. Butterworths, Boston London, pp 141–142
5. Chaussy C (1982) Extracorporeal shockwave lithotripsy. New aspects in the treatment of kidney stone disease. Karger, Basel
6. Chaussy C, Schmiedt E, Jocham D, Brendel W, Forssmann B, Walter V (1982) First clinical experience with extracorporeally induced destruction of kidney stones by shockwaves. J Urol 127:417–420
7. Chaussy C, Schmiedt E, Jocham D, Schuller J, Brendel W, Liedl B (1984) Extracorporeal shockwave lithotripsy for treatment of urolithiasis. Urology 23:59–66
8. Delius M, Enders G, Xuan Z, Liebish HG, Brendel W (1988) Biological effects of shockwaves: kidney damage by shockwaves in dog-dose dependence. Ultrasound Med Biol 1:117–122
9. Gilbert BR, Riehle RA, Vaughan ED (1988) Extracorporeal shockwave lithotripsy and its effects on renal function. J Urol 138:482–485
10. Grantham JR, Millner MR, Kaude JV (1986) Renal stone disease treated with extracorporeal shockwave lithotripsy: short-term observations in 100 patients. Radiology 158:203–207
11. Hegazy AR, Ishak AE, El-Kateb S (1987) The effect of ESWL on the kidney: histopathological study. Fifth World Congress on Endourology and ESWL. Cairo, Egypt
12. Jocham D (1987) Clinical studies documenting renal changes after ESWL. In: Riehle RA (ed) Principles of extra corporeal shockwave lithotripsy. Churchill Livingstone, New York Edinburgh London Melbourne
13. Kaude JV, Williams CH, Millner MR, Scott KN, Finlayson B (1986) Renal morphology and function immediately after extracorporeal shockwave lithotripsy. AJR 15:305–313
14. Kishimoto T, Yamamoto K, Yashihara H, Mackawa M (1986) Side effects of extracorpreal shockwave exposure in patients treated by extracorporeal shockwave lithotripsy for upper urinary tract stones. Eur Urol 12:308–313
15. Knapp PM, Kulb TB, Lingeman JE (1988) Extracorporeal shockwave lithotripsy induced perirenal hematoma. J Urol 139:700–703
16. Lingeman JE, Kulb TB (1987) Hypertension following extracorporeal shockwave lithotripsy. J Urol 137:45A
17. Lingeman JE, Newman DM, Mertz JHD, Mosbaugh PG, Steele RE, Kahhoski RJ, Caury TA, Woods JR (1986) Extracorporeal shockwave lithotripsy: the Methodist Hospital of Indiana experience. J Urol 135:1134–1137
18. Muschter R, Schmeller N, Kutscher KR, Reimers I, Hofstädter F (1986) Morphologische Nierenveränderungen durch die Anwendung der extrakorporalen Stoßwellenlithotripsie und ihr klinisches Korrelat. 38. Kongress der Deutschen Gesellschaft für Urologie e.V. Würzburg, Federal Republic of Germany
19. Newman RC, Hacket RL, Senior DF, Brock KA, Feldman J (1987) ESWL pathological effects on canine renal tissues. Urology 29:194–200
20. Newman RC, Williams CM, Kaude J, Petterson J, Thomas WC (1987) Hypertension following ESWL. 5th World Congress on Endourology and ESWL. Cairo, Egypt
21. Newmark RC (1986) Effect of shockwaves on canine renal and neurologic tissue. In: Gravenstein JS, Peta K (eds) Extracorporeal shockwave lithotripsy for renal stone disease. Technical and clinical aspects. Butterworths, Boston London, pp 143–144
22. Recker F, Rüben H, Hofstädter F, Bex A (1988) Ultramorphological acute and longterm lesions of ESWL in rat kidney. 6th World Congress on Endourology and ESWL. Paris, France
23. Rubin JI, Anger PH, Pollack HH, Bonner MP, Coleman BG, Mintz MC, Van Ansdalen KN (1987) Kidney changes after extracorporeal shockwave lithotripsy: CT evaluation. Radiology 162:21–24
24. Ruiz-Marcellan FJ, Ibarz Servio L (1986) Evaluation of renal damage in extracorporeal lithotripsy by shockwaves. Eur Urol 12:73–75
25. Schulze H, Falkenberg FH, Mondorf AN, Engelmann O, Senge T (1988) Enhanced excretion of kidney-derived antigens in the urine of patients after ESWL. J Urol 139:323A
26. Steinmann J, Wilbert DM, Strohmeier WL, Fluchter SH, Bichler KH (1988) Glomerular and tubular changes after ESWL measured by urinary proteins. 6th World Congress on Endourology and ESWL. Paris, France
27. Waldthausen W, Schuldes H, Behrmann-Küster A, Nagel R (1987) Renale Hämatome nach ESWL-Verlaufsbeobachtungen. Aktuel Urol 18:93–197
28. Williams CH, Kaude JV, Newman RC, Peterson JC, Thomas WC (1988) Extracorporeal shockwave lithotripsy: longterm complications. AJR 130:311–315

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