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Morphological changes following ESWL in the rat kidney

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Summary. Fifty four Wistar rats were treated with 500, 1,000 or 2,000 shock waves, using the modified DORNIER HM 3 system with the new SG40 shock wave generator. The animals were sacrificed after a period of 24 hours, 7 days or 35 days. Histological examination, scanning electron microscopy (SEM) and magnetic resonance imaging (MRI) were used to evaluate acute and long term effects after extracorporeal shock-wave lithotripsy (ESWL). Acute morphological changes such as glomerular bleeding, tubular dilatation, atrophy and partial necrosis occured immediately after ESWL throughout the kidney. SEM revealed a tubular loss of microvilli and cilia. There was restitutio ad integrum of these diffuse lesions. The extent of the long term lesions was determined by the following mechanism: venous rupture occured during ESWL, especially in thin arcuatae veins which are, tortuous their and run between two different tissue densities. This resulted in interstitial haematoma, demonstrable by MRI; in the long term groups, the haematomas progressed to interstitial fibrosis with segmental retraction of renal convexity. The blood supply in these areas was reduced and secondary changes such as glomerular-tubular atrophy and sclerosis followed. The degree to which long-term renal lesions resulted was determined by the extent of these changes, which were shock-wave dose dependent up to a dose of 2,000 shock waves.

Key words: Extracorporeal shock wave lithotripsy – Renal morphology – Scanning electron microscopy – Magnetic resonance imaging – Rats

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Introduction

Since 1980, ESWL has rapidly established itself throughout the world as a new, non-invasive method of treating urolithiasis. This new era was ushered in by the appearance of the DORNIER lithotriptor [3–5, 13]. A second generation of lithotriptors, distinguished by an extended-diameter elipsoid and a new shock wave generator, has since been developed [10, 14]. Second generation lithotriptors permit treatment without anaesthesia and allow administration of analgesics to be reduced or even dispensed with. The number of shock waves required to destroy the kidney stones has, however, increased.

Unlike early investigations by Chaussy et al. [6], which revealed no pathological findings in the renal tissue of ESWL-treated dogs, recent reports [8, 9] describe renal parenchymal damage.

Clinically, some renal lesions due to ESWL have been reported [12]. Studies document a decreased effective renal plasma flow in 30% of the patients immediately following ESWL [7]. Magnetic resonance imaging (MRI) indicated acute focal intrarenal areas of higher or lower signal intensity following ESWL [1], whose morphological background could not be revealed in all cases. In addition subcapsular hematomas occured. These findings, in conjunction with the gross haematuria encountered shortly after ESWL, suggested that this effective treatment was traumatic to renal tissue. Optical and scanning electron microscope studies were necessary to establish what acute intrarenal morphological changes occur after ESWL and to what extent they may develop into long-term lesions following different ESWL doses. The

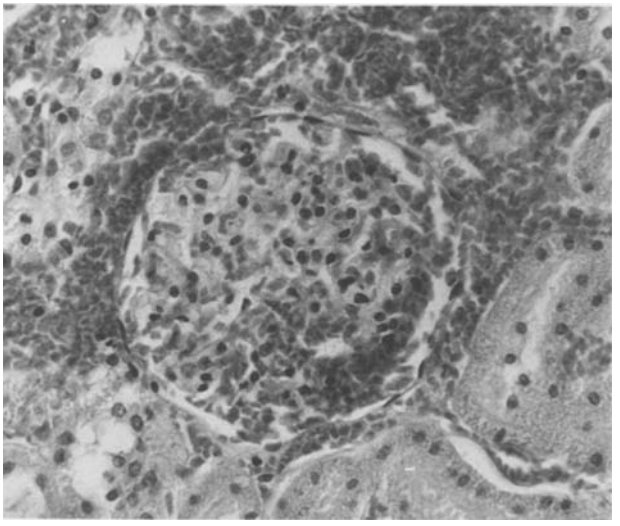

Fig. 1. Glomerular bleeding acute after ESWL with 1,000 shock waves, partially caused by rupture of the glomerular capillaries or fracture of the Bowman's capsule near an interstitial haemorrhage

Table 1. Primary diffuse intrarenal lesions (24 hours group) corresponding to shock waves given. Group 1 received 500, group 2 1,000 and group 3 2,000 shock waves

Groups		1	2	3
glomerular	bleeding	ø	+	+
tubular	dilatation	+	+	++
	atrophy	ø	+	++
	red blood cells/ proteinaceaous cast	+	+	++
	necrosis	ø	+	+
venous	dilatation	+	++	++
	thrombotic fragments	+	+	++

+ = slight; ++ = moderate

course of renal haematomas should be observed by MRI.

