HIGHLIGHTS

• By PNL, the progression of CKD may be halted. While significant improvement was observed in early-stage CKD, sometimes unexpected deterioration could occur in patients at end stages of renal diseases.
• Our results indicated that most patients presenting with kidney stone disease and renal insufficiency will experience improvement or stabilization of renal function after PNL.

ABSTRACT

Introduction
The principles of nephrolithiasis therapy in patients with chronic kidney disease are the same as in patients with normal kidneys. Percutaneous nephrolithotomy (PNL) is the standard treatment for patients with complex or large-volume upper urinary tract calculi. We reported the characteristics and outcomes of patients following percutaneous nephrolithotomy according to their preoperative renal function levels.

Methods
In this prospective cohort study, data on 53 consecutive patients treated with percutaneous nephrolithotomy in 6 months were collected. Patients were divided into 3 groups by estimated glomerular filtration rate (eGFR) including chronic kidney disease (CKD) stages 0, 1 and 2 (eGFR ≥ 60 mL/min/1.73 m²), stage 3 (eGFR = 30 to 59 mL/min/1.73 m²) and stages 4 and 5 (eGFR < 30 mL/min/1.73 m²).

Results
31 patients with CKD stages 0, 1, and 2, 17 patients with CKD stage 3, and 5 patients with stages 4 and 5 were followed up for at least three months. The mean eGFR before and after PNL was 80.1 vs. 85.9, 47.6 vs. 49.1, and 23.5 vs. 23.4 mL/min/1.73 m² in the mild, moderate, and severe CKD groups, respectively. Based on the statistical analysis, eGFR in the mild group had been significantly increased compared to the other groups, whereas there was no considerable difference between the moderate and severe groups.

Conclusions
By the removal of kidney stones, the progression of CKD may be halted. While significant improvement was observed in early-stage CKD, sometimes unexpected deterioration could occur in patients at end stages of renal diseases.

Keywords: Nephrolithiasis; Renal Insufficiency; Chronic; Nephrolithotomy; Percutaneous

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Introduction

Percutaneous nephrolithotomy (PNL) remains the first-line treatment for kidney stone burdens 2 cm and greater unless significant contraindications are present (1). Urinary calculi may be associated with various degrees of renal insufficiency. The etiology of renal insufficiency in patients with nephrolithiasis is multifactorial and includes renal obstruction, urinary infection, frequent surgical interventions, and coexisting medical diseases (2).

PNL is now commonly used for urolithiasis treatment with minimal morbidity compared to the conventional open surgery. It would also have several advantages in patients with different associated diseases such as chronic kidney disease (CKD) (3,4).

Regarding the importance of finding an optimal therapeutic method for urolithiasis in patients with CKD and paucity of consistent data in the literature, this study was conducted to evaluate the effects of PNL on the estimated glomerular filtration rate (eGFR) of patients affected by chronic kidney disease.

Materials and Methods

A cohort of fifty-three consecutive PNL operations for removal of large renal stones was performed in Shariati hospital from May 2017 until October 2018 by a single surgeon (SS), and the results were studied prospectively. PNL was performed only in the patients with renal stones larger than 20 mm or in whom shock wave lithotripsy (SWL) had failed. The standard PNL procedure was performed within the prone position and under the fluoroscopy. Stone fragmentation was done using a Swiss LithoClastTM pneumatic lithotriptor through a 28Fr amplatz sheath. In the end, an 18Fr foley catheter was inserted as a nephrostomy tube.

Patients’ preoperative clinical information counting age, sex, body mass index (BMI), and stone burden were recorded. The eGFRs of adult patients were calculated utilizing the Modification of Diet in Renal Disease (MDRD) formula, and the patients were categorized according to the Kidney Disease Outcome Quality Initiative CKD classification framework (7).

Patients were divided into 3 groups by glomerular filtration rate including chronic kidney disease stages 0, 1, and 2 (eGFR = 30 to 59), and stages 4 and 5 (eGFR < 30 ml/min/1.73 m3). The effect of PNL on eGFR was analyzed by comparing the preoperative eGFR with the eGFR just before discharge and at postoperative month 3.

