

## Do the applied shock wave numbers and the application side affect pancreatic exocrine functions in patients who have undergone extracorporeal shock wave lithotripsy for upper urinary tract calculi?

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**Aim:** To investigate the effect of extracorporeal shock wave lithotripsy (ESWL) on the pancreatic exocrine functions related to the number of high-energy shock waves and the ESWL-applied kidney side for upper urinary tract stones.

**Materials and methods:** Included in the study were 76 patients undergoing ESWL for proximal ureteral or kidney stones. The right kidney group (RKG) consisted of 40 patients who underwent ESWL for right kidney stones and the left kidney group (LKG) consisted of 36 patients who underwent ESWL for left kidney stones.

**Results:** The observed changes in plasma amylase and lipase levels were not statistically significant compared with the pre-ESWL values in both groups. The relationship between the number of applied shock waves (SWs) and the serum amylase and lipase after ESWL showed a statistically significant positive correlation in the RKG but not in the LKG.

**Conclusion:** There were no statistically significant differences between the pre- and post-ESWL serum amylase and lipase levels. However, a statistically significant positive correlation was found between the number of SWs applied and the post-ESWL amylase and lipase levels in the RKG. Although clinical and experimental studies have shown the safety of ESWL, avoiding excess sessions and an unnecessarily high number of SWs may be helpful in the prevention of the potential risks of ESWL.

**Key words:** Pancreatic exocrine functions, ESWL, urinary stone

### Üst üriner taş nedeniyle ESWL uygulanan hastalarda uygulama tarafı ve şut sayısı pankreas ekzokrin fonksiyonları etkiler mi?

**Amaç:** Üst üriner sistem taşları için uygulanan ESWL'nin pankreas ekzokrin fonksiyonları üzerindeki etkisinin şok sayısı ile ve ESWL uygulanan böbrek tarafı ile ilişkisini araştırmak.

**Yöntem ve gereç:** Bu prospektif çalışma üst üreter ve böbrek taşları için ESWL uygulanan ardışık 76 hastayı içermektedir. Sağ böbrek taşı nedeniyle ESWL uygulanan 40 hasta sağ böbrek gurubu (RKG), sol böbrek taşı nedeniyle ESWL uygulanan 36 hasta da sol böbrek gurubu (LKG) olarak adlandırıldı.

**Bulgular:** ESWL sonrası serum amilaz ve lipaz değerlerindeki değişiklikler ESWL öncesi değerlerle karşılaştırıldığında istatistiksel olarak anlamlı değildi. Serum amilaz ve lipaz değerleriyle uygulanan şok dalga sayısı arasındaki ilişkiye bakıldığında ise RKG'da pozitif korelasyon varken, bu korelasyon LKG'da tespit edilmedi.

**Sonuç:** Bu çalışmada, ESWL sonrası serum amilaz ve lipaz değerlerinde istatistiksel olarak anlamlı bir artış bulmadık. Ancak, RKG' da uygulanan şut sayısı ile ESWL sonrası serum amilaz ve lipaz değerleri arasında pozitif bir korelasyon gördük. Klinik ve deneysel çalışmalar ESWL'nin genel olarak güvenli olduğunu işaret etse de gereğinden fazla seans ve şut sayısından kaçınmak ESWL'nin potansiyel risklerini önlemek için faydalı olabilir.

**Anahtar sözcükler:** Pankreas ekzokrin fonksiyonlar, ESWL, üriner taş

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## Introduction

The introduction of extracorporeal shock wave lithotripsy (ESWL) during the early 1980s dramatically changed the management of urinary tract stones (1,2). Nowadays, ESWL is a preferred treatment in patients with renal and ureteral calculi because of its effectiveness, ease of use, and minimally invasive nature (3). In fact, indications for ESWL have expanded, such that 80%-90% of calculi can be treated successfully with ESWL (4). Although shock wave (SW) lithotripsy is the most common treatment for urolithiasis, it can cause serious side effects and acute and long-term complications in the treated organs and surrounding structures. Acute complications are renal hematoma, sepsis, cardiac arrhythmias, vascular injury involving rupture of abdominal aortic aneurysms, pulmonary injury, muscle damage, urinary fistulas, fertility effects, and injuries of the liver, spleen, pancreas, stomach, duodenum, and small and large bowel (5). Data on the long-term complications of ESWL are rare and controversial. The reported development of hypertension as a late complication in some studies (4,6) could not be confirmed by others (7,8). Recently, the development of diabetes mellitus (DM) was proposed to be a late complication of ESWL (9). Several authors reported acute pancreatitis associated with ESWL treatments (10-13). The mechanism leading to acute pancreatitis after ESWL is under discussion; while the pancreas, lying close to the kidneys within the retroperitoneum, might be subject to accidental SWs, other mechanisms involving vasoconstriction are being discussed. ESWL's established efficacy has been associated with a number of side effects and complications that are being increasingly recognized along with its widespread availability and use (4). The aim of this study was to investigate the effect of ESWL on pancreatic exocrine functions related to the number of high-energy SWs and the ESWL-applied kidney side for upper urinary tract stones.