Materials and methods

Fifty-four female Wistar rats with body weights ranging from 250–300 g were randomly divided into three groups. Group 1 received 500, group 2 1,000 and group 3 2,000 single shock waves at 15 kV spark discharge. A third of each group was sacrificed 24 h, 7 or 35 days after ESWL. Treatment was performed using the new DORNIER HM3 system with the new SG40 shock-wave generator and the wider E 1.68 ellipsoid. Pressure at the focal point was 625 bar at a spark discharge of 15 kV. The anaesthetised rats (100 µg/g body weight phenobarbital) were fixed to a gantry-suspended frame and lowered into the water bath. In each case, the left kidney was treated after localisation by means of two video fluoroscopic systems and intravenous injection of 0.7 ml contrast medium (Conray 70). Prior to ESWL, immediately after ESWL and prior to necropsy, imaging was performed using a 1.5 T superconductive system (Magnetom, Siemens, Erlangen) in the half the individuals of each group. The rats were placed in a supine position on a coil with a circular surface diameter of 12.5 cm, centred over the kidney region. Multisectional axial and coronal imagages of both kidneys were obtained using T1 and T2 weighted pulse sequences.

At the end of the observation period, the anaesthetised rats were laparotomised and the abdominal section of the aorta catheterised via the aortic bifurcation, using a 1.3 × 50 mm teflon catheter, which was positioned under the renal hilum. 0.9% sodium chloride and 2.5% glutaraldehyde (in 0.1 M cacodylate buffer, pH 7.4) were inflated, the kidneys perfused, removed and bisected; half of each specimen was used for SEM examination as described by various authors [2]. The remaining half was stored in 10% formaldehyde, embedded in paraffin and stained with haematoxylin-eosin (HE) for optical microscopy.

Results

Morphological renal changes following ESWL may be divided into acute (primary) and long-term (secondary) lesions. The various renal structures (glomeruli, tubuli and vessels) were judged in relation to their intrarenal localisation. It was important to draw a distinction between lesions appearing throughout the renal parenchyma and those appearing in the region of intrarenal haematomas. The extent of morphological change was related to the number of shock waves administered.

Primary lesions

Throughout the whole kidney, rats subjected to high doses of 1,000 or 2,000 shock waves showed slight to moderate glomerular bleeding acute after ESWL (Fig. 1, Table 1). This was partially caused by the rupture of glomerular capillaries (demonstrable under SEM) or fracture of the Bowman's capsule near an interstitial haemorrhage. The tubular epithelium showed vacuolisation, dilatation and particularly atrophy. Numerous distal segments contained lumina plugged with red blood cells and proteinaceous cast. The extent of these diffuse lesions was greater in groups 2 and 3 than in group 1 (Table 1). There was sporadic tubular necrosis with high shock doses. A loss of microvilli was apparent under SEM, especially in the thin ascending distal tubule. The tubular cells were swollen and acute diffuse desquamation was noted after ESWL (Fig. 2).

The commonest acute renal changes after ESWL in the left kidney subjected to shock-wave treatment were intrarenal haematomas. The most significant haemato-

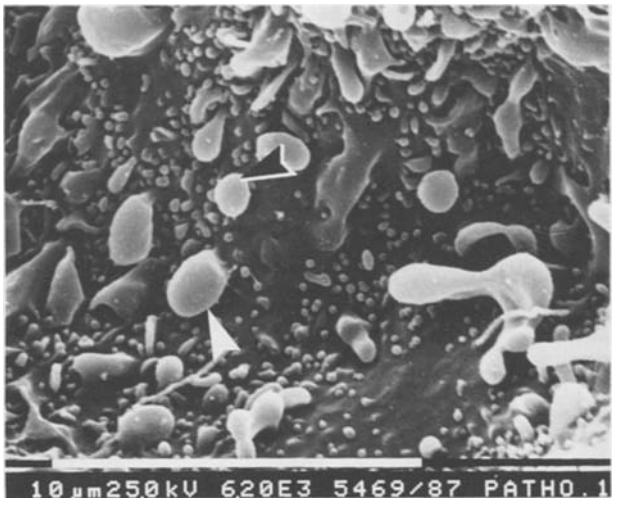

Fig. 2. Looking into the ascending thin loop of Henle, scanning electron microscopy revealed a loss of microvilli and cilia with swollen cells (arrow) and diffuse desquamation acute after ESWL

