## ORIGINAL PAPER

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# Long-term effects of percutaneous nephrolithotomy on renal morphology and arterial vascular resistance as evaluated by color Doppler ultrasonography: preliminary report

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Abstract We evaluated the long-term effects of percutaneous nephrolithotomy (PNL) on renal morphology and vascular resistance. Parenchyma thickness, echogenicity and resistive index (RI) of upper, middle and lower poles of operated and contralateral kidneys of 41 patients with 82 renal units who underwent unilateral PNL with single pole access between 2000 and 2002 were examined separately by color Doppler ultrasonography. Mean patient age and duration between PNL and evaluation time were  $\pm$  11.53 years and 46.44  $\pm$  10.9 months, respectively. In operated kidney, mean RI, parenchyma thickness and echogenicity of the access pole were not statistically different than those of the adjacent two poles (0.608  $\pm 0.053$  vs.  $0.608 \pm 0.052$  for RI, P = 0.895;  $11.46 \pm 2.58$  $11.41 \pm 2.68$  mm for parenchyma thickness, P = 0.838;  $0.049 \pm 0.31$  vs.  $0.073 \pm 0.33$  for parenchyma echogenicity, P = 0.160, respectively). Although mean RI and parenchyma thickness of access pole were statistically significantly different than the mean values contralateral kidney  $(0.562 \pm 0.032)$  $14.31 \pm 1.37$  mm, respectively), no statistical difference was found between mean parenchyma echogenicities of both of them (echogenicity of contralateral kidney was 0, P = 0.317). No significant difference was found between the average echogenicities of the three poles of the operated and contralateral kidneys  $(0.063 \pm 0.32 \text{ vs.})$ 0, P = 0.080). In 14 patients RI decreased from  $0.694 \pm 0.058$  to  $0.602 \pm 0.056$  in operated kidney

(P=0.001) and from  $0.604\pm0.06$  to  $0.559\pm0.031$  in contralateral kidney (P=0.018) following PNL. It seems that PNL does not cause renal scarring, renal parenchymal loss or increase in renal vascular resistance in the long term. However, prospective studies must be performed for more definitive conclusions.

**Keywords** Renal stone disease · Percutaneous nephrolithotomy · Color Doppler ultrasonography · Resistive index · Renal damage

## Introduction

Urinary stone disease is one of the important health care problems. Incidence of nephrolithiasis is about 10–12% in Caucasian people [1]. Additionally, it has a high recurrence potential, which is about 50% at 5 years in people who have a tendency to develop stones [2]. Stone disease also affects children and the recurrence rate in children is greater than in adults due to the longer risk period [1, 3].

Although there is no definitive treatment, except the secondary cases to some diseases, the goals of treating such a disease with high incidence and recurrence potential are to achieve maximal stone clearance with minimal morbidity and maximal nephron preservation and to take precautions to delay the recurrence. Therefore, shock wave lithotripsy (SWL) and minimally invasive surgical treatment methods are currently preferred over open surgery [1, 3].

Shock wave lithotripsy is the first alternative for upper urinary tract stone disease. However, the size, composition and position of stones and the presence of some renal anomalies limit SWL use. Stones greater than 2 cm, composed of cystine and calcium oxalate monohydrate and positioned in the lower pole are not suitable for SWL. It also has a low success rate when the infundibular angle is lower than 70°, the calyx neck is narrow or UPJ obstruction is present. However, percu-

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taneous nephrolithotomy (PNL) can be applied easily, safely and effectively in all these conditions. The only contraindication of PNL is bleeding diathesis. Compared to open surgery, patients have lower postoperative discomfort and quicker convalescence. Therefore, since the work of Fernstrom and Johansson [4] in 1975, PNL is commonly used in clinical practice and is the standard treatment method for kidney stones if SWL is not suitable or unsuccessful.

