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Does lithotripsy increase stone recurrence? A comparative study between extracorporeal shockwave lithotripsy and non-fragmenting percutaneous nephrolithotomy

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Extracorporeal shockwave lithotripsy;
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Fragmentation

ABBREVIATIONS

ESWL, extracorporeal shockwave lithotripsy;
HR, hazards ratio;
KUB, plain abdominal radiograph of the kidneys, ureters and bladder;

Abstract ***Objectives:*** To investigate the effect of stone fragmentation on late stone recurrence by comparing the outcome of extracorporeal shockwave lithotripsy (ESWL) and non-fragmenting percutaneous nephrolithotomy (PCNL), and to investigate factors contributing to recurrent calculi.

Patients and methods: We evaluated stone recurrence in 647 patients who initially achieved a stone-free status after ESWL and compared the outcomes to 137 stone-free patients treated with PCNL without stone fragmentation. Patients were evaluated every 3 months during the first year and every 6 months thereafter to censorship or time of first new stone formation. Stone recurrence rates were calculated using the Kaplan–Meier method. The effects of demographics, stone characteristics, and intervention on the recurrence rate were studied using the log-rank test and the Cox-regression analysis.

Results: For ESWL the recurrence rates were 0.8%, 35.8% and 60.1% after 1, 5 and 10 years, which were comparable to the 1.5%, 35.5% and 74.9%, respectively found in the PCNL group ($P = 0.57$). Stone burden (>8 mm) and a previous history of stone disease were significantly associated with higher recurrence rates regardless of the method of stone intervention ($P = 0.02$ and $P = 0.01$,

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NCCT, non-contrast CT;
OSS, open stone surgery;
PCNL, percutaneous nephrolithotomy;
US, ultrasonography

respectively). In the ESWL group, a stone length of >8 mm showed a higher recurrence rate ($P = 0.007$). In both the ESWL and PCNL groups, there was a significant shift from baseline stone location, with an increased tendency for most new stones to recur in the calyces as opposed to the pelvis.

Conclusions: In comparison with PCNL, ESWL does not increase long-term stone recurrence in patients who become stone-free. The stone burden appears to be the primary factor in predicting stone recurrence after ESWL.

Introduction

Since the introduction of extracorporeal shockwave lithotripsy (ESWL) by Chaussy et al. [1] in the early 1980s, the management of renal calculi has changed dramatically. Currently, ESWL is the recommended primary treatment option for renal stones of <2 cm, whereas percutaneous nephrolithotomy (PCNL) is preferred for large, complex or staghorn calculi [2].

Although the efficacy of ESWL in treating urolithiasis in adults and children has been established [3,4], there is concern about the increasing rate of new stone formation after ESWL compared with other techniques. Looking carefully at published data identifies marked variability in reported recurrence rates after ESWL ranging from 5% to 20.3% [5–8], and in one study the recurrence rate was higher, reaching up to 70% after 9 years [9]. This might be attributable to the presence of microscopic residual stone fragments left in the collecting system that may act as nidi for stone recurrence [10]. If this hypothesis is true; this would question the long-term efficiency of ESWL.

Previous reports have investigated the recurrence rate after ESWL compared with PCNL to test this hypothesis [11–15]. However, most of those studies [12–15] neglected that stone fragmentation during PCNL might be a contributing factor for stone recurrence exactly as for ESWL. In addition, small sample sizes in some of the publications [11–13] is a hindering factor for adequate interpretation of the results.

The previous controversy and limitations were the trigger to address the issue of late stone recurrence after ESWL. In the present study, a large number of patients were included who initially were stone-free after ESWL and compared the findings for stone-recurrence rates in stone-free patients treated with PCNL without stone fragmentation. Also, we investigated factors predicting late stone recurrence.

Patients and methods

After approval of the Institutional Review Board, the computerised patients' records of 2252 adult patients (aged >18 years), who had a stone-free status at 3 months after the last session of ESWL (from January 1999 through December 2011), were retrospectively reviewed. Another group of 278 adult patients who were stone-free after PCNL using mechanical extraction only (from January 1998 through December 2005) were also retrospectively reviewed.

