Shock Wave Lithotripsy is More Effective for Residual Fragments after Percutaneous Nephrolithotomy than for Primary Stones of the Same Size: A Matched Pair Cohort Study

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Abstract
Aims: To compare the outcome of shock wave lithotripsy (SWL) on post-percutaneous nephrolithotomy (PCNL) residual fragments (RFs) versus primary stones of the same size through a matched pair study. Methods: Patients with a single 5–15 mm fragment 3 months after PCNL were enrolled (study group n = 59). The control group (n = 67) consisted of all adult patients with a single 5–15 mm renal stone. Results: The success rate of SWL was significantly higher in the study group (81.4 vs. 59.7%; p = 0.008; OR: 2.95). With a cutoff point of Hounsfield units (HU) 750: the success rate was significantly lower in patients with a stone HU ≥ 750 (OR: 3.488). This HU cutoff value had no effect on the outcome of SWL in patients with post-PCNL RF (p = 0.14). On the other hand, the outcome of SWL was significantly more favorable in control group when HU < 750 (p = 0.02). Conclusion: The success rate of SWL was 2.95-fold higher for post-PCNL RFs than in a stone burden-matched control group. The likelihood of stone clearance after SWL was 3.488-fold greater when HU was less than 750. This effect of HU was more prominent in patients receiving SWL for their primary stones while SWL was evenly effective on post PCNL RFs with different HUs.

Introduction

Since percutaneous nephrolithotomy (PCNL) was established as the standard of care for managing large renal stones, the stone-free rate (SFR) after PCNL and the use of ancillary procedures to manage residual stones have attracted growing interest. The average SFR after PCNL is between 74 and 83% [1, 2]; the exact figure depends on the postoperative imaging modality used to detect residual fragments (RFs) and the cutoff value for considering a RF “clinically” significant, and both criteria remain controversial. Associated stone-related events such as RF growth, emergency hospitalization for obstruction or renal colic, and the need for ancillary procedures make the diagnosis and management of post-PCNL RFs a hot topic [3, 4].
In the era of shock wave lithotripsy (SWL), the term “clinically insignificant residual fragment” has been coined to represent RFs smaller than 4–5 mm that are asymptomatic, non-obstructive and not associated with urinary tract infection. Ganpule et al. [5] analyzed the outcome of RFs in 187 out of 2,469 patients who underwent PCNL. They found that the most common site of post-PCNL RF was the lower calyx (57.7%), and that fragments in the renal pelvis and/or smaller than 25 mm² had the best chance of spontaneous passage. However, more than half of the patients with post-PCNL RF required secondary intervention. Several modalities such as SWL, flexible ureteroscopy and re-PCNL have been proposed for delayed management of post-PCNL RF; among them SWL remains the least invasive procedure.

To compare the outcome of SWL on post-PCNL RF versus primary stones of the same size, we designed a matched pair study. We hypothesized that the energy delivered directly to the stone by intracorporeal lithotripsy during PCNL is transmitted to all parts of the stone and may weaken the bonds within the stone by vibration. Therefore, when any residual fragment of the stone, which had already absorbed energy, received extracorporeal shock waves, the disintegration effect would be enhanced.

**Patients and Methods**

**Patients**

Study group: After obtaining approval from our institutional review board, between January 2014 and March 2016 all patients who had a single 5–15 mm RF from the primary stone, confirmed by follow-up computerized tomography (CT) scan 3 months after PCNL were considered for this study. Fluoroscopic guided tubeless PCNL using pneumatic lithotriptor had been done for all patients.

Exclusion criteria were solitary kidney or renal anomalies such as duplex system, horseshoe kidney and ectopic kidney, serum creatinine level > 2 mg/dl, uncontrolled hypertension, pregnancy, persistent urinary tract infection after adequate antibiotic therapy, irreversible coagulopathy, ureteral obstruction, morbid obesity and skeletal malformations. We used a 3-dimensional CT reconstruction technique to calculate the volume of the treated stone with the triaxial ellipsoid volume formula: \( V = \frac{a \times b \times c \times \pi}{6} \).

**Control Group**

During the same period, all adult patients with a single 5–15 mm renal stone who had not have any of the exclusion criteria noted above were scheduled for SWL and enrolled in the study. These patients had no previous history of any intervention for their stones, and the volume of their stones was calculated with the formula noted above.

All patients had negative urine culture before SWL. A Dornier lithotripter (Dornier MedTech GmbH, Germering, Germany) was used.