All interventions which are done to clear stones cause little or much harmful effects on kidney. Therefore, it is normal to think that PNL can deteriorate renal morphology and functions. However, the literature does not support this conception. Many studies have suggested that PNL has no or minimal deleterious effects on kidney. The effect of minimally invasive techniques on renal function is presumed to be negligible [5]. However, results reported in the literature are not long term. Furthermore, to our knowledge, no study assessing long-term renal morphological changes associated with PNL by color Doppler ultrasonography has been published to date. We hypothesized that following operation, the determination of a significant decrease in parenchyma thickness and significant increases in intrarenal resistive index (RI) and parenchymal echogenicity over a relatively long-term period might indicate PNL-associated renal parenchymal damage. Renal parenchymal echogenicity, the sonographic parameter that correlates best with pathologic findings, results from scarring [6] and is determined primarily by tubular atrophy and interstitial inflammation [7]. Scarred kidneys also show higher RI values [8]. Therefore, the present retrospective study aimed to compare the RI, parenchyma thickness and echogenicity of the access pole of the operated kidney (renal pole through which percutaneous access into the renal collecting system was obtained) with values of the adjacent poles of the same kidney and with those of the contralateral kidney as evaluated by color Doppler ultrasonography.

#### **Materials and methods**

Archives of the urology department from 2000 to 2002 were reviewed and patients who underwent PNL operation with single renal pole access due to unilateral stone disease were determined. Patients with multiple PNL sessions and having a history of SWL or open surgery in the same kidney were excluded. The purpose of the study was explained to the remaining ones over the telephone and they were asked to come to the hospital for further evaluation. Forty-one patients (15 females, 26 males) with 82 renal units were examined with color Doppler ultrasonography after general systemic examination, brachial blood pressure and renal function test measurements and urine culture examinations. The patients' characteristics are given in Table 1.

No systemic disorder (cardiac, renal or hepatic, hypertension and diabetes mellitus) or a history of drug use for their systemic diseases was determined in any patient. Heart rates of the patients ranged between 56 and 90 beats/min during examination.

#### Technical method of PNL

Over a 0.038 in. guide wire (Scimed®, Boston Scientific Corporation, New York, USA), the nephrostomy route was dilated up to 30 Fr using an Amplatz-type graduated renal dilatation set (Microvasive<sup>®</sup>, Boston Scientific International, France). The Amplatz nephrostomy working sheath with 30 Fr inner and 34 Fr outer diameters (Microvasive®, Boston Scientific International) was positioned over the no. 30 Fr dilatator and passed into the collecting system. The 26 Fr nephroscope (Karl Storz®, Germany) was used for stone removal. Stones were fragmented via pneumatic lithotripter (Calculith lithotripter, PCK, İstanbul, Turkey) before extraction. Percutaneous access was performed through the middle pole in 11 operations and the lower pole in the remaining 30 operations.

Serum creatinine and blood urea nitrogen levels were within the laboratory ranges in all the patients preoperatively and currently (laboratory ranges for creatinine: 0.6–1.2 mg/dl and for BUN: 5–24 mg/dl). Patients with bacteriologic evidence of urinary infection were examined after treatment with appropriate antibiotics. Due to technical insufficiency, stone component analysis was not performed in any patient.

NSAIDs were stopped 24 h before color Doppler ultrasonography examination because they might affect RI measurements [9, 10]. Since measuring objective kidney parameters (parenchymal thickness, echogenicity and RI) by color Doppler ultrasonography is highly variable and subjective, to minimize subjective results as far as possible, all examinations were performed in the fasting state after 30 min of rest while supine and under similar ambient conditions on the operated and contralateral kidney, which served as controls, using a wall filter (50 Hz) and convex 2–5 MHz transducers attached to a Doppler unit (HDI 5000; Philips Medical Systems, Bothell, WA, USA), separately for upper, middle and lower poles by the same highly experienced roentgenologist, who was unaware of which one of the renal poles was the access pole. Blood flow rate was obtained using the fast Fourier transform method. Before the RI measurement, the renal parenchyma thickness was determined as the shortest distance from the renal sinus fat to the renal capsule. Echogenicity of the renal parenchyma was measured qualitatively according to an ordinal system based on the echogenicity of the liver (Grade 0: echo lower than that of liver; Grade 1: echo equal to that of liver; Grade 2: echo greater than that of liver). The degree of the pyelocaliectasis was graded according to ultrasonography findings as absent, mild, moderate and significant.