Patients were excluded if they had a ureteric stone or if any type of intracorporeal disintegration (Lithoclast, ultrasonic or laser) was used during PCNL. Patients with a follow-up of <6 months or with inadequate follow-up data were also excluded. Similarly, patients with evident metabolic or anatomical disorders such as cystinuria, hyperparathyroidism, and congenital renal anomalies (e.g. horseshoe kidney and polycystic kidney) were excluded because of the high rate of stone recurrence.

Pretreatment evaluation included a careful medical history; physical examination; routine blood tests; urine analysis; urine culture; plain abdominal radiograph of the kidneys, ureters and bladder (KUB); urinary ultrasonography (US); and IVU or non-contrast CT (NCCT). Stone length was defined as the largest cross-sectional diameter in a single stone measured on KUB or NCCT in a single stone or the sum of the largest diameters for multiple stones

All patients underwent ESWL using a Dornier Lithotriptor S (Dornier MedTech GmbH, Germering, Germany). The technique of PCNL was previously described in detail [16]. Briefly, a renal puncture was made with the patient prone, using multidirectional C-arm fluoroscopic guidance (BV Pulsera, Philips Medical Systems, Eindhoven, the Netherlands). The tract was dilatated using Alken's coaxial dilators (Karl Storz Endoskope, Tuttlingen, Germany) to 30 F. A 26-F rigid nephroscope (Karl Storz Endoskope) was used through an Amplatz sheath (Boston Scientific Corp., Natick, MA, USA). The stone was removed using forceps. A 22-F nephrostomy tube was placed at the end of the procedure and left *in situ* for 24–48 h.

Follow-up

After treatment, stone-free status was determined in an outpatient clinic setting at 3 months postoperatively

for PCNL and after the last session of ESWL. Patients were evaluated every 3 months during the first year and every 6 months thereafter or when symptoms developed by urine analysis, urine culture, KUB and urinary US or NCCT, whenever indicated. The patients were followed to censorship or time of first new stone formation. During follow-up we advised patients to maintain a high fluid intake and avoid excessive intake of salt, oxalate containing foods and animal proteins, together with adequate intake of citrate containing fruits.

Statistical analysis

Stone and patients characteristics were compared between the ESWL and PCNL groups using the chi-square test for categorical data and *t*-tests for continuous data. Kaplan–Meier estimates of the probability of stone recurrence were plotted. The effects of various factors such as patient age, sex, stone side, site, size, previous stone disease, radio-opacity, stone multiplicity, and type of intervention on the recurrence rate were studied using the log-rank test and Cox regression analysis. A threshold value of 8 mm was used for stone size; this value was of maximal sensitivity and specificity for prediction of stone recurrence and was determined using a receiver operating characteristic curve. Statistical analysis was done using IBM SPSS software version 20 (IBM Corporation, Armonk, NY, USA) and statistical significance was defined as a $P < 0.05$.

Results

The present study included 647 and 137 patients in the ESWL and PCNL groups, respectively. The clinical and radiographic findings were compared between the groups and are summarised in Table 1. While there were statistically significance differences in most of the variables between the groups at baseline, they are unlikely to be of clinical significance, as both groups were stone free after treatment.

Stone recurrence rates at 1, 5 and 10 years after ESWL and PCNL are summarised in Table 2. Our data showed a comparable stone recurrence rate at 1 and 5 years after ESWL compared with PCNL. With longer follow-up, at 10 years there was a trend towards higher new stone formation rate in the PCNL group compared with the ESWL group, but this did not reach statistical significance. The Kaplan–Meier curve in Fig. 1 shows stone recurrence over time in both groups.

Within the ESWL group, there were no patients or stone characteristics associated with time-to-stone recurrence except stone length (Table 2). The log-rank test showed that the rate of stone recurrence was significantly greater ($P = 0.007$) with stone lengths of >8 mm compared with smaller stones. Within the PCNL group stone recurrence was significantly associated with stone multiplicity ($P = 0.015$; Table 2).

Table 1 The patients' and stone characteristics at baseline in the ESWL and PCNL groups.