Human rights were respected under the Helsinki Declaration 1975, as revised in 1983. The ethical committee of Tehran University of Medical Sciences (IR. TUMS.MEDICINE.REC.1398.469) approved the study. The informed consent was taken from the patients as well as from parents and first relatives. Statistical analysis was carried out using the STATA software version 11.2. Categorical data across groups were compared by T-test and continuous variables were compared by one-way analysis of variance (ANOVA). The Bonferroni post hoc test was also used to counteract the problem of multiple comparisons among these three groups. Statistical significance was considered with the two-sided P value of less than 0.05.

Results

The study group consisted of 19 females and 34 males with the mean patient age of 58.9 ± 12.7 years. The mean follow-up time was 3 months. Mean BMI and GFR were 27.3 ± 3.3 kg/m2 and 64.3 ± 24.2 ml/min, respectively. Thirty-one of the 53 patients (58.5%) had CKD stages 0, 1, and 2, 17 patients (32%) had CKD stage 3 and the remaining 5 patients (9.5%) had CKD stages 4 and 5 (Table 1).

The stones size ranged from 1.5 to 6 cm. Primary stones location varied, but the majority were lodged in the renal pelvis or the lower pole. The mean eGFR before and after PNL was 80.1 vs. 85.9, 47.6 vs. 49.1, and 23.5 vs. 23.4 in the mild, moderate, and severe CKD groups, respectively. The percentage of change in the eGFR was measured by comparing the preoperative and postoperative values. A 5% change in renal function was found the main indicator between these three groups: (Table 2)

Group 1, with an eGFR increase of >5% (+7.3%); group 2, with an eGFR increase of ≤5% (+2.7%) and group 3, with an eGFR decrease of <5% (-0.6%). A one-way between-groups analysis of variance was conducted to explore the impact of eGFR at the base on the rate of eGFR change at month 3. Patients were divided into 3 groups according to their base eGFR: group 1 with mild CKD (eGFR>60), group 2 with moderate CKD (30≤ eGFR<60), and group 3 with severe CKD (eGFR<30). There was a statistically significant difference at the p-value<0.05 level in the rate scores for the three CKD groups (p-value<0.0001).

Despite reaching statistical significance, the actual difference in mean scores between the groups was small. Post-hoc comparisons using the Bonferroni HSD test indicated that the mean score for the mild CKD group (M=107.34, SD=3.00) was significantly different from the moderate CKD group (M=107.725, SD=7.24) (p-value=0.008) and also from the severe CKD group (M=99.36, SD=94.64) (p-value=0.004). The moderate CKD group did not differ significantly from the severe CKD group (p-value=0.54).
Outcomes of PNL According to Renal Function Levels

Discussion
PNL is the standard treatment for patients with complex or large-volume upper urinary tract calculi. Although ureteroscopy technology has progressed, recent data suggest that the utilization of ureterorenoscopy (URS) and SWL has declined for the patients with large calculus, whereas that of PNL is steadily increasing (8).

The principles of nephrolithiasis therapy in patients with chronic kidney disease are the same as in patients with normal kidneys. Owing to a large number of patients with nephrolithiasis suffering from various degrees of renal failure in our referral center, we planned to assess the adequacy and results of PNL to treat kidney stones in patients with chronic renal insufficiency. Some prospective studies have already evaluated the outcomes of percutaneous nephrolithotomy in patients with chronic renal insufficiency (9,10).

In one study, there were no statistically significant differences between patients with normal and impaired renal function for success and complication rates (p-value=0.376, and p-value=0.184, respectively). In a mean follow-up of 15.6 months, mean serum creatinine decreased from 2.8 to 2.6 mg/dl (p-value=0.273) in patients of the impaired renal function group. Similar stone clearance and complication rates were obtained with PNL in patients with impaired and normal renal function. Surgery did not cause biochemical deterioration in patients with compromised renal function before treatment (4).

In another study, patients with CKD had a noteworthy improvement in the GFR after the surgery. In postoperative month 3, the mean GFR was more than 60 mL/min/1.73 m² in 25% of the patients with CKD and less than 60 mL/min/1.73 m² in 75%. While all patients with stage 5 CKD improved to better stages, some other patients’ conditions declined to stage 5 from better stages at the end of postoperative month 3. No patient needed dialysis. The presence of urinary tract infections tended to affect GFR negatively (5).