**Table 1** Characteristics of the patients

Mean age (range) (years)	All patients (no.: 41): 38.29 ± 11.53 (19–60) Males (no.: 26): 36.35 ± 10.21 (19–54) Females (no.: 15): 41.67 ± 13.21 (19–60)		
Side of the operated kidney	( ( (		
Right	15 patients		
Left	26 patients		
Time between PCNL and current evaluation time	$46.44 \pm 10.9 \ (30-58) \ months$		
Degree of preoperative hydronephrosis in operated kidney (no. of patients, %)			
Absent	10 (24.4%)		
Mild	7 (17.07%)		
Moderate	16 (39.02%)		
Significant	8 (19.51%)		
Degree of hydronephrosis at present time in operated			
kidney (no. of patients, %)			
Absent	35 (85.37%)		
Mild	5 (12.2%)		
Moderate	1 (2.43%)		
Significant	0		
Mean preoperative stone load in operated kidney (range) (cm <sup>2</sup> )	$4.66 \pm 1.78 \ (1.8 - 9.6)$		
Preoperative stone location in operated kidney			
(no. of patients)			
In only renal poles	25		
In only renal pelvis	7		
In both renal poles and pelvis	9		
Mean stone load in operated kidney at present time (range) (cm <sup>2</sup> )	$0.42 \pm 0.53 \; (0-1.9)$		

Doppler spectra were obtained from arcuate arteries at the corticomedullary junction. The Doppler angle was maintained between 30° and 60° to correct for the angle between the axis of the beam and the vessels for all measurements. At least three measurements were obtained in the cranial portion, midportion and caudal portion and averaged for each kidney at each session. The waveforms were optimized by adjusting the pulse repetition frequency to the lowest possible level that would not produce aliasing. A spectrum was considered optimal if 3–5 consecutive similar-appearing waveforms were noted. Peak systolic and end-diastolic velocities of the arteries were recorded, and intrarenal RI values were measured automatically by the software of the ultrasound system using the equation: RI = (systolic peak velocity – diastolic peak velocity)/systolic peak velocity. Although Mostbeck et al. [11] suggested a regression equation to correct the RI to a heart rate of 80 beats/ min, their findings have been refuted in a study of Kublickas et al. [12], who observed no reason to correct the RI for heart rate in the ranges considered clinically normal (60-90 beats/min). Also in a recent study, no correlation was found between the heart rate and renal RI [13]. In our study heart rates were in the normal range in all patients, so we did not need to adjust the RI.

The RI, parenchyma thickness and echogenicity values obtained from two poles adjacent to the access pole of the operated kidney and three poles of the contralateral kidney were averaged arithmetically. Statistical comparison was made between these arithmetic means and the access pole.

## Statistical analysis

Values represent means  $\pm$  standard deviation. All statistics were made by SPSS 10.0 for Windows software. Distribution of parameters was tested using Kolmogorov–Smirnov's goodness of fit test. According to the results of this test, in-group analysis was made with paired samples or Wilcoxon signed rank tests. For between-group analysis, independent samples or Mann–Whitney U tests were used. P < 0.05 was accepted as significant.