Variable	ESWL	PCNL	*P*
Number of patients	647	137	
Mean (SD) age, years,	40 (10)	47.6 (10)	<0.001
N (%):			
Gender			<0.001
Male	490 (75.7)	83 (60.5)	
Female	157 (24.3)	54 (39.5)	
Renal morphology			<0.001
Normal	449 (69.4)	58 (42.3)	
Pyelonephritis	46 (7.1)	10 (6.3)	
Hydronephrotic	152 (23.5)	69 (50.4)	
Solitary kidney			<0.001
No	631 (97.5)	116 (84.6)	
Yes	16 (2.5)	21 (25.4)	
Mean (SD) stone size, mm	13.8 (6)	9.4 (1.3)	<0.001
N (%):			
Stone nature			<0.001
De novo	535 (82.7)	93 (67.9)	
Recurrent	112 (17.3)	44 (32.1)	
Stone number			<0.001
Single	507 (78.4)	60 (43.8)	
Multiple	140 (21.6)	77 (56.2)	
Stone opacity			<0.001
Opaque	640 (98.9)	103 (75.2)	
Lucent	7 (1.1)	34 (24.8)	
Side			0.7
Right	312 (48.2)	64 (46.8)	
Left	335 (51.8)	73 (53.2)	
Stone site			<0.001
Pelvis	515 (79.6)	63 (46)	
Calyx	52 (8)	45 (32.9)	
Multiple	80 (12.4)	29 (21.1)	

When we combined patients who underwent ESWL and PCNL as one group, the rate of stone recurrence was significantly higher with a stone length of >8 mm ($P = 0.023$) and a previous history of stone disease ($P = 0.01$; Table 2, Figs 2 and 3). By Cox regression, patients with a stone length of >8 mm were more likely to develop stone recurrence with time [hazards ratio (HR) 1.297, 95% CI 1.015–1659; $P = 0.038$]. In addition, a history of stone disease was also found to be significant for time-dependent stone recurrence (HR 1.257, 95% CI 1.041–1.562; $P = 0.019$).

The site of stone recurrence within the pelvis or calyces was analysed for both groups and compared with baseline site of the original stone (Table 3). In both the ESWL and PCNL groups, there was a shift from baseline stone location, with an increased tendency for most new stones to recur in the calyces as opposed to the pelvis.

Discussion

Several authors have reported long-term stone recurrence rates after ESWL, but their results have been

Table 2 Factors significantly associated with time-dependent recurrence for patients who underwent PCNL and ESWL.

	Time-to-recurrence, months	Recurrence-free status,%			*P*
	Median (95% CI)	1 year	5 years	10 years	
Overall					
Stone nature					0.01
De novo	84 (75.5–92.4)	99	65	38.6	
Recurrent	72 (61.8–82.1)	99.4	61	28	
Stone size, mm					0.023
⩽8	118 (95.5–140.4)	99.2	75.6	48	
>8	72 (65.2–78.7)	99	62.3	38.5	
Intervention					0.058
ESWL	78 (70.9–85)	99.2	64.2	38.9	
PCNL	75 (60–89)	98.5	64.5	25.1	
ESWL group sub-analysis					
Stone size, mm					0.007
⩽8	121 (93–148)	98.8	76.6	56.5	
>8	72 (65–78.8)	99.3	62.3	36.1	
PCNL group sub-analysis					
Stone number					0.015
Single	109 (75.5–142.4)	98	72.4	36.8	
Multiple	66 (57.6–74.3)	98.7	59	17.4	