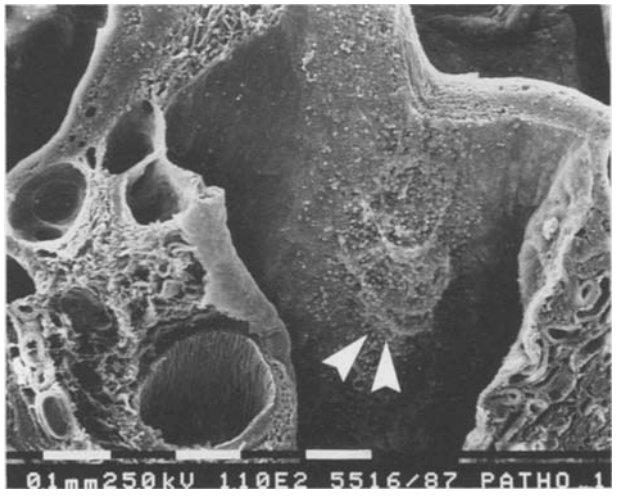

Fig. 3. Scanning electron microscopy showed acute after ESWL (1,000 shock waves) dilated v. arcuatae with thrombotic fragments (arrow) as evidence of reparative process after endothelial lesions. The arterial system (bottom left), was generally preserved

mas were localised at the cortical medullary junction, which enlarged particularly into the papillary region. The outer cortex was not involved. Haematomas occured more frequently in the high shock-wave groups than in groups 1. Haematomas which were macroscopically detectable also proved to be demonstrable by T1 and T2 – weighted magnetic resonance imaging as a area of reduced signal intensity. Optical microscopy revealed dilatation, endothelial lesions and ruptured veins, especially in the arcuate veins in the region of cortical medullary haematomas. Examination under the scanning electron microscope showed a large number of endothelial lesions in the arcuate veins with thrombotic fragments as evidence of reparative processes (Fig. 3). Occurence of endothelial lesions was minimal in the arterial as compared to the venous system.

Apart from this characteristic localisation, there were diffuse radially oriented haemorrhages and haemorrhagic streaks in the parenchyma. These were more frequent in the high shock wave groups than in group 1, but were less frequent than cortical medullary haematomas. They were not apparent to macroscopic and magnetic resonance examination.

The occurence of subcapsular haematomas was dose dependent to shock wave treatment. In group 1, 4 of 6 haematomas were macroscopically demonstrable and could be evaluated by means of MRI as a region of reduced signal intensity in T1 and T2 weighted magnetic resonance imaging. In high shock wave groups, subcapsular haematomas appeared more frequently. In each group 6 out of 8 haematomas could be distinguished macroscopically.

There were rare occurences of the subtransitional haematomas in the renal pelvis. Only in grous 2 and 3 did these changes prove.

Secondary lesions

These changes were observed in the 35-day group. A distinction was drawn between long-term lesions in the area of primary haematomas, demonstrated by MRI directly after ESWL being judged in their course and long- term lesions throughout the renal tissue.

Unlike subcapsular haematomas, which produced no reduction in renal convexity, primary cortical medullary haematomas caused segmental fibrotic shrinkage of the renal capsule after 35 days. Glomerular atrophy and sclerosis were identifiable throughout in regions of interstitial fibrosis. Extensive tubular damage was also observed. Dilatation, atrophy and necrosis were encountered more frequently in groups 2 and 3. Some epithelial cells contained abundant haemosiderin. Focal calcification was found in the damaged areas. A dense hyalinised scar surrounded the arcuate veins, which were dilated. The characteristics of acute failure were found in the neighbourhood of interstitial fibrosis. In contrast to these severe, demarcated secondary lesions following ESWL, the remaining renal parenchyma was free of long-term lesions. Apart from rare sporadic glomerular atrophy and sclerosis or tubular dilatation and atrophy, no histological abnormalities were noted in the kidneys. Scanning electron microscopy revealed no residual diffuse lesions in the kidneys.

