

Prevalence of acute kidney injury following percutaneous nephrolithotomy

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Background: The objective is to evaluate the prevalence of acute kidney injury (AKI) as an early complication of the percutaneous nephrolithotomy (PCNL) procedure. **Materials and Methods:** From May 2022 to October 2022, we conducted a retrospective study on patients undergoing PCNL procedures in two of the tertiary medical centers affiliated with Isfahan University of Medical Sciences. Patients' baseline characteristics, laboratory values, perioperative data, and stone features were documented. AKI was defined either as a ≥ 0.3 mg/dL increase in the serum creatinine level within 2 days, or a ≥ 1.5 -fold increase in baseline serum creatinine level within 7 days after the operation. Laboratory values were measured 1 day before PCNL and daily thereafter until discharge. Patients were followed 1 week later to detect all of the possible cases of AKI. **Results:** The final analysis was performed on 347 individuals. AKI developed in 16 (4.61%) cases. The two groups were comparable regarding age ($P = 0.887$), gender ($P = 0.566$), and underlying comorbidities including diabetes mellitus ($P = 0.577$) and hypertension ($P = 0.383$). The mean body mass index (BMI) ($P < 0.001$) and both frequency and severity of hydronephrosis ($P < 0.001$) were significantly different. A higher mean PCNL duration ($P < 0.001$), period of hospitalization ($P < 0.001$), and blood loss volume ($P < 0.001$) were observed in those who developed AKI. Overall, 56.3% (9) of patients in the AKI group and 2.7% (9) in the non-AKI group required the establishment of more than one access tract, during the procedure ($P < 0.001$). A lower preoperative hemoglobin level was observed in the AKI group ($P < 0.001$). Those with AKI had significantly larger stones (3.08 ± 0.46 vs. 2.41 ± 0.23 cm, $P < 0.001$) and higher Hounsfield units ($P < 0.001$). In addition, in the AKI group, most of the calculi (81.3%, 13) were of staghorn type, whereas in the non-AKI group, calculi were most frequently located in the middle calyx (30.2%, 100), ($P < 0.001$). **Conclusion:** The prevalence of post-PCNL AKI is approximately 4.61%. The mean BMI, preoperative hemoglobin level, PCNL duration, intraoperative blood loss volume, and hospitalization period were significantly higher among patients who developed AKI. Those with AKI had significantly larger stones with higher Hounsfield units and more frequently of staghorn type. The two groups were not statistically different regarding age, gender, and presence of comorbidities (hypertension and diabetes mellitus).

Key words: Acute kidney injury, percutaneous nephrolithotomy, prevalence

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INTRODUCTION

Nephrolithiasis is an inseparable part of the daily urologic practice with an approximate prevalence ranging from 1% to 13% in different regions across the globe. Given its high recurrence rate and complications, it imposes a large socioeconomic burden on the health-care system.^[1] In recent years, major progress

has been made in the management strategies of nephrolithiasis. Percutaneous nephrolithotomy (PCNL) is now considered the gold standard treatment option for upper urinary tract calculi larger than 2 cm, as well as selected smaller ones. The minimally invasive nature of the PCNL procedure is combined with relatively higher efficacy and lower complications rate. Nevertheless, it still holds certain shortcomings.^[2]

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Postoperative acute kidney injury (AKI) is a significant complication in urology patients with an occurrence rate of 6.7%–38.2%.^[3] The impact of PCNL on renal function has been a matter of debate. Although in general, stone removal can improve the baseline renal function by eliminating obstruction and eradicating underlying infection,^[4] AKI has been reported as a serious complication of the PCNL procedure, with limited data available regarding its nature. AKI is defined as an acute decline in renal function. Its pathogenesis involves a complex interplay between vascular, tubular, and inflammatory elements,^[5] mostly due to the injuries caused by direct dilating and puncturing of the renal tissue throughout the stone removal procedure. Besides, obstructive uropathy induced by the remaining calculus particles may play an additional part in the pathogenesis of AKI.^[6] Postoperative AKI carries a substantial risk for unfavorable adverse outcomes such as prolonged hospitalization, postoperative urinary tract infection (UTI), development of new chronic kidney disease (CKD), and higher mortality rates,^[3] which could impose a burden on both patients and health-care system.^[7] Several predisposing factors such as age, obesity, metabolic acidosis, certain pharmaceutical agents, and systemic underlying diseases could contribute to the development of AKI.^[8]

The literature is inadequate regarding the evaluation of post-PCNL AKI and no study of this kind has been conducted in Iran; therefore, given the importance of this complication and the necessity of its prevention, we conducted this study to assess the prevalence of post-PCNL AKI and emphasize the importance of detecting high-risk individuals to take timely relevant measures for their management.

MATERIALS AND METHODS

Participants

Men and women between 18 and 80 years of age, who underwent PCNL procedures and had a complete medical record were eligible for being included in this study. Exclusion criteria were: (1) solitary kidney, (2) active UTI, (3) anatomical abnormalities of the genitourinary system, (4) body mass index (BMI) ≥ 35 , (5) history of previous open laparoscopy, and (6) dissent to take part in the program.

