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A decrease in blood pressure following pyelolithotomy but not extracorporeal lithotripsy

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Abstract Our aim was to evaluate the hypothesis that relief of renal obstruction lowers the arterial blood pressure if the procedure of stone removal does not injure the kidney itself. Sixty patients with unilateral renal stone were evaluated at baseline and 3 months after electrical shockwave lithotripsy (ESWL, $n=30$) or Gil-Vernet intrasinus pyelolithotomy ($n=30$). Blood pressures were measured noninvasively and renal vascular resistances were obtained from radionuclide measurements of renal blood flow. At baseline, the renal vascular resistance of the obstructed kidney was 2 and 2.5 times greater than of the unobstructed kidney in the ESWL and pyelolithotomy groups, respectively. After 3 months in operated patients, the blood pressure decreased (from 87 to 81 mm Hg, $P=0.002$, in case of diastolic, and from 140 to 132 mm Hg, $P<0.0001$, in case of systolic pressure), while the vascular resistances of both kidneys were equal and normal. In contrast, in the ESWL group the blood pressures and vascular resistances of the treated kidney did not differ from the baseline values. Surgical relief of renal obstruction chronically lowers the arterial blood pressure, possibly by normalizing the renal vascular resistance. ESWL does not change the blood pressure or renal vascular resistance, which could reflect a balance between the relief of obstruction and kidney lesions induced by shock waves.

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Introduction

Extracorporeal shock wave lithotripsy (ESWL) is the preferred way of treating uncomplicated kidney stones smaller than 3 cm in diameter. Acute complications after using ESWL are rare, and it was believed that collateral lesions to paralithiasic tissue, which are due to imperfect focusing of the shock waves, regress later. This was based on the observation that after ESWL the function of the lithiasic kidney is acutely depressed but returns to pretreatment values with time [1, 2]. We challenged this view by showing that the obstructed kidney function improves after removing the stone by pyelolithotomy, an open surgery that saves the renal parenchyma, but not after ESWL [3]. If the renal obstruction-related lesions are potentially reversible, the results of ESWL should be reinterpreted. In particular, the restoration of pretreatment renal function may only reflect a balance between treatment-induced lesions and relief after obstruction. What is important is that ESWL is unable to improve the function of the treated kidney, which can be achieved by the other method of stone removal.

We hypothesized that the same reasoning is valid for the impact of ESWL on arterial blood pressure. The hemodynamic effects of chronic renal obstruction in humans have been uninvestigated. Nonetheless, it is reasonable to hypothesize that substantial renal obstruction may cause an increase in blood pressure that can be reversed by removal of the obstruction. If so, the current controversy as to whether ESWL causes an increase in blood pressure or not can be reformulated into why ESWL does not lower the blood pressure.

We report the measurements of arterial blood pressure and renal vascular resistance before and after pyelolithotomy and ESWL. Data on kidney function are presented in the previous report [3].

Patients and methods

A total of 82 subjects with unilateral renal stone entered the study after giving their informed consent. Sixty of these completed the study protocol. The stone was removed by electromagnetic lithotripsy ($n=30$) or Gil-Vernet intrasinus pyelolithotomy ($n=30$). The subjects were evaluated several days before the treatment and after 3 months. In majority of pyelolithotomies, the stone was a staghorn or greater than 3 cm. However, in several cases war-related problems due to communication difficulties with the medical center where the lithotripsy was performed (Zagreb) and the lack of percutaneous lithotripsy influenced the operative indications. Double-J stents were routinely applied in cases of stones larger than 2 cm in ESWL group ($n=9$) and intra-operatively in six pyelolithotomy patients. During pyelolithotomy, general anesthesia was maintained by isoflurane. This study was approved by the Ethics Committee of the University Hospital Split.

Lithotripsy

An electromagnetic lithotripter with biplane fluoroscopy was used. The patient was given an analgesic and lidocaine cream was applied to the skin. The generation of shock waves was synchronized with the repolarization phase of the cardiac cycle and the last third of the expiration phase of the respiratory cycle. From 1,800 to 3,200 waves were applied for 20–60 min. The peak value of the potential pulse ranged from 12.3 to 15 kV.

