ORIGINAL ARTICLE

Renal function markers in single-kidney patients after percutaneous nephrolithotomy: A pilot study

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Background: The present study was performed to investigate and compare renal functions of single-kidney patients after 12 h of percutaneous nephrolithotomy (PCNL) surgery through assessing major markers of renal function with focus on serum level of cystatin that performs a consistent accuracy in various conditions. **Materials and Methods:** This pilot quasi-experimental study was done on 92 patients with single kidney having staghorn calculus who had undergone PCNL and were referred to the Al-Zahra Hospital, Isfahan, Iran, during 2019–2021. Serum levels of cystatin C, creatinine, estimated glomerular filtration rate (eGFR), and neutrophil gelatinase-associated lipocalin (NGAL) urine level were evaluated before and 12 h after surgery. **Results:** The mean cystatin C decreased significantly 1.58 ± 0.55 versus mg/L 1.46 ± 0.52 after 12 h after surgery ($P < 0.001$). Furthermore, the mean levels of creatinine (2.04 ± 0.71 vs. 1.89 ± 0.60 mg/dL) and NGAL (39.72 ± 12.87 vs. 24.05 ± 10.89 μg/ml) were decreased significantly after 12 h of procedure ($P < 0.05$) while the mean eGFR (57.62 ± 27.59 vs. 64.68 ± 31.88 ml/min/1.73 m^2) was increased significantly after 12 h ($P < 0.001$). **Conclusion:** Due to significant improvement in all markers of renal after PCNL, this procedure can be considered a potentially effective and safe approach for treating large stone in single-kidney patients.

Key words: Cystatin C, neutrophil gelatinase-associated lipocalin, percutaneous nephrolithotomy, renal function markers, single-kidney patients

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INTRODUCTION

Percutaneous nephrolithotomy (PCNL)[1] is a minimally-invasive procedure to remove stones from the kidney by a small incision wound through the skin. It is most suitable to remove stones of more than 2 cm in size, which are present near the pelvic region.[2] This method is mainly used for removal of cystine radiopaque kidney stones with diameter of more than 2 cm.[3]

PCNL is one of the effective monotherapies for removal of kidney stones and is also associated with least mortality and complication rates.[4,5]

Studies have indicated that PCNL has efficient long-term results even in patients with high risks, such as the elderly, children, and patients with chronic kidney diseases (CKDs), but very few studies have investigated the effects of PCNL on kidneys within the 1st day after this procedure.[6] Complications of PCNL could be due to the following reasons: inappropriate patient's selection, insufficient equipment, technical problems, vascular injuries, and hemorrhage. Vascular injuries could also lead to postoperative bleeding and might require surgical interactions if persistent for more than 3 weeks.[7,8]

Evaluation of estimated glomerular filtration rate (eGFR) is one of the best methods of assessing renal functions. The eGFR assessments could help us to evaluate the exact renal functions. This process could be performed using different agents, such as inulin, iohexol, 125I-iothalamate, and cystatin C.[9,10]

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Creatinine is the most widely used biomarker of kidney function. However, it is inaccurate at detecting mild renal impairment, and its levels can vary with muscle mass but not with protein intake. Urea levels might change with protein intake.[11] Cystatin C has a low molecular weight (approximately 13.3 kilodaltons), and it is removed from the bloodstream by glomerular filtration in the kidneys. If kidney function and glomerular filtration rate decline, blood levels of cystatin C rise. Cross-sectional studies have suggested that serum levels of cystatin C are a more precise measure of kidney function than serum creatinine levels. There are a limited number of longitudinal studies, but some of them have shown promising results.[12,13] Although studies are somewhat divergent, most studies have found that cystatin C levels are less dependent on age, gender, ethnicity, diet, and muscle mass compared to creatinine, and that cystatin C is equal or superior to the other available biomarkers in a range of different patient populations including diabetic patients in CKD and after kidney transplant.[14,15]

According to the UK's National Institute for Health and Care Excellence guideline for assessment and management of CKD in adults, using serum cystatin C to estimate eGFR is more specific for important disease outcomes than the use of serum creatinine, and may reduce overdiagnosis in patients with a borderline diagnosis, reducing unnecessary appointments, patients' worries, and also the overall burden of CKD on population.[16,17]