## Materials and methods

Included in this prospective trial were 76 consecutive patients undergoing ESWL for proximal ureteral or kidney stones from March to October 2010, in our department. Exclusion criteria were ages below 18 years, history of pancreatic disease, existing DM,

coagulopathy, the presence of a congenital and/or acquired obstructive uropathy, urinary tract infection, and nonfunctioning kidneys, or signs and symptoms of any gastrointestinal abnormality. All of the patients gave written informed consent before they were enrolled in the study, which was approved by the institutional review board. Patient characteristics (age, sex, and body mass index (BMI)) were recorded; the stone characteristics (stone size, location and side, and number of applied SWs and sessions) were also recorded.

Standard evaluation of the patients before ESWL included renal function tests, urinalysis, urine culture, and intravenous pyelography and/or renal ultrasonography to rule out congenital urinary disorders (such as horseshoe kidney, duplicated systems, and ectopic kidney) and to investigate the suitability of ESWL treatment.

The patients were divided into 2 groups according to the side of the ESWL-treated kidney. The right kidney group (RKG) consisted of 40 patients who underwent ESWL for right kidney stones and the left kidney group (LKG) consisted of 36 patients who underwent ESWL for left kidney stones. All of the patients received only the one-side ESWL application in the supine position. The double-J ureteral stent and nephrostomy tube were not used prior to or after the ESWL procedure. None of the patients had previously received ESWL.

A piezoelectric SW emitter system, the Piezolith 3000 (Richard Wolf, Knittlingen, Germany), was used for ESWL treatment. The Piezolith 3000 was designed to offer 20 power levels and is capable of treatment at 60 or 120 Hz. Testing began at level 11 and the energy level was gradually elevated to level 20. All of the patients were maintained at this energy level. In this study, 120 Hz was chosen as the ESWL treatment rate for all of the patients and the total number of SWs applied during a treatment session varied from 1500 to 4000. For analgesia, the patients received 75 mg of diclofenac sodium intramuscularly 45 min prior to the procedure. None of the patients required general anesthesia or sedation. Blood samples were taken after fasting for 8 h, before starting the procedure; at 1 h after ESWL to evaluate the plasma levels of amylase and lipase as markers for early exocrine pancreatic cell damage; and again

after 1 week. Amylase and lipase were measured in a routine clinical laboratory. Standard radiological follow-up studies, including renal ultrasonography and/or plain abdominal radiography, were performed 1 week postoperatively.

Data were analyzed using SPSS 11.5 for Windows (SPSS, Inc., Chicago, IL, USA). The distribution of the groups was analyzed with the one-sample Kolmogorov-Smirnov test. Both groups showed normal distribution, and therefore parametric statistical methods were used to analyze the data. The results are presented as mean  $\pm$  standard deviation (SD), with statistical significance determined using the chi-square test, Student's t -test, Pearson's correlation, and repeated-measures analysis of variance (ANOVA) with  $P < 0.05$  considered as statistically significant.

## Results

The mean age, BMI, stone diameter, operative time, and number and power of applied SWs were similar in both groups. The patient characteristics are shown in Table 1.

The observed changes in plasma amylase and lipase levels were not statistically significant compared with the pre-ESWL values in both groups. All of the measured serum amylase and lipase values

are shown in Table 2. The relationship between the number of applied SWs and the serum amylase and lipase levels after ESWL showed a statistically significant positive correlation in the RKG but not in the LKG (Table 3). No major complications such as renal hematoma or acute pancreatitis were observed in any of the patients. Failure to respond to treatment was observed in 8 patients (20%) in the RKG and 6 patients (16%) in the LKG; therefore, these patients were further treated with ureteroscopy.

## Discussion

ESWL is a revolutionized treatment for patients suffering from urinary stones. Many patients with urinary tract stones receive benefit from this technology. Although ESWL is noninvasive and safe (14,15), clear evidence also suggests that ESWL can cause acute tissue damage and long-term renal scar formation. In fact, almost every abdominal organ has been reported to be injured during clinical ESWL treatment (16). Therefore, since the kidney can potentially experience significant damage secondary to ESWL, the potential for the development of long-term renal dysfunction has been a significant concern. The injury usually has limited clinical impact, but there is potential for serious acute and long-term effects.

Table 1. Demographics, stones, and treatment characteristics of the patients (mean  $\pm$  SD).

	RKG (n = 40)	LKG (n = 36)	P
Age (years)	37.0 $\pm$ 11.6	40.2 $\pm$ 14.5	ns
BMI (kg/m <sup>2</sup> )	24.9 $\pm$ 3.1	24.9 $\pm$ 3.0	ns
Men/women	29/11	21/15	ns
Stone size (mm)	12.6 $\pm$ 4.0	12.4 $\pm$ 4.8	ns
Number of SWs	2926 $\pm$ 863	2793 $\pm$ 957	ns
Number of sessions	2.1 (range: 1-4)	2.2 (range: 1-4)	ns
Operative time (min)	31 $\pm$ 9.8 (range: 15-50)	32 $\pm$ 9.6 (range: 15-50)	ns
Power (kV)	17 $\pm$ 2.3 (range: 11-20)	17 $\pm$ 2.7 (range: 11-20)	ns

BMI: body mass index, RKG: right kidney group, LKG: left kidney group, ns: nonsignificant.