Blood pressure measurements

The pretreatment and follow-up measurements of blood pressure were done using a mercury sphygmomanometer, with the patient laying supine for at least 5 min. Three measurements were done in succession, separated by 2 min, and the average values of systolic and diastolic blood pressure were recorded. The dominant arm was always used.

Dual renal scintigraphy

The patient was hydrated with 400 ml of water 20 min before the study and lay in a prone position with a gamma camera (Siemens, LFOV) head above the lumbar area and tilted caudally at 10°. The cocktail of around 185 MBq (5 mCi) technetium-99m diethylenetriaminepentaacetic acid (99m-Tc DTPA) and the 13 MBq (350 μCi) of ortho-iodine-131 hyppuric acid (131-OIH) bolus were given intravenously, with a simultaneous start of data acquisition in 12 s frames over 25 min.

Total renal function

Two blood samples, 44 and 150 min after injection of the radioindicator cocktail, were taken and compared with the dose aliquot count rates of 131-I (44 min sample) or 99m-Tc (150 min sample). From the "volumes of distributions" of 99m-Tc DTPA and 131-OIH so obtained, the total glomerular filtration rate (GFR) and effective renal plasma flow (ERPF), respectively, were calculated using the regression equations of Tauxe et al. [4]. The total renal filtration fraction (FF) was equated as GFR/ERPF.

Separate renal functions

Separate renograms of the left and right kidney parenchyma and a radiohistogram of the left ventricular area were generated. From these data, using the matrix deconvolution technique [5], the relative functions of each kidney (percents in total GFR or ERPF) were calculated. The individual kidney functions (ERPF or GFR of each kidney in ml/min) were obtained by multiplying the total kidney function (ERPF or GFR in ml/min) with the relative function of each kidney (in % of total function).

Renal vascular resistances were obtained as the mean arterial blood pressure/kidney blood flow, where the mean arterial blood pressure was assessed as: (2/3)diastolic blood pressure + (1/3)systolic blood pressure, and the kidney blood flow was equated to: ERPF/(1−hematocrit ratio).

In this way, the total vascular resistance of both kidneys can be calculated, as well as the individual vascular resistance of the treated or untreated kidney.

Other evaluations

In addition to the radionuclide evaluations, all patients underwent an ultrasound examination, planar abdominal x-ray, excretory urography and routine laboratory tests, before the treatment, from 6 to 9 days after treatment, and at the 3-month follow-up.

Statistics

The changes in blood pressure and kidney function following ESWL or pyelolithotomy were evaluated by paired *t*-tests (the variables were approximately normally distributed, i.e. $P>0.2$ by the Kolmogorov-Smirnov test, in each case). The test was first performed for each group of patients separately. Next, in an attempt to account for the differences in possible predictors of blood pressure changes between the study groups, all patients were entered as cases. The changes in blood pressures were then evaluated by two way (study phase×study group) ANOVA, with stone size and baseline vascular resistance of the treated kidney as covariates (ANCOVA). The effect studied was the covariate independent interaction between the study phase (before/after stone removal: intra-subject variability) and study group (ESWL/operation: inter-subject variability) in predicting the arterial blood pressure. The associations between metric variables were tested by linear regression. All tests were performed using SPSS 11.0.3 software (SPSS, USA).

Results

A total of 22 patients (10 ESWL and 12 operated) did not complete the 3-month follow-up phase. They either did not come for the 3-months radionuclide evaluations ($n=18$), refused to repeat the dual renal scintigraphy due to paravenous bolus injection, or data failed due to computer errors in data acquisition ($n=4$). Neither group developed acute complications from ESWL or renal surgery.