The neutrophil gelatinase-associated lipocalin (NGAL) is a small glycosylated protein that is filtered in the glomerular membrane and also it is reabsorbed in proximal tubule. The urinary level of NGAL is a biomarker for renal function and renal tubular injury.[18]

PCNL for large stones in patients with CKD, particularly in single-kidney patients, poses an important challenge and potential threat or progression of CKD. As we are aware, there is no previous study evaluating the effect of PCNL in single-kidney patients suffering from large stones. Therefore, the current pilot study has been conducted to evaluate the efficacy and safety of PCNL in these patients through evaluating the improvement in major markers of renal function including serum levels of cystatin C, creatinine, eGFR, and NGAL urine level.

MATERIALS AND METHODS

Study design and participants

This pilot quasi-experimental study was done on 92 patients with single kidney having staghorn calculus who had undergone PCNL and were referred to the Al-Zahra Hospital, Isfahan City, Isfahan Province, Iran, during 2019–2021. The protocol of the current study was approved (IR.BMSU.BAQ.REC.1399.008) by the Baqiyatallah University of Medical Sciences, Tehran, Iran. Furthermore, informed consent was obtained from all the subjects for participation in the study. Inclusion criteria included the patients with solitary kidney aged more than 10 years with kidney stone (diameter of more than 2 cm and staghorn calculus based on multidetector computed tomography [MDCT] scan findings) who were willing to cooperate in the study. Furthermore, the patients with two kidneys and normal kidney function, renal failure (eGFR below 15 ml/min/1.73 m^2), heavy bleeding (over than 1000 cc), or low blood pressure (under 90/50 mmHg) during surgery and patients who had recently undergone extracorporeal shock wave lithotripsy were excluded from the study.

Surgical procedure and main study outcomes evaluation

All patients underwent the same general anesthesia with thiopental sodium (5–7 mg/kg), atracurium besilate (0.4–0.5 mg/kg), fentanyl (50–100 μg/kg), and propofol. A 5–6-Fr ureteral catheter was placed in ureter for patients and then secured to a Foley catheter. Position of patients was placed prone and a pad was used for under pressure protection. An 18-gauge Chiba needle and a guidewire were used to access calyx under fluoroscopic guidance. Amplatz dilators up to 28 Fr were used for tract dilation. After screening with nephroscopy, stones were fragmented with pneumatic LithoClast (SWISS LithoClast) and then removed of kidney. After ensuring the absence of stones in pyelocaliceal subguide of fluoroscopy, 4.8-Fr ureteral stent and 16-Fr nephrostomy tube were placed in renal pelvis.

The blood sample (3 cc) was taken from patients 6 h before surgery and 12 h after surgery, and blood samples (at a temperature range of 2°C–4°C) were sent to laboratory to evaluate the serum level of cystatin C and then serum level of cystatin was evaluated with enzyme-linked immunosorbent assay (ELISA) (Human Cystatin C Quantikine ELISA Kit DSCTC0: R&D Systems, USA) kit based on manufacturer's instructions.

Serum level of creatinine was evaluated with 3 cc of blood samples before and 12 h after surgery. The urine sample (4 cc) were collected from patients 2 h before and 12 h after procedure and sent to laboratory for measurement of NGAL urinary levels with using ELISA assay by kit produced via R&D Systems Company (USA). Furthermore, eGFR of patients was calculated using cystatin level before and 12 h after surgery; the formula for measurement of eGFR was 100/cystatin c-14 formula.[19,20]

Complications and other variables

Complications following PCNL included bleeding during surgery, thoracic complication (pneumothorax, hemothorax,

and nephropleural fistula), injury and obstruction to renal pelvic and renal collecting ducts, colon perforation, spleen and liver injury, postoperative fever, sepsis, and neurologic complication (facial nerve injury, blurry vision, hemiplegia, paraplegia, neurovascular disease, and comma).[21] These complications were evaluated during and after surgery, so MDCT scan was performed for suspected patients to organ injury.