**Table 1. Comparison of demographic characteristics between the 2 groups**

|                      | Study group (n = 59) post-PCNL fragments | Matched control group (n = 67) primary stones | p  |
|----------------------|----------------------------------------|---------------------------------------------|----|
| Age, years           | 46.45±14.94                           | 45.91 ± 14.25                              | 0.83|
| Gender               |                                        |                                             | 0.12|
| Male                 | 39 (66.1%)                             | 42 (62.7%)                                 |     |
| Female               | 20 (33.9%)                             | 25 (37.3%)                                 |     |
| Body mass index, Kg/m² | 24.72 ± 3.9                       | 24.47 ± 3.8                                | 0.93|
| Stone side           |                                        |                                             | 0.75|
| Right                | 28 (47.5%)                             | 36 (53.7%)                                 |     |
| Left                 | 31 (52.5%)                             | 31 (46.3%)                                 |     |
| Mean stone size (Max diameter), mm | 10.2 ± 3.14                     | 9.3 ± 5.52                                  | 0.06|
| Mean stone volume, mm³ | 532.8 ± 413.3             | 491.4 ± 246.2                              | 0.06|
| Location of stone    |                                        |                                             | < 0.001|
| Lower calyx          | 32 (54.2%)                             | 20 (29.9%)                                 |     |
| Mid calyx            | 9 (15.3%)                              | 6 (9%)                                      |     |
| Upper calyx          | 6 (10.2%)                              | 3 (4.4%)                                    |     |
| Renal pelvis         | 12 (20.3%)                             | 28 (41.8%)                                 |     |
| Ureteropelvic junction | 0 (0%)                           | 10 (14.9%)                                 |     |
| Stone Opacity        |                                        |                                             | 0.85|
| Opaque               | 27 (45.7%)                             | 31 (46.3%)                                 |     |
| Semiopaque           | 9 (15.3%)                              | 8 (11.9%)                                   |     |
| Lucent               | 23 (39.0%)                             | 28 (41.8%)                                 |     |
| Stone density (HU)   | 738.39 ± 325.29                        | 942.42 ± 327.01                            | 0.001|
|                      | 939.12 ± 357.6 (Before PCNL)           |                                             | 0.64|

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used for lithotripsy. Fluoroscopy (for opaque and semi opaque stones) or ultrasonography (for radiolucent stones) was used for stone localization.

Study Outcome

In both groups, demographic data and stone characteristics [largest stone diameter, stone volume, location and density in Hounsfield units (HU)] were recorded before SWL. Non-contrast CT scan was used to determine the final outcome of SWL after 3 months. Stone-free status (no identifiable stone) or the volume and size of any post-SWL residual stones were recorded. Preoperative and postoperative variables were compared between the 2 groups.

Statistical Analysis

All statistical analyses were done with SPSS V.17 (SPSS Inc. Chicago, IL). We used Student’s t test to compare continuous variables, and the chi-squared test for categorical parameters. Logistic regression and receiver operating characteristic curves were used to detect predictors of SFR after SWL.

Results

During the study period 59 patients received SWL for post-PCNL management of a residual stone (study group) and 67 patients underwent SWL for their primary stone (control group). Table 1 summarizes the demographic characteristics of all patients. The 2 groups were similar in age, gender distribution, body mass index, maximum stone diameter and volume. Likewise, patients in the study group before undergoing PCNL had comparable stone density, in terms of HU, with patients receiving SWL (939.12 ± 357.6 vs. 942.42 ± 327.0, p = 0.64). However, most RFs after PCNL (study group) were in the lower calyx (54.2%) whereas in the control group most stones were in the renal pelvis (41.8%) (p < 0.001) (table 1).

The success rate of SWL (no identifiable stone after 3 month) was significantly higher in the study group [81.4% vs. 59.7%; p = 0.008; odds ratio (OR): 2.95, 95% confidence interval (CI): 1.301–6.66]. Interestingly, this was independent of stone location (table 2). Despite that before PCNL, patients in both groups had similar stone density, mean stone HU decreased significantly after PCNL in the study group (from HU = 939.12 ± 357.6 to 738.4 ± 325.3, p = 0.001). Therefore, mean stone HU was lower in patients with previous PCNL compared to control group (738.4 ± 325.3 vs. 942.4 ± 327.0; p = 0.001) (table 1). Likewise, mean stone HU was significantly lower in patients with a successful SWL outcome (790.7 ± 336.46 vs. 945.7 ± 316.8; p = 0.005, 95%CI: 313.71–56.24).

Receiver operating characteristic curve analysis determined a cutoff point of 750 HU (fig. 1). The success rate of SWL (no identifiable stone after 3 month) was significantly higher in the study group [81.4% vs. 59.7%; p = 0.008; odds ratio (OR): 2.95, 95% confidence interval (CI): 1.301–6.66]. Interestingly, this was independent of stone location (table 2). Despite that before PCNL, patients in both groups had similar stone density, mean stone HU decreased significantly after PCNL in the study group (from HU = 939.12 ± 357.6 to 738.4 ± 325.3, p = 0.001). Therefore, mean stone HU was lower in patients with previous PCNL compared to control group (738.4 ± 325.3 vs. 942.4 ± 327.0; p = 0.001) (table 1). Likewise, mean stone HU was significantly lower in patients with a successful SWL outcome (790.7 ± 336.46 vs. 945.7 ± 316.8; p = 0.005, 95%CI: 313.71–56.24).