Patient baseline characteristics and therapy outcome

The groups were anthropometrically matched, but differed in stone size, the degree of obstruction and baseline renal function (Tables 1, 2). There were two cases of intrarenal hematoma after ESWL. In six ESWL patients and one operated patient, the residual stone fragments (concrements larger than 5 mm immediately after treatment) were treated by ESWL after follow-up. During the follow-up period, recurrent stones (concrements larger than 5 mm at 3 months, but not immediately after treatment) developed in two ESWL patients and in eight operated patients. Thus, at 3 months follow-up there were similar stone-free rates in both groups

Table 1 Comparison of patients with nephrolithiasis treated operatively and with extracorporeal lithotripsy

n	Pyelolithotomy 30	Lithotripsy 30
Anthropometry		
Men/women	13/17	9/21
Age (years)	51 ± 11	51 ± 11
Hheight (cm)	170 ± 9	169 ± 11
Body mass (kg)	74.7 ± 12	79.3 ± 12
Stone		
Size (cm)	3.2 ± 0.7	1.8 ± 1.1
Calcium stone (no. patients)	28	26
Infecting stone (no. patients)	17	22
Obstructing stone (no. patients)	9	14
Clinical outcome		
Intrarenal hematoma (no. patients)	2	0
Residual concrements (no. patients)	6	1
Rersistent infection (no. patients)	1	1
Stone-free rate at 3 months	22/30	21/30
Partial obstruction at 3 months (no. patients)	3	3

Table 2 The chronic effects of kidney stone removal on renal vascular resistance (RVR) and filtration fraction in 30 patients treated with pyelolithotomy and 30 patients treated with extracorporeal lithotripsy (ESWL). All values are means ± SD. The paired *t*-test was used to determine the probability (*P*)

	At baseline	At 3 Months	*P*
Pyelolithotomy			
Treated kidney			
RVR (mm Hg/ml/min)	0.52 ± 0.3	0.22 ± 0.1	2×10^{-6}
Filtration fraction	0.20 ± 0.03	0.21 ± 0.03	0.11
Untreated kidney			
RVR (mm Hg/ml/min)	0.26 ± 0.1	0.21 ± 0.1	0.002
Filtration fraction	0.20 ± 0.03	0.22 ± 0.04	0.006
ESWL			
Treated kidney			
RVR (mm Hg/ml/min)	0.41 ± 0.38	0.39 ± 0.29	0.48
Filtration fraction	0.20 ± 0.05	0.20 ± 0.05	0.77
Untreated kidney			
RVR (mm Hg/ml/min)	022 ± 0.06	0.23 ± 0.08	0.38
Filtration fraction	0.20 ± 0.04	0.21 ± 0.05	0.05

(absence of stone concrements larger than 5 mm). The excretory urography and dynamic scintigraphy confirmed that about a third of these residual or recurrent stone fragments caused the partial extra-parenchymal obstruction at 3 months in both groups (Table 1).

Blood pressure

The baseline values of the diastolic blood pressure were greater than 90 mm Hg in ten patients (33%) treated with ESWL and in 12 patients (40%) treated with pyelolithotomy (Fig. 1). However, no patient in either group was treated for hypertension before or during the study. At 3 months after stone removal, the blood pressures returned to baseline values in subjects treated with ESWL, but decreased significantly in subjects treated with pyelolithotomy (Table 2, Fig. 1).

Renal vascular resistance

The pretreatment renal vascular resistance of the treated kidney was greater in pyelolithotomy than in ESWL patients, however, these values were roughly doubled in comparison with the untreated kidney in both groups (Table 2). At 3 months follow-up, the renal vascular resistance of the treated kidney in the pyelolithotomy group was completely normalized, not differing from the untreated kidney, which also decreased slightly with respect to baseline. In contrast, in the ESWL group the renal vascular resistance of the treated kidney remained at the baseline elevated level (Table 2).