Demographic, clinical, and surgical informations such as age, gender (male, female), body mass index (BMI, kg/m^2), glomerular filtration rate (eGFR), side of involved single kidney (right, left), cause of having single kidney (atrophy as renal stone or trauma, hypoplasia as pyelonephritis, congenital agenesis, atresia, and nephrectomy), size of renal stone, place of kidney stone (upper, middle, lower), number of access, and duration of surgery and hospitalization were recorded in baseline.

Statistical analysis

All statistical analyses were performed by using SPSS version 24 (SPSS Inc., Chicago, Ill., USA). Continuous and categorical data were reported as mean ± standard deviation and frequency percentage. Normality of continuous variables was evaluated by Kolmogorov–Smirnov test and Q-Q plot. Change from baseline for continuous variables was evaluated using paired samples *t*-test.

RESULTS

The current study was performed on 92 single-kidney patients (63 males and 29 females) with a mean age of 44.29 ± 12.55 years. The mean of kidney stone size was 2.78 ± 0.65 cm, and most of stones were placed in lower region of kidney. Table 1 presets the complete demographic and clinical features of included patients in the current study.

The mean cystatin C decreased significantly 1.58 ± 0.55 vs. 1.46 ± 0.52 mg/L after 12 h after surgery ($P < 0.001$). Furthermore, the mean levels of creatinine (2.04 ± 0.71 vs. 1.89 ± 0.60 mg/dL) and NGAL (39.72 ± 12.87 vs. 24.05 ± 10.89 µg/ml) were decreased significantly after 12 h of procedure ($P < 0.05$) while the mean eGFR (57.62 ± 27.59 vs. 64.68 ± 31.88 ml/min/1.73 m^2) was increased significantly after 12 h ($P < 0.001$) [Table 2].

Three patients (3.2%) had fever after procedure that these patients were afebrile within 4 days and then discharged from hospital. Furthermore, two cases (2.1%) had gross hematuria (following acute kidney injury [AKI] and raising of creatinine) after procedure that these patients underwent complete bed rest, hydration therapy, and received pack cells and then these patients were recovered after 5 days of procedure.

Table 1: Clinical and demographical data of patients

Variables	Patients (*n*=92), *n* (%)
Age (years)	44.29±12.55
Gender	
Male	63 (68.5)
Female	29 (31.5)
Cause of single kidney	
Atrophy as renal stone or trauma	30 (32.6)
Hypoplasia as pyelonephritis	14 (15.2)
Congenital agenesis, atresia	27 (29.3)
Nephrectomy	21 (22.8)
Side of single kidney	
Right	38 (41.3)
Left	54 (58.7)
Size of kidney stone (cm)	2.78±0.65
Place of kidney stone	
Upper	5 (5.4)
Middle	18 (19.6)
Lower	69 (75)
Number of placed accesses	
One	80 (87)
Two	12 (13)
BMI (kg/m^2)	24.58±3.20
Durations	
Surgery (min)	115.59±40.26
Hospitalization (days)	2.10±0.52

Continuous and categorical variables have been presented as mean±SD and frequency (%). BMI=Body mass index; SD=Standard deviation

Table 2: Changes in renal function markers before and 12 h after percutaneous nephrolithotomy

Markers of renal function	Before	After 12 h	*P**
Cystatin C serum level (mg/L)	1.58±0.55	1.46±0.52	<0.001
Creatinine serum level (mg/dl)	2.04±0.71	1.89±0.60	0.02
NGAL urine level (µg/ml)	39.72±12.87	24.05±10.89	<0.001
eGFR (ml/min/1.73 m^2)	57.62±27.59	64.68±31.88	<0.001

*Paired samples test. eGFR=Estimated glomerular filtration rate, NGAL=Neutrophil gelatinase-associated lipocalin

DISCUSSION

In the present study, 92 patients undergoing PCNL were examined and our results showed that mean serum levels of cystatin and creatinine were decreased significantly within 12 h after surgery. Furthermore, the means of NGAL urine level were significantly decreased after 12 h of procedure and the means of eGFR were significantly increased after 12 h.