## **Results**

### Parenchyma thicknesses

Without determining the parenchyma thickness of each renal pole of the operated and contralateral kidneys separately, parenchyma thickness of the whole kidney had been determined preoperatively as the average of three poles. Pre- and postoperative parenchyma thicknesses were  $12.12\pm2.54$  and  $11.43\pm2.55$  mm in operated kidney (P < 0.0001),  $14.76\pm1.32$  and  $14.31\pm1.37$  mm in contralateral kidney (P < 0.0001), respectively. Both pre- and postoperative values were statistically significantly lower in operated kidney than in contralateral kidney (P < 0.0001 for both).

Postoperative assessment performed for each of the renal poles separately revealed that the parenchyma thickness of the access pole was not statistically different

Table 2 Range and mean RI, parenchyma thickness and echogenicity of operated and contralateral kidney

	Operated kidney			Contralateral kidney	
	Access pole (A)	Adjacent two poles (B)	P <sup>a</sup>	Average of three poles (C)	$P^{\mathrm{b}}$
RI Parenchyma thickness (mm) Parenchyma echo	0.608 ± 0.053 (0.52–0.76) 11.46 ± 2.58 (6–16) 0.049 ± 0.31 (0–2)	0.608 ± 0.052 (0.53–0.74) 11.41 ± 2.68 (6–16) 0.073 ± 0.33 (0–2)	0.895 0.838 0.160	$0.562 \pm 0.032 \ (0.51 - 0.65)$ $14.31 \pm 1.37 \ (11.7 - 17.3)$	<0.0001 <0.0001 0.317

<sup>&</sup>lt;sup>a</sup>Between A and B

than that of the adjacent two poles and was statistically lower than the average parenchyma thickness of the contralateral kidney (Table 2).

#### Parenchyma echogenicity

No assessment could be made of the postoperative alterations in parenchyma echogenicities of the operated and contralateral kidneys due to the absence of records on the preoperative condition. However, no statistically significant difference was currently found between the average echogenicity of the three poles of the operated and contralateral kidneys  $(0.063 \pm 0.32 \text{ vs. } 0, P = 0.080)$ .

Similar to the parenchyma thickness results, the mean echogenicity level of the access pole was not statistically different from that of the adjacent two poles (Table 2). Additionally, no statistical difference was found between mean parenchyma echogenicities of the access pole and contralateral kidney.

## Resistive index

The mean RI value of the three poles of 41 operated kidneys was statistically higher than that of the contralateral kidney  $(0.61\pm0.053~{\rm vs.}~0.562\pm0.032,~P<0.0001)$ . Comparison between the renal poles revealed that the mean RI of the access pole of the operated kidney was not statistically different than that of the adjacent two poles, although it was significantly higher than the mean RI value of the contralateral kidney (Table 2).

Determination of RI had been performed before the operation in the operated and contralateral kidneys in only 14 patients. In these patients, mean pre- and post-operative RI values were  $0.694 \pm 0.058$  and  $0.602 \pm 0.056$  in operated kidney (P = 0.001) and  $0.604 \pm 0.06$  and  $0.559 \pm 0.031$  in contralateral kidney (P = 0.018). RI was statistically greater in operated kidney than in contralateral kidney both in pre- and postoperative periods (P = 0.0001 and P = 0.018, respectively).

## **Discussion**

Open surgery was the standard therapy for urinary calculi up to about 30 years ago. However, the

development of minimally invasive treatment methods, such as SWL, and simultaneous endourological procedures like ureterorenoscopy and PNL has replaced open stone surgery almost completely.