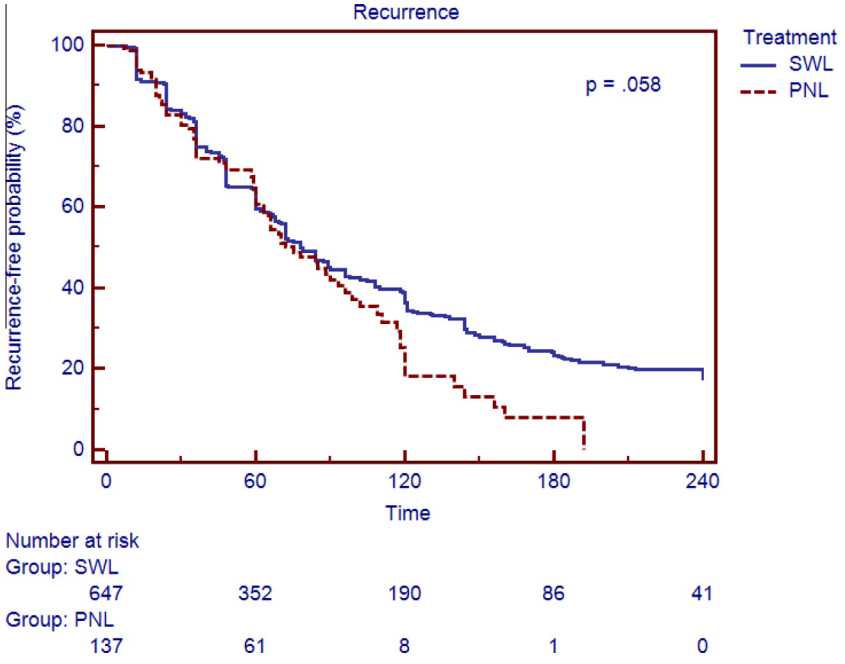

Figure 1 Kaplan–Meier plot for stone recurrence in the ESWL (SWL) and PCNL (PNL) groups. Time, months.

contradictory, with stone recurrence rates ranging from 5% to 20.3% [6–8]. Some claim that the recurrence rate after ESWL is similar to the natural recurrence rate and that ESWL has particular effect on true stone recurrence [6]. On the other hand, Sun et al. [9] reported the highest recurrence rate of 51% in 436 patients at a mean follow-up of 7.1 years; also late recurrences were noted in up to 70% of their patients after 9 years. They concluded that the frequent late recurrences support the speculation that ESWL might lead to higher recurrence rates.

A problem when analysing long-term stone recurrence is the large number of patients who withdraw from the study. The Kaplan–Meier method allowed us to draw long-term conclusions from the data on the remaining cases still being followed. In our present study, the recurrence rates at 1, 5 and 10 years after ESWL were 0.8%, 35.8% and 60.1% using Kaplan–Meier analyses. Other studies have also calculated cumulative recurrence rates using the Kaplan–Meier method [17,18]. In one study [17], the overall ipsilateral

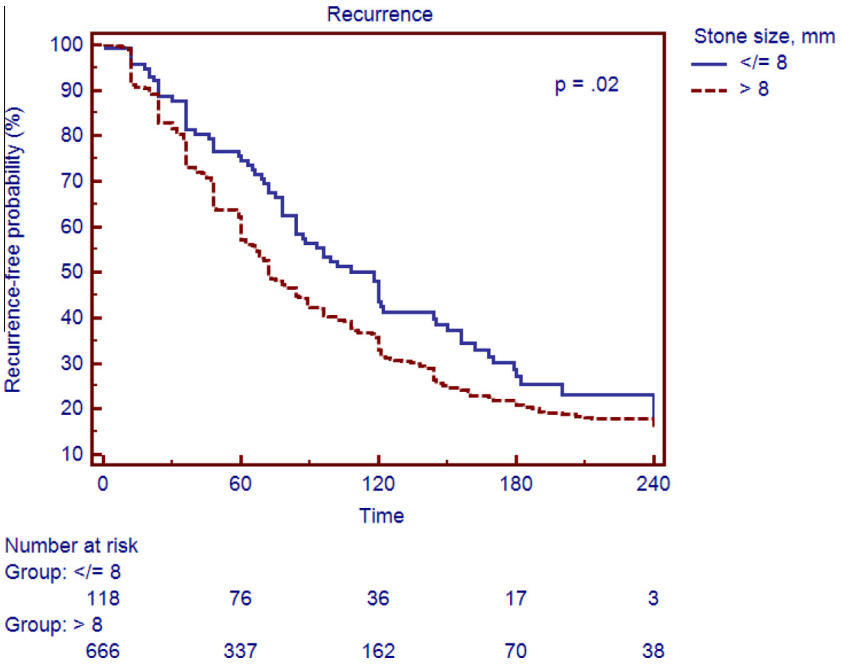

Figure 2 Kaplan–Meier plot for stone recurrence in all 784 patients according to stone length (⩽8 vs >8 mm). Time, months.