Table 2. The time course of serum variables before and after ESWL (mean  $\pm$  SD).

		Before ESWL	One hour after ESWL	One week after ESWL	P
Amylase	RKG	68.3 $\pm$ 17.4	69.0 $\pm$ 19.3	66.3 $\pm$ 17.9	ns
	LKG	60.4 $\pm$ 16.1	58.6 $\pm$ 17.6	61.1 $\pm$ 18.8	ns
Lipase	RKG	34.4 $\pm$ 16.3	36.2 $\pm$ 17.6	33.0 $\pm$ 15.5	ns
	LKG	32.0 $\pm$ 11.1	33.2 $\pm$ 11.6	29.8 $\pm$ 11.1	ns

Amylase reference values: 26-102 U/L, lipase reference values: 10-73 U/L.

Repeated-measures ANOVA.

RKG: right kidney group, LKG: left kidney group, ns: nonsignificant.

Table 3. The relationship between the numbers of applied SWs and serum amylase and lipase values.

		One hour after ESWL		One week after ESWL	
		Amylase	Lipase	Amylase	Lipase
RKG	r	0.584	0.507	0.591	0.531
	P	<0.001	0.002	<0.001	0.001
LKG	r	0.078	0.160	-0.042	-0.180
	P	0.689	0.406	0.828	0.350

RKG: right kidney group, LKG: left kidney group.

The delivery of SW energy to the kidney results in some degree of acute renal injury, including interstitial bleeding and disruption of small to medium renal arteries and veins (17). This may result in intrarenal bleeding (hematoma), which may extend into the perinephric tissue. The reported incidence of renal hematoma varies between 0.28% and 4.1% in large series (18). The risk factor most commonly associated with the development of hematoma is hypertension, especially when it is poorly controlled. The issue of DM after SW lithotripsy treatment is also controversial. Krambeck et al. (9) reported a greater risk of DM after ESWL for proximal ureteral and kidney calculi in a 19-year follow-up. Patients who had been treated conservatively for urinary tract calculi served as controls in that study. The authors reported new-onset DM in 16.8% of their patients treated with ESWL, compared to 6.7% of

patients in the control group. They suggested that the increased incidence of DM might be a consequence of pancreatic trauma caused by ESWL, with the consecutive destruction of islet cells leading to an insufficiency of endocrine pancreatic function. However, current studies suggested that ESWL did not enhance new onsets of DM (19). In this study, we aimed to evaluate only the exocrine function of the pancreas. Aside from the therapeutic use of ESWL for urinary tract stones, it has repeatedly been described as a safe and efficient method for treating pancreatic duct stones (20). However, acute pancreatitis after ESWL was reported in up to 5.4% of patients, indicating that SWs directed at the pancreas lead to a higher risk of pancreatic tissue damage than SWs focused on urinary tract stones (20). Data on acute damage of the pancreas after ESWL for urinary stones are rare and controversial. Lingeman et al.

(4) showed that there is a rise in pancreatic enzymes after ESWL. Kirkali et al. (21) also reported a slight increase in blood amylase and lipase after ESWL for upper urinary tract stones, but the increase was only moderate and other variables remained within their normal laboratory limits. Therefore, this increase was not assessed as pathological by the authors. In contrast to these studies, Deliveliotis et al. (22) and Apostolov et al. (23) found no increase in serum amylase and lipase values.

In the present study, the observed changes in plasma amylase and lipase levels were not statistically significant compared with the pre-ESWL values in both groups.

We did not obtain any clear finding indicating that the right side application has a far more serious effect on pancreatic tissue than the left side application of the high-energy SWs of ESWL, but we did notice that the pancreatic tissue in right side application was affected more seriously by the number of SWs compared to left side application. There was a statistically significant positive correlation among the number of SWs applied in the RKG and the post-ESWL amylase and lipase values. The same

correlation was not seen in the LKG. It was interesting that the number of cases published relating to acute pancreatic damage as a result of right side treatment was observed to be rather high compared to left side ESWL applications.

Although no acute pancreatitis cases were observed in our study, to our knowledge, approximately 6 cases of acute pancreatitis or necrotizing pancreatitis in ESWL treatment to renal calculi were reported in the literature. ESWL was applied for right renal calculi in 4 of these cases (12,13,24,25), for bilateral calculi in 1 case (12), and for left kidney calculi in 1 case (26).

We did not find any statistically significant differences between the pre- and post-ESWL serum amylase and lipase levels. However, this study demonstrated a statistically significant positive correlation between the number of SWs applied and the post-ESWL amylase and lipase levels for patients who underwent the right side ESWL applications for upper urinary tract stones. Although clinical and experimental studies have shown the safety of ESWL, avoiding excess sessions and an unnecessarily high number of SWs may be helpful in the prevention of the potential risks of ESWL.

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