Filtration fraction

The pretreatment filtration fractions of the treated kidney were normal, i.e., not different from the untreated

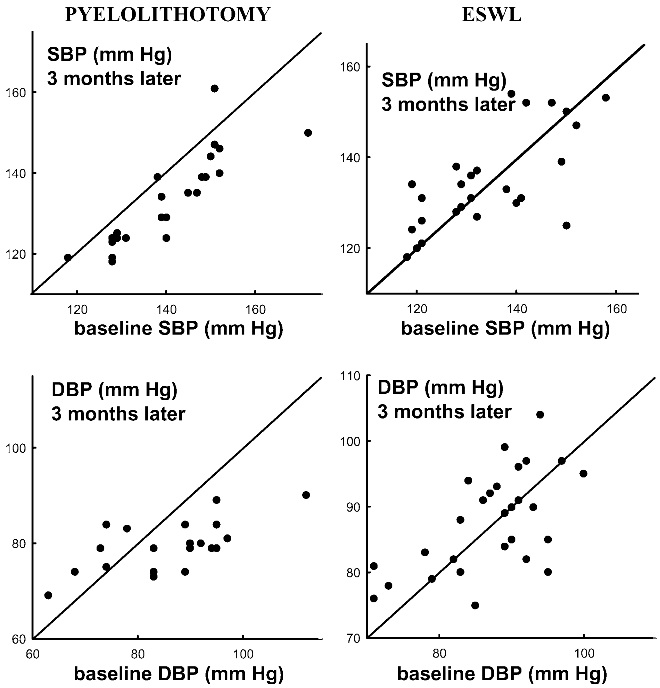

Fig. 1 The diastolic and systolic blood pressures decreased in almost all of the 30 patients with unilateral kidney stone at 3 months after pyelolithotomy (*data below the line of identity*), but were unchanged in the 30 patients treated with extracorporeal lithotripsy (*data around the line of identity*)

kidney in either group of patients. At 3 months follow-up, in the ESWL group, these values did not change, except for a marginal increase in the filtration fraction of the untreated kidney. In the pyelolithotomy group, the filtration fractions of both kidneys were slightly increased at 3 months after stone removal (Table 2).

Multivariate analysis

The only significant variable in the repeated measures ANCOVA was the interaction between the study phase and study group, and this only in the case of systolic blood pressure as the outcome (dependent) variable ($P = 0.045$).

Correlations

Total renal vascular resistance increased with increasing systolic blood pressure at baseline and at the follow-up in subjects treated with pyelolithotomy (linear correlation coefficient, r, ranged from 0.78 to 0.81, $P = 0$ in each case), and less strongly in subjects treated with ESWL (r ranged from 0.43 to 0.59, $P < 0.01$ in each case). The intra-individual chronic changes in renal vascular resistance (differences between RVR at 3 months and at baseline) correlated with the respective changes in the mean blood pressure in operated patients ($r = 0.43$, $P = 0.017$), but not in patients treated with ESWL.

Patient subgroups

All analyses were repeated by excluding the patients with residual or recurrent stones at the 3-month follow-up. Aside from minor changes in P-values, the results were not different. Moreover, taking in account only patients with residual/recurrent stones, the same response in blood pressure following ESWL (no change) or pyelolithotomy (apparent, but not statistically significant decrease) was observed.

Discussion

Chronic arterial hypertension adversely affects renal function. Conversely, several pathologies of the kidney may cause hypertension. These include renal artery stenosis, renal artery embolism, chronic pyelonephritis, acute interstitial nephritis, polycystic kidney and obstructive uropathy [6]. Bilateral obstructive nephropathy due to bladder outflow obstruction, clinically presenting as a high pressure chronic retention of urine, may cause bilateral hydronephrosis and, eventually, uncontrollable hypertension [7, 8]. However, even unilateral hydronephrosis has been reported in association with hypertension that was reversed after the relief of obstruction [9].