It is well recognized that in the western world, a percutaneous approach is preferred to open surgery for most cases of complex renal calculi resistant to SWL. Monotherapy with PNL is safe and effective in the management of staghorn and complex renal calculi in one single hospital stay. The safety and efficacy of PNL have been proved by a number of studies investigating injuries to the kidney by various techniques, such as excretory urogram, antegrade nephrostography, grayscale ultrasound, computerized tomography, DMSA and DTPA renal scintigraphy, mercaptoacetyl triglycine nuclear renography, SPECT (single photon emission computed tomography), renal subtraction angiography, experimental studies, histopathologic examination and serum creatinine-serum and urinary enzyme levels (NAG: N-acetyl-glycosaminidase)-glomerular filtration rate measurements. However, to our knowledge, its adverse effects on the kidney morphology have not been evaluated by color Doppler ultrasonography to date. In the present study, the safety of PNL was tried to be determined by the differences in renal parenchyma thickness, parenchyma echogenicity and intrarenal RI between the operated and contralateral kidneys, between the access pole of the operated kidney and contralateral kidney and between the access pole and adjacent two poles of the operated kidney.

Technetium—99m-DMSA renal scintigraphy is otherwise considered a reference investigation for the diagnosis of renal scarring [14, 15]. However, it is an invasive method that is not readily accessible in all centers, exposes the patients to radiation and an intravenous agent injection and may not differentiate between old scarring and acute parenchymal involvement [16]. On the other hand, the advantages of Doppler ultrasonography are obvious: no ionizing radiation, no need for intravenous contrast medium, low cost and greater availability. For these reasons, we did not compare color Doppler ultrasonography results with those of renal scintigraphy in this study. We think that this may be the subject of another study.

The results of the present study suggest that PNL does not cause renal parenchyma damage. Supporting this finding, we could not determine statistically significant differences between parenchyma thicknesses and

<sup>&</sup>lt;sup>b</sup>Between A and C

echoes of access pole and adjacent poles and between parenchyma echoes of access pole and contralateral kidney and between parenchyma echoes of operated and contralateral kidneys. It is strongly possible that significant differences in parenchyma thicknesses between contralateral and operated kidneys or access pole at evaluation time are associated with the preoperative parenchymal status of the stony kidney, rather than the devastating effect of PNL on kidney, since there was also a significant difference in parenchyma thicknesses before the PNL. Most probably, parenchymal destruction due to urinary obstruction resulting from the stone effect is the cause of significant differences in parenchyma thickness. Although the difference between preoperative and current parenchyma thicknesses in operated kidney was statistically significant, it was quantitatively small (approximately 0.6–0.7 mm) and might possibly be caused by the sensitivity of ultrasonography in spite of all attempts to increase the sensitivity such as the use of the same sonography equipment by the same operator. Additionally, parenchyma thickness was still in the normal range for adults postoperatively. From these findings, it seems that PNL does not result in parenchyma loss. Furthermore, almost normal-appearing parenchyma echogenicity in the access pole suggested to us that scarring associated with PNL was negligible. Our findings are consistent with the published literature. It is generally believed that transparenchymal access to the pelvocaliceal system through percutaneously established large tracks seems to cause limited damage which resolves in minor scars. Desai et al. [17] and Mor et al. [18] performed radioisotope scans before and after PNL and showed no evidence of scarring in patients with staghorn or complex renal calculi. Lechevallier et al. [19] evaluated local uptake and scarring of the treated area in patients treated with SWL (12 patients) or PNL (10 patients) by SPECT before and 30 days after stone treatment. In the SWL group, all the kidneys demonstrated a loss of local uptake, whereas 7 of the 10 in the PNL group did so. In the SWL group, 4 of the 12 kidneys had a local loss exceeding 4% but only 2 of 10 kidneys in the PNL group. There were seven scars in the treated area in the SWL group and six in the PNL group. In an experimental study, mean estimated scar volume of the 30 and 11 Fr PNL tracts was 0.29 and 0.40 cm<sup>3</sup>, which translated into a mean fractional loss of parenchyma of 0.63 and 0.91%, respectively (P not significant) [20].