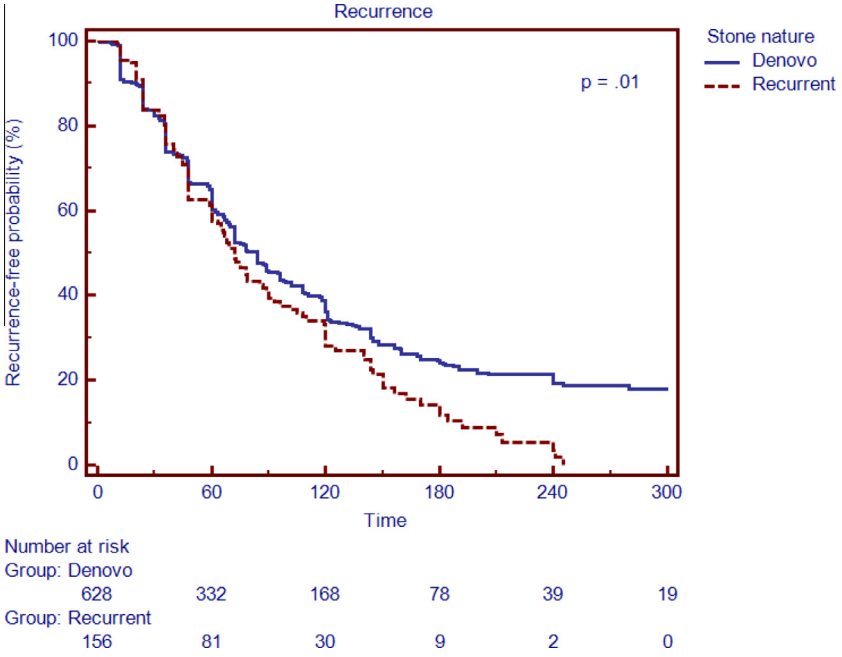

Figure 3 Kaplan–Meier plot for stone recurrence in all 784 patients according to previous history of stone disease (de novo vs recurrent). Time, months.

recurrence rates were 3.5%, 21.2%, 34.7% after 1, 3 and 5 years, respectively; and the contralateral stone recurrence rates were 1.9%, 7.5%, 12.8%, respectively. In another study, the cumulative recurrence rates were 2.0% at 1 year, 13.1% at 3 years, 23.9% at 5 years, 30.7% at 7 years, and 40.7% at 10 years [18].

The differences in recurrence rates between ESWL and other methods of stone management remain controversial. A single study noted a greater recurrence rate after conventional open stone surgery (OSS) [19]. The recurrence rate was 31.8% within a mean of 40 months in the OSS group, whereas this figure was 13.9%, with a mean period of 46 months in the ESWL group ($P < 0.05$). The mean periods of recurrence in the ESWL and OSS groups were 20 and 11 months, respectively ($P < 0.05$). However, for comparable stone burdens, the recurrence rate was similar. The results of that study show that stone burden may be

Table 3 Distribution of site of stone recurrence in both the ESWL and PCNL groups.

Site	ESWL, *n* (%) (*N* = 469)		*P*	PCNL, *n* (%) (*N* = 80)		*P*
	Baseline	Follow-up		Baseline	Follow-up	
Upper calyx	43 (9.2)	58 (12.4)	<0.001	4 (5)	2 (2.5)	0.01
Middle calyx	42 (9)	71 (15.1)		2 (2.5)	8 (10)	
Lower calyx	113 (24.1)	131 (27.9)		25 (31.2)	31 (38.8)	
Pelvis	213 (45.4)	136 (29)		30 (37.5)	13 (16.2)	
Multiple sites	58 (12.4)	73 (15.6)		19 (23.8)	32.5 (22.5)	

the primary risk factor for stone recurrence after ESWL and OSS.