Previous studies have also evaluated the effects of PCNL on kidney functions. Sairam *et al*. evaluated data of 5644 patients from 96 centers and followed them for 1 year. They showed that impaired renal functions could negatively influence results of PCNL, but no evidence was observed on the negative effects of PCNL on kidney functions. They also explained that serum creatinine and kidney function

indicators did not increase immediately after PCNL.[1] Our results were in line with the findings of this study. Akman *et al*. (2011) evaluated outcomes of PCNL in 47 patients with solitary kidney. They showed that PCNL is a safe and beneficial technique, especially in patients with single kidney accompanied by no immediate complication and negative effects on kidney functions. However, a 10.6% complication rate was observed within a mean follow-up time of 18.7 ± 11.8 (6–60) months.[22] Hosseini *et al*. conducted a study on 412 single-kidney patients in 2015. They found that PCNL had no significant adverse effects on kidney functions and was considered a safe method for removal of kidney stone in patients with single kidney. They also suggested that more attention should be given in order to prevent even minor complications.[23]

Our findings emphasize that PCNL is safe and had minimal adverse effects on patients with single kidney. Most of the previous studies have evaluated kidney function within long follow-up times, but here, kidney function was investigated 12 h after PCNL. Basiri *et al*. studied the safety and efficacy of PCNL for management of large renal stones in 60 patients with single-functioning kidneys and double-functioning kidneys, respectively. They used quantitative single-photon emission computed tomography (CT) measurement of technetium-99m dimercaptosuccinic acid scan uptake and showed that renal function was preserved or even was often improved after percutaneous stone removal, and the procedure had no detrimental effects on renal function in both groups. They also showed no statistically significant difference between these groups in terms of morbidity and stone clearance.[24] In the current study, the serum levels of cystatin and creatinine were investigated and both factors were found to significantly decrease after PCNL showing effectiveness of this method.

There have been also some other studies that indicated the effectiveness of PCNL in patients with kidney problems, and they have reported no significant complications.[25,26] Based on the results of our study, improvements in renal functions were also detected whether PCNL might become transiently worse kidney functions within hours after the procedure. Furthermore, significant direct correlations were found between serum cystatin and creatinine levels with age, BMI, and length of hospital stay. Therefore, this procedure is suggested to be performed on older patients with higher BMI with more care, as mentioned in the study by Bozzini *et al*.[27]

Spahillari *et al*. compared serum level of cystatin C and creatinine for detection of AKI and showed that serum level of cystatin C was less sensitive than creatinine to detect AKI and also cystatin C and creatinine were among markers to detect mortality and dialysis outcomes.[28] However, the results of another study indicated that serum level of cystatin C was better than creatinine to estimate kidney function.[29]

In a study by Mohammadi and Ghamari, who evaluated urinary NGAL for patients with double kidneys underwent PCNL. The authors conducted that urinary NGAL and serum creatinine were increased after the procedure compared to before. GFR was also decreased after the procedure compared to before. These changes were observed based on AKI in patients.[30] In our study, patients with single kidney underwent PCNL, so eGFR was increased and urinary NGAL and creatinine were decreased after procedure. The current study is a novel study about the effect of PCNL in single kidney so previously and also cystatin C and NGAL were measured for first time in patients with single kidney under PCNL. The main limitation of our study is the lack of a control group to compare the effectiveness of PCNL with normal subjects.

CONCLUSION

Significant improvement was observed in all markers of renal function, particularly in serum level of cystatin after PCNL, in our study patients. An observed significant improvement in cystatin C is a promising biomarker for better estimate of kidney function in this population in the current study that provides primary evidence on considering PCNL as a potentially effective and safe approach for treating large stone in single-kidney patients. Randomized clinical trials for comparing the effectiveness of PCNL with competitors' other standard approaches are suggested.

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The protocol of the current study was approved (IR.BMSU.BAQ.REC.1399.008) by the Baqiyatallah University of Medical Sciences, Tehran, Iran.

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Conflicts of interest

There are no conflicts of interest.

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