The etiology of hypertension related to obstructive uropathy is not known. The possibilities include volume expansion, high renin state, increased sympathetic tonus, impaired renal function and the loss of renomedullary vasodilatative substances. However, such reports are rare and it is generally accepted that the obstructed kidney is able to maintain the homeostasis of sodium and water despite the burden of reduced glomerular filtration and blood flow. Nonetheless, even the best control mechanism requires some shift of the control variable. Thus, theoretically, renal obstruction should have some effect on blood pressure. We can further expect a correlation between the degree and duration of renal obstruction and a change in blood pressure with respect to the pre-obstructive state. Due to the high morbidity caused by nephrolithiasis, even a small effect on blood pressure would be important, and this issue should not be addressed only in terms of induction of blunt hypertension.

Animal data on the hemodynamic impact of renal obstruction are scarce and hardly applicable to humans. Several epidemiological studies have demonstrated a link between renal lithiasis and raised blood pressure [10, 11, 12]. These data were interpreted in two ways: (1) that hypertensive subjects have a greater risk of renal stone formation, especially when hypertension is associated with excessive body weight, but also (2) that renal obstruction increases the risk of subsequent hypertension [11]. In humans it is not possible to experimentally evaluate the pre-obstructive versus post-obstructive states. However, we can evaluate the effects of the therapy for nephrolithiasis, but in order to study the effects of stone removal per se, the stone should be removed without collateral damage to kidney or other organs that can mediate post-treatment changes in blood pressure. ESWL is not a good model for evaluating the effect of stone removal on blood pressure. Besides the relief of obstruction, ESWL may cause lesions to treated and even untreated kidneys and possibly other organs, especially in obese patients [3], when focusing of shock waves may be hampered by the different acoustic properties of fat and other soft tissues. In contrast, spontaneous stone passage, urethrocistoscopy or open surgery that saves the renal parenchyma (pyelolithotomy) are probably better models to assess the impact of renal obstruction on renal function and blood pressure. Our data suggest that even partial unilateral renal obstruction may increase the arterial blood pressure and that the relief of obstruction should lower it if the procedure of stone removal does not injure the kidney itself.

Surprisingly, we have found only few data on the impact of these methods on blood pressure. Lingeman et al. [13] reported that in 171 patients with urinary stones treated with uretroscopy ($n = 166$) or spontaneous stone passage ($n = 5$), the diastolic pressure apparently decreased by 0.88 mm Hg, which was not a statistically significant change. Strohmaeir et al. [14] followed blood pressure changes after various types of urinary stone therapy in 252 patients for 2 years. At 24 months, in all patient groups regardless of the stone location and type of treatment, blood pressure was increased. They concluded that renal stone disease, rather than the type of treatment, was the cause of the observed increases in systolic and diastolic blood pressure at 24 months after the relief of obstruction in their patients. At first sight, it appears that this report contradicts our findings. However, out of 252 patients reported by Strohmaier et al. there were 84 with renal stones and only eight of these underwent percutaneous nephrolithotomy or open surgery (the rest received ESWL or no treatment). The authors did not specify how many of these eight patients underwent open surgery and what the type of operation was. Thus, less than eight and maybe none of their patients with renal stones underwent pyelolithotomy or another parenchymal saving procedure. Therefore, the results from our patients with renal stones treated with pyelolithotomy cannot be compared with those of Strohmaeir et al.

The chronic decrease in blood pressure following pyelolithotomy in this study was observed in parallel with the decrease in renal vascular resistance. Moreover, the extent of change in renal vascular resistance could completely account for the change in blood pressure in this group. To make this clear, recall that the kidney accommodates about 1/5 of the cardiac output. Since the blood flow to an organ is proportional to its vascular conductance (1/vascular resistance), it follows that the kidney's vascular system accounts for 1/5 of the total peripheral vascular conductance. This means that a 60% increase in (total) renal vascular conductance, observed at 3 months after pyelolithotomy, implies about a 12% increase in total peripheral vascular conductance. If cardiac output (the product of mean arterial blood pressure and total peripheral conductance) was unaffected, this 12% increase in vascular conductance would result in about a 10% decrease in mean arterial blood pressure. This roughly agrees with the observed 7% decrease in mean arterial blood pressure in operated patients. This simple explanation of the sustained decrease in blood pressure following pyelolithotomy is substantiated by the observed correlations between the arterial blood pressure and renal vascular resistance.