Study design

This retrospective study was conducted from May 2022 to October 2022 at the Department of Urology of Al-Zahra and Khorshid Hospitals, Tertiary Medical Centers Affiliated with Isfahan University of Medical Sciences. The study protocol was approved by the internal review board and the ethical approval code was received from the Institutional Research Ethics Committee (IR.MUI.MED.REC.1401.206).

We implemented a convenience nonprobabilistic sampling method. The enrollment algorithm is illustrated in Figure 1. Initially, 413 individuals undergoing the PCNL procedure were assessed. Among them, 347 patients were eligible to be recruited in the study and provided written informed consent.

We extracted the following data from the patients' medical records and documented them in a checklist. In cases of uncertainty regarding a portion of the medical record, the patient was contacted through telephone call. (1) Patient's demographics and baseline characteristics including age, gender, BMI, comorbidities (diabetes mellitus and hypertension), and severity of hydronephrosis. (2) Stone features such as stone's size, location, and Hounsfield unit. (3) Perioperative data consisting of PCNL duration, requirement of more than one access tract, and the volume of blood loss. (4) Postoperative outcomes in the aspect of AKI occurrence and hospitalization period. (5) Pre- and postoperative laboratory values including serum hemoglobin and creatinine levels, as well as estimated glomerular filtration rate (eGFR).

A diagnosis of diabetes mellitus and hypertension was formulated based on the patients' past medical history documents. Besides, a cutoff point of 100 mg/dL for fasting plasma glucose and 140/90 mmHg for blood pressure was applied to identify the cases.

The estimated blood loss volume was extracted from the anesthesia report and calculated using the following formula provided by the "Agreement of surgical blood loss estimation methods:"^[9]

Estimated blood loss = weight \times average blood volume \times $(\text{Hb}_1 - \text{Hb}_2) / \text{Hb}_1$

Average blood volume was estimated at 75 mL/kg in men and 65 mL/kg in women. Hb_1 and Hb_2 represented pre- and postoperative hemoglobin levels, respectively. Preoperative hemoglobin level was measured 1 day before surgery and postoperative hemoglobin was defined as hemoglobin level at day 2 after the surgery.

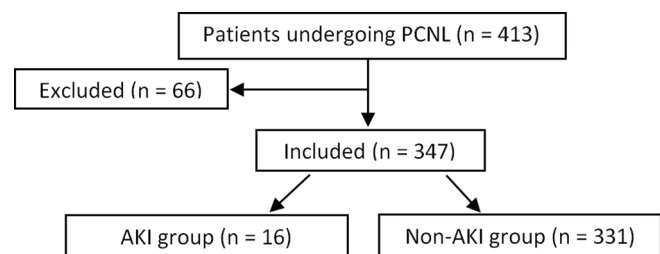


Figure 1: Study flow chart for patient enrollment

We diagnosed AKI according to the criteria provided by the “kidney disease: improving global outcomes (KDIGO),” which is defined either as a ≥ 0.3 mg/dL increase in the serum creatinine level within 2 days or a ≥ 1.5 -fold increase in baseline serum creatinine level within 7 days after the operation.^[10] Each of the selected subjects had undergone a computed tomography (CT) scan before booking the procedure to identify the severity of hydronephrosis and the stone’s characteristics. We measured the paraclinical values 1 day before PCNL and daily thereafter until discharge from the hospital. In addition, we re-evaluated the patients 1 week later to detect all of the possible cases of AKI. Finally, we divided the individuals into 2 groups based on the occurrence of AKI and examined any possible correlation between the underlying characteristics and AKI occurrence.

Percutaneous nephrolithotomy procedure

All procedures were conducted by two experienced urologists using the same method. Under general anesthesia, a 5F ureter catheter was placed in the lithotomy position with cystoscopic guidance. Percutaneous access was obtained with C-armed fluoroscopy combined with retrograde contrast injection through the ureteral catheter. After placing a guidewire, Amplatz dilation was performed and a 30F sheath was inserted. A 26F rigid nephroscope was used to visualize the field. Stones were disintegrated by a pneumatic lithotripter. The procedure was completed by placing a 16F nephrostomy tube through the puncture site.

Statistical analysis

Data were analyzed with Statistical Package for Social Sciences (SPSS) version 18. Qualitative variables were compared between the two groups using the Chi-square and Fisher’s exact tests and are reported as frequency and percentage. After evaluating for normality by Kolmogorov–Smirnov test, either an independent samples *t*-test or a Mann–Whitney *U*-test was applied for the comparison of quantitative variables and they are shown as mean \pm standard deviation. The level of significance was set at 0.05.

RESULTS

The final analysis was performed on 347 consecutive individuals. AKI developed in 16 (4.61%) patients and the sample was divided into AKI ($n = 16$) and non-AKI ($n = 331$) groups, accordingly. Patients’ demographics and baseline characteristics, laboratory values, perioperative data, and stone features are compared and summarized in Table 1.