Patients who present with varying severity of obstructive urolithiasis behave differently after the treatment. Some patients recover with improved renal function while others progress to renal failure. A preoperative prognostic model for the renal functional outcome after the treatment of bilateral obstructive urolithiasis in patients with chronic kidney disease was also defined in another clinical trial study (8).

Combined cortical width (p-value≤0.001), proteinuria (p-value=0.01), positive urine culture (p-value=0.004), and nadir preoperative GFR post-bilateral percutaneous nephrostomy (p-value=0.016) were statistically significant factors affecting renal deterioration on multivariate analysis. Combining these parameters in a prediction table yielded a renal deterioration index (RDI) score ≥12 being associated with high odds risk (odds ratio=11.2) of treatment failure. So, they could objectively quantify which patients would progress to renal failure after treatment for obstructive urolithiasis (8).

Here is our short-term follow-up data from patients with kidney stones and chronic kidney disease. Our main goal would be to present our long-term follow-up data from patients with kidney stones and chronic kidney disease to identify the factors that could help predict the likelihood of long-term deterioration in renal function in addition to preoperative eGFR. We also plan to analyze the factors predictive of functional improvement or impairment in these patients who were submitted to PNL. However, the small sample size and the relatively short follow-up time were the main limitations of our study.

Conclusions
eGFR, as a strong indicator of renal function, is probably influenced by PNL surgery. Whereas noteworthy renal function improvement was observed in the early-stage CKD patients, conversely in some end-stage CKD patients the deterioration of renal function may unexpectedly be encountered.

Our results indicated that some patients presenting with kidney-stone disease and renal insufficiency could experience improvement or stabilization of renal function after PNL. Patients with mild to moderate renal failure

Table 1. Demographic data and stone characteristics

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>N</td>
<td>53</td>
</tr>
<tr>
<td>Mean age±SD (years)</td>
<td>58.9±12.7</td>
</tr>
<tr>
<td>Male/female</td>
<td>34/19</td>
</tr>
<tr>
<td>Mean BMI ± SD (kg/m2)</td>
<td>27.3±3.3</td>
</tr>
<tr>
<td>CKD status N (%)</td>
<td></td>
</tr>
<tr>
<td>Mild</td>
<td>31 (58.5%)</td>
</tr>
<tr>
<td>Moderate</td>
<td>17 (32%)</td>
</tr>
<tr>
<td>Severe</td>
<td>5 (9.5%)</td>
</tr>
<tr>
<td>Mean Stone size ± SD (mm)</td>
<td>30.8±13.8</td>
</tr>
<tr>
<td>Mean GFR ± SD (ml/min) 3 months</td>
<td>68.2±26.3</td>
</tr>
</tbody>
</table>

Table 2. Patient perioperative CKD stage and postoperative GFR changes

<table>
<thead>
<tr>
<th>Postop GFR changes</th>
<th>GFR-0 (ml/min)</th>
<th>GFR-month 3 (ml/min)</th>
<th>Change (%)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mild CKD</td>
<td>80.2</td>
<td>85.9</td>
<td>+7.3</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Moderate CKD</td>
<td>47.5</td>
<td>49.1</td>
<td>+2.7</td>
<td>0.213</td>
</tr>
<tr>
<td>Severe CKD</td>
<td>23.5</td>
<td>23.4</td>
<td>-0.6</td>
<td>0.749</td>
</tr>
</tbody>
</table>
showed the best improvement in renal function, reducing or maybe preventing the need for future renal replacement therapy.

**Authors’ contributions**
ShSh was the responsible of study conception and design, AM and AK wrote the manuscript and provided data, SRY supervised the process and edited the manuscript. All authors reviewed the results and approved the final version of the manuscript.

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**Conflict of interest**
The authors declare that there are no conflicts of interest regarding the publication of this manuscript.

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**Ethical statement**
Not Applicable.

**Data availability**
Not Applicable.

**Abbreviations**
- BMI: Body mass index
- CKD: Chronic kidney disease
- eGFR: Estimated glomerular filtration rate
- MDRD: Modification of diet in renal disease
- PNL: Percutaneous nephrolithotomy
- RDI: Renal deterioration index
- SS: Single surgeon
- SWL: Shock wave lithotripsy
- URS: Ureterorenoscopy

**References**