After the first Doppler ultrasonography study on the analysis of renal arterial system by Arima et al. in 1979, new insight into the physiology of the kidney has emerged, enabling the detection of subtle renal blood flow changes associated with various pathophysiological conditions [10, 21]. Doppler ultrasonography is capable of not only producing morphologic images, but also calculating the RI by characterizing altered waveforms in response to elevations of renal vascular resistance and may possibly be used to discriminate among various pathophysiological conditions [10]. Additionally, as

different from the radionuclide renography, Doppler ultrasonography gives precise information about the vascular anatomy or blood flow rates in different branches of the renal arteries [22]. Furthermore, Doppler ultrasonography has been found to be sensitive and specific in determining renal damage [16]. Therefore Doppler ultrasonography has undergone extended use in the diagnosis of various renal disorders.

Assessment of the intrarenal RI, a physiological parameter reflecting the degree of renal vascular resistance, is a noninvasive diagnostic modality for studying changes in the renal arterial system. RI has the benefit of being independent of the Doppler angle. Since it is measured at an artery in the renal parenchyma, RI is elevated in diseases involving the tubulointerstitial or vascular system. For this reason, RI has proved to be a sensitive tool for monitoring vascular and tubulointerstitial disorders of the kidney. It is widely used to detect intrarenal edema, which occurs in transplant rejection, acute tubular necrosis and obstructive pyelocaliectasis. In all these conditions RI levels greater than 0.70 are considered to indicate pathological changes [22].

Despite the wide use of Doppler ultrasonography in the assessment of the renal vascular system, only one study has reported the results of intrarenal RI alteration following PNL operation in the literature to date [23]. In this study, Kilic et al. evaluated patients who underwent unilateral PNL for UPJ stone, which caused partial urinary obstruction, with color Doppler ultrasonography preoperatively and during 30 postoperative days. RI dropped to levels lower than 0.70 after the seventh postoperative day in the kidneys with preoperative RI≥0.70 and no change was observed in those kidneys with preoperative RI  $\leq$  0.70. The authors concluded that a threshold RI level of 0.70 might indirectly reflect the presence or absence of functionally significant obstruction in chronic partially obstructed kidneys and that decrease and normalization of RI was a rapid process following the relief of obstruction by PNL.

We performed this present study to determine whether there were any alterations in renovascular resistance in the long term that were attributable to PNL. Compared to adjacent renal poles and contralateral kidney, a significant increase in RI in the access pole of the operated kidney would indicate negative effects of PNL on the renal vascular system and morphology. However, we did not observe any significant difference between access pole and adjacent poles in operated kidney. Although it was statistically greater than the RI value of contralateral kidney, mean RI of access pole was very low and still in the normal range for adults. Therefore we conclude that PNL did not cause renal vascular damage, supporting published literature. In an experimental study, corrosion casts and renal subtraction angiography performed after PNL demonstrated no significant vascular defects [24].

A significant decrease in RI in the contralateral normal kidney of our study patients after the operation is in

concordance with the findings of an experimental study by Shokeir et al. [9]. In this study mean RI of the contralateral kidney decreased significantly versus baseline at the end of 8 weeks of unilateral obstruction and remained stable after relief of obstruction.

## **Conclusions**

Although, from the results, it seems possible to consider that PNL does not deteriorate renal morphology and vascular system in the long term, it is really difficult to draw a definitive conclusion with only the results of a postoperative assessment study since the scarring, echo patterns and low resistive indices may have been present prior to surgery. The absence of preoperative examinations limits the outcomes of the current study. Therefore, the present work should be considered as a preliminary report to build a prospective one. A prospective study is currently in progress for more definitive conclusions, and results will be reported later.

In addition, color Doppler ultrasonography is a study evaluating renal morphology and vascular system macroscopically, so it must be remembered that the sensitivity of color Doppler ultrasonography is not enough to detect minor change in the limited area, such as a very small part of the access pole, in which renal dilatators and nephrostomy working sheath perforate the renal parenchyma. In that case, it is still possible that PNL might cause minor injuries in the limited area around the access pole. Therefore, this problem may be elucidated in the studies of color Doppler ultrasonography combined with the histopathology or angiography examinations.

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