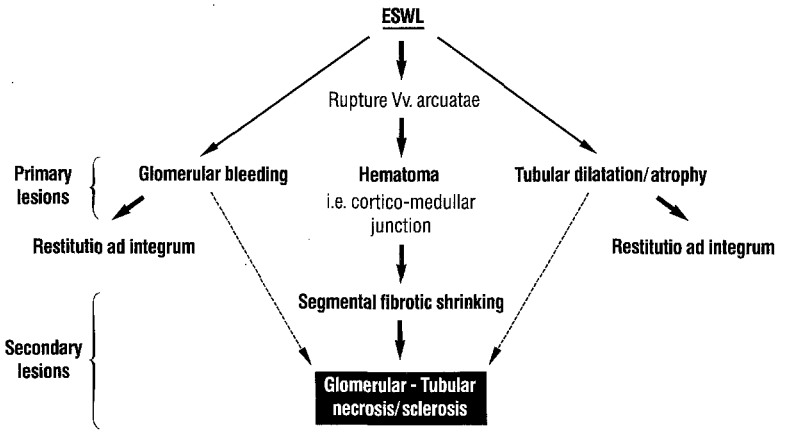

Fig. 4. Morphological pathomechanism following ESWL. Main long term lesions (secondary: glomerular/tubular necrosis) are dependent from the extent of intrarenal haematomas, generally caused by rupture of the Vv. arcuatae. Sporadically occuring glomerular bleeding and tubular dilatation throughout the whole kidney generally led to restitutio ad integrum

Discussion

The histological structure of the cortex and medulla in rats is comparable to that in human kidneys [11]. The number of shocks administered were used to determine maximum damage to renal tissue. The kV value (15 kV) was lower than for humans (18–21 kV), but the effective pressure at the kidneys was comparable, since the shock wave loses 20% of its pressure in passing through 6 cm of muscle and fatty tissue.

Renal damage needed to be differentiated into primary and secondary lesions (Fig. 4). Acute glomerular bleeding and tubular dilatation or atrophy occured after ESWL. The tubules were filled with the red blood cells and proteinaceous cast. These findings explain the gross haematuria evident in all animals until the day after lithotripsy. Generally, there was restitutio ad integrum in the long-term groups. Only a few diffuse, localized glomeruli and tubules showed signs of sclerosis or necrosis. Their numbers were quantitatively lower than the damaged glomerula and tubules in the acute groups.

The following pathomechanism (Fig. 4) seemed to be responsible for the long-term lesions: ESWL causes venous rupture, especially of the arcuate veins. These are the vessels predominantly exposed to shock waves. 1. Throughout their course, they run in a circular path parallel to then renal outline and are more exposed to shock waves. 2. Their normal function is governed by water reabsorption, so that they are extremely thin-walled and thus highly vulnerable. 3. They also run along the borderline separating two different tissue densities (cortex and medulla), where ESWL effects are most likely to occur.

Ruptures of the arcuate veins led to haematomas in the region of the cortical medullary junction. These could be detected using MRI and their subsequent development was observed. Segmental fibrotic shrinking, accompanied by retraction of renal convexity, resulted. The interstitial fibrosis compressed the vessels, diminishing the blood supply and leading to the destruction of tubules and glomeruli. The extent of these damages was dose dependent to the number of shock waves up to 2,000. The question of whether this partly reduced blood flow is accompanied by activation of the renin angiotensin system in respect of hypertension remains unsolved.

Data on the extent of renal damage cannot be extrapolated to humans. In these series, the whole kidneys lay in the field of shock waves, whereas in human kidneys only a part of parenchyma is exposed to shock waves. Nevertheless the vulnerability of structures and the consequences of lesions may be comparable. Further studies will be necessary to determine whether there must be more caution in patients with preexisting renal pathology and whether it is preferable to administer shock waves to a stone in one or a number of sessions, and there should be a longer period between treatments.

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