Few studies have compared late stone recurrence after ESWL and PCNL, and they also show conflicting findings [11–15]. Krambeck et al. [12] reported that at 19 years of follow-up stone recurrences were less frequent after PCNL compared with ESWL. A similar conclusion was reported by Carr et al. [11], who reported that new stones formed in 22.2% of their patients after ESWL and in 4.2% after PCNL at 1 year ($P = 0.004$), and in 34.8% vs 22.6%, respectively, at 2 years ($P = 0.190$). More recently in a study by Chongruksut et al. [14] and during 3 years of follow-up, the overall stone recurrence rates were 15.5% and 12.6% in the ESWL and PCNL groups, respectively. Contrary to these findings; Carlson et al. [15] reported that stone recurrence rates in the first 2 years after ESWL and PCNL were similar in both groups, and there was no significant difference in stone recurrence for patients treated with ESWL. In accordance with the findings of Carlson et al. [15]; Trinchieri et al. [13] reported that the overall recurrence rates for ESWL and PCNL were very similar (37% and 39%, respectively).

A major concern about the findings of these previous studies is that most of them [12–15], except those of Carr et al. [11], did not exclude patients with PCNL who underwent intracorporeal lithotripsy. It is clearly obvious that intracorporeal lithotripsy may lead to formation of microscopic fragments similar to those that occur in ESWL. Therefore, the previous findings should be interpreted with caution. Another concern is the small number of patients included [11–13].

In our present study, a large number of patients who were stone-free after ESWL were included, as well as patients treated by PCNL without any attempt at intracorporeal lithotripsy. Our present data showed no significant difference in recurrence rates in patients treated by ESWL and PCNL. The Kaplan–Meier analyses showed high recurrence rates following either ESWL or PCNL after 5 and 10 years, respectively. These findings confirm the significance of long-term follow-up after stone removal and the need to find an effective prophylactic therapy to prevent recurrence.

In the study by Carr et al. [11], the location of stone recurrences for the ESWL group showed a shift from the baseline location before treatment to a higher incidence for recurrence within the calyces. In another study [5], the distribution of the location of the original stone was unrelated to recurrence but calculi predominantly recurred in the lower calyx (68%). The explanation for higher recurrence in the lower calyx after ESWL may be due to microscopic stone debris remaining following ESWL, which gravitate to dependent calyces and act as nidi for new stone growth. In our present study, there was a similar trend of higher new stone formation in the lower calyx compared with the original sites.

Stone size, site, multiplicity and composition, a positive history of stone disease and UTI after ESWL were identified previously as factors influencing stone recurrence [6,8,17,18]. In our present study, a stone size of >8 mm was a significant predictor of stone recurrence after ESWL. A positive history of urolithiasis was another predictive factor among the patients included in our present study.

Finally, we acknowledge some limitations in our present study. Firstly, a large number of patients were lost to follow-up. Another source of bias within our study is that patient demographics or risk factors for stone recurrence were not possible to control for between treatment groups. Metabolic evaluation or stone analysis was not done routinely for all patients; if these factors were not similar within the ESWL and PCNL groups stone recurrence rates may have been changed. Prospective trials are warranted to avoid these potential risk factors.

Conclusions

The Kaplan–Meier recurrence rates following ESWL were 0.8%, 35.8% and 60.1% after 1, 5 and 10 years, respectively. The recurrence rates in the ESWL and PCNL groups were comparable. Our present results demonstrated that ESWL does not increase long-term stone recurrence in patients who become stone free after ESWL. The stone burden appears to be the primary factor in predicting stone recurrence after ESWL. The recurrence rate in all patients was also influenced by positive history of urolithiasis. More new stones recurred in the calyces compared with baseline location in the ESWL and PCNL groups. The high recurrence

rates at 5 and 10 years after ESWL and PCNL show the importance of long-term follow-up and the need for an effective prophylactic therapy to prevent recurrence.

Conflicts of interest

None.

Source of funding

None.

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