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Discussion

PCNL is the preferred standard of care for large renal stones. However, post-PCNL residual stones are not uncommon, and several modalities have been proposed to manage these fragments after a period of observation for spontaneous passage. Second-look flexible nephroscopy through an established tract has been shown to have a SFR up to 97% [7]. However, nephroscopy is an invasive and costly procedure requiring operating room facilities and possible anesthesia; moreover, it deprives the patient of a period of expectant management for spontaneous passage and it cannot be done if tubeless PCNL has been contemplated. The use of retrograde intrarenal surgery (RIRS) with flexible ureteroscopy to manage RFs has recently been studied [8, 9]. Hamamoto et al. [8] showed that combining RIRS with PCNL can significantly improve the SFR from 38.9 to 81.7% in patients with large stones (mean size 34.6–39.2 mm). Similarly, Xu et al. [9] used RIRS to manage post-PCNL RF and obtained an overall SFR of 91.3% after 3 months. However, the cost-benefit ratio of this procedure compared to less invasive modalities remains unclear.

SWL remains the mode of therapy of first choice for small renal stones (≤ 10–20 mm) [10], and thanks to its non-invasive nature it seems very promising for the management of RFs after PCNL, which are usually small fragments. Especially when delayed rather than immediate management of the RF is planned. In the present study, we compared a group of patients with a single post-PCNL RF ≤ 15 mm and a cohort of patients with intact single primary stone of the same size to determine whether previous PCNL affected the outcome of future SWL. Interestingly, we found that in patients with RF after PCNL the success rate of SWL was significantly higher (OR 2.95) despite the fact that more stones in this group were located in the lower calyx. This finding may reflect the effect of manipulation of the primary stone and collecting system during PCNL: intracorporeal lithotripsy during PCNL may have disintegrated or loosened the RFs. As shown, while the stone HU before PCNL was similar between the 2 groups, it decreased significantly after the PCNL. Moreover, expansion of the collecting system which occurs during PCNL may result in a better response to future SWL by increasing the stone-fluid interface.

To the best of our knowledge, no matched pair studies have been published that compare the efficacy of SWL on intact versus post-PCNL stones. Xu et al. [11] retrospectively compared the efficacy of SWL versus RIRS for the management of residual stones after PCNL, and found RIRS to be better (3-month SFR 72.9 vs. 91.3%). Their SFR after SWL was similar to ours, but in contrast to our study, they measured only the largest diameter of stones with ultrasonography. Zhang et al. [12] compared the effect of SWL on RFs after different procedures (i.e. ureteroscopic lithotripsy, PCNL and open surgery), and found the lowest clearance rate for RF after open surgery with SWL (73.0%) compared to ureteroscopy (100%) or PCNL (83.3%).

In accordance with the standards of reporting PCNL outcomes recently published by Opondo et al. [13], we evaluated stone-free status by CT scan. Several studies have confirmed the superiority of unenhanced CT scanning to evaluate RFs [12, 13]. This modality has a sensitivity of 100% for RF detection, and can significantly reduce the need for ancillary procedures to manage RFs [12, 13]. The predictive value of HU for SWL outcome has been studied in recent years. Although the cutoff points range from 600 to 1,200 among different studies, the lower the HU, the higher SFR after SWL [14–18]. In consonance with these findings, we found that the likelihood of stone clearance after SWL was almost 3.5-fold greater when the HU was < 750. Interestingly, we found that the effect of HU is more prominent in patients re-

![Receiver operating characteristic curve analysis of stone-free rate after shock wave lithotripsy according to stone density in HU. The cutoff value was 750 (area under the curve = 0.663).](image-url)
ceiving SWL for their primary stones. In other words, SWL is evenly effective on post-PCNL RFs with different HUs (table 2). As a limitation of our study, we did not evaluate or analyze stone composition as a potential variable that might affect the outcome of SWL. Instead, we used HU as a quantitative marker of stone density. Given the fact that in clinical situations most stones have mixed components and SWL may clear only 1 component, a quantitative variable such as HU seems more reliable for outcome assessment [16].

In the present study, in an attempt to homogenize the groups, all patients had a single stone to be treated by SWL and the stone size and volume were similar in both groups but in more patients with post-PCNL group, residual stones were located in the lower pole. The lack of homogeneity notwithstanding, SFR was higher in this group. We thus can conclude that if we had matched patients in the 2 groups for stone location, SFR after SWL would have been even higher in the group with post-PCNL RFs. A prospective cohort study to compare the effectiveness, costs, complications and their impact on quality of life can provide better evidence to decide the modality of choice for post-PCNL RF management.

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Ethical Approval

All procedures performed in this study were in accordance with the ethical standards of the Shiraz University of Medical Sciences research committee and with the 1964 Helsinki declaration and its later amendments.

Informed Consent

Informed consent was obtained from all individual participants included in the study for using their procedural outcome in the research project.

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