The mechanisms by which the kidney regulates blood pressure are complex and only partially worked out in an animal model [15]. Although this important kidney function is rather a robust one, it is not surprising that it cannot be perfectly executed in the substantially altered pressure conditions of urine flow in obstructive uropathy. Our original hypothesis was that even unilateral renal obstruction impairs the homeostasis of salt and water, leading to water retention and a rise in blood pressure. We cannot exclude the involvement of this mechanism, but the documented decrease in renal vascular resistance was great enough to fully explain the observed decrease in the arterial blood pressure after the relief of obstruction.

The increased vascular resistance of the obstructed kidney may reflect an altered vasomotor tone which is abolished by surgical relief of obstruction. One can speculate that the pain induced by the kidney stone increases the sympathetic tone, which in turn increases the peripheral vascular resistance, especially in well innervated organs like kidneys. However, the baseline RVR was mainly increased in the obstructed kidney in both patient groups. This speaks against a significant contribution from a sympathetically mediated elevation of renal vascular resistance in patients with kidney stones. We also observed a decrease in RVR of the untreated kidney at 3 months after pyelolithotomy. This suggests the presence of renorenal reflexes, elaborated in animal models [16].

In contrast to operated patients, the vascular resistance of the treated kidney did not change at 3 months after ESWL. This lack of change in RVR was observed in parallel with the unchanged renal plasma flow and indexes of obstruction, reported previously. In particular, in spite of removing the cause of obstruction, ESWL did not accelerate the flow of filtrate, i.e. the post-treatment renogram was still of an obstructive type [3]. The fact that ESWL did not lower the blood pressure in this, as well as in other studies, could reflect the relatively small obstruction in these patients compared to operated patients. Clearly, a small renal obstruction or its removal may have no hemodynamic impact. The baseline RVR was increased more in operated patients, which could account for the different response in blood pressure following the relief of obstruction. Therefore, we do not suggest that either group of patients in this study can be considered as a control group in evaluating the effect of relief of renal obstruction on blood pressure. Still, one should not overlook the fact that the baseline RVR was substantially increased even in the ESWL group. Also, the results of the multivariate analysis suggest that sustained changes in blood pressure depended on the type of treatment (ESWL or pyelolithotomy), irrespectively of the baseline RVR or size of the stone. Therefore, we put forward the hypothesis that ESWL causes both blood pressure lowering (relief of obstruction) and blood pressure raising effects (renal damage) which roughly cancel each other. If this hypothesis is true, the current controversy about whether ESWL causes a small raise in blood pressure in some patients appears to be a superficial one. One should first answer the question of why ESWL does not lower the blood pressure, at least in patients with significant obstruction at baseline.

In our patients, the filtration fraction appeared to be a robust parameter of kidney function, practically insensitive to the presence of obstruction or its cessation. In normal conditions, the changes in renal blood flow, by affecting the colloid oncotic pressure in the glomerular capillaries, cause similar changes in GFR, which acts to keep the filtration fraction constant. It is reasonable to hypothesize that urinary obstruction increases the hydrostatic pressure in Bowman's capsule, accounting for the observed decrease in GFR [3]. By mechanisms that cannot be inferred from this study, the urinary obstruction also increases renal vascular resistance, which decreases the renal blood flow in proportion to the decrease in GFR, so that the filtration fraction is unchanged. Thus, these two mechanisms of preservation of filtration fraction in normal conditions and in obstructive uropathy have a common endpoint but opposite cause-effect relationships.

In conclusion, the surgical relief of renal obstruction lowers the arterial blood pressure, which can be explained by a decrease in renal vascular resistance. The fact that in this, as well as in other studies, ESWL did not decrease the blood pressure could reflect a relatively small obstruction in these patients, or a balance between blood pressure raising and lowering effects.

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