There was no significant difference between the groups regarding their age ($P = 0.887$), gender ($P = 0.566$), and underlying comorbidities including diabetes mellitus ($P = 0.577$) and hypertension ($P = 0.383$). Of those

who developed AKI, 37.5% (6) were diabetic and 37.5% (6) had a history of hypertension; besides, in the non-AKI group, diabetes mellitus and hypertension were observed in 29.6% (98) and 26% (86) of the population, respectively. Nevertheless, the mean BMI ($P < 0.001$) and both frequency and severity of hydronephrosis ($P < 0.001$) were significantly different between the two groups.

A higher mean PCNL duration (140.31 ± 18.39 vs. 91.79 ± 12.24 min, $P < 0.001$), period of hospitalization (5.00 ± 0.37 vs. 2.09 ± 0.34 days, $P < 0.001$), and blood loss volume (1581.25 ± 258 vs. 1058.61 ± 231 mL, $P < 0.001$) were observed in those who developed AKI. Overall, 56.3% (9) of patients in the AKI group and 2.7% (9) in the non-AKI group required the establishment of more than one access tract, during the procedure ($P < 0.001$). Preoperative serum hemoglobin level was 12.31 ± 0.81 and 13.65 ± 0.65 mg/dL in AKI and non-AKI groups, respectively. A lower preoperative hemoglobin level was observed in the AKI group ($P < 0.001$), whereas preoperative eGFR did not differ significantly ($P = 0.987$). Moreover, patients with AKI revealed a lower hemoglobin level after PCNL ($P < 0.001$) compared to those without AKI.

The mean stone size was 3.08 ± 0.46 and 2.41 ± 0.23 cm in AKI and non-AKI groups, respectively ($P < 0.001$). Stone’s Hounsfield unit was significantly higher in those with AKI ($P < 0.001$). In addition, in the AKI group, most of the calculi (81.3%, 13) were of staghorn type, whereas in the non-AKI group, calculi were most frequently located in the middle calyx (30.2%, 100), ($P < 0.001$).

DISCUSSION

Percutaneous nephrolithotomy’s impact on renal function

The long-term effect of PCNL on renal function is well established; most of the literature uniformly states that renal function either remains unchanged or ameliorates after PCNL.^[11,12] Nevertheless, an acute decline in renal function is reported within the early postoperative days,^[13,14] which then rises toward back to baseline values after 72–96 h.^[15] Besides the local trauma and ischemia caused by direct dilating and puncturing of the parenchyma, which is undoubtedly expected at the introduction site, PCNL could also elicit an acute failure in renal filtration, perfusion, and excretory function bilaterally.^[14] Elevated plasma concentrations of renin and aldosterone during the PCNL procedure result in a reno-renal reflex mediated by the sympathetic nervous system and must be considered as a contributor to bilateral renal vasoconstriction.^[16] Coherent with previous results, we observed a rise in serum creatinine and a decline in glomerular filtration rate (GFR) levels within the first 2 postoperative days, which occurred among the whole population, regardless of the occurrence of AKI.

Table 1: Baseline characteristics, laboratory values, perioperative data, and stone features

Variables	Non-AKI group (n=331)	AKI group (n=16)	P ^a
Demographics and baseline characteristics			
Age (years)	52.70±13.32	53.37±18.53	0.887
Gender, n (%)			
Female	149 (95.51)	7 (4.49)	0.566
Male	182 (95.29)	9 (4.71)	
BMI (kg/m ²)	25.70±2.61	30.12±3.26	<0.001
Diabetes, n (%)			
No	233 (95.88)	10 (4.12)	0.577
Yes	98 (94.23)	6 (5.77)	
Hypertension, n (%)			
No	245 (96.08)	10 (3.92)	0.383
Yes	86 (93.48)	6 (6.52)	
Hydronephrosis, n (%)			
No	31 (72.09)	12 (27.91)	<0.001
Mild	63 (96.62)	2 (3.08)	
Moderate	104 (99.05)	1 (0.95)	
Severe	133 (99.25)	1 (0.75)	
Laboratory values			
Preoperative GFR (mL/min)	79.55±22.665	78.25±28.906	0.825
Postoperative GFR (mL/min)	73.22±20.91	34.06±9.96	<0.001
Preoperative Hb (g/dL)	13.65±0.65	12.31±0.81	<0.001
Postoperative Hb (g/dL)	13.47±0.69	10.59±0.37	<0.001
Peri-operative data			
PCNL duration (min)	140.31±18.39	91.79±12.24	<0.001
Multi-tract access, n (%)			
No	323 (97.87)	7 (2.13)	<0.001
Yes	9 (50.00)	9 (50.00)	
Blood loss volume (mL)	1058.61±231.42	1581.25±258.76	<0.001
Hospitalization period (days)	2.09±0.34	5.00±0.37	<0.001
Stone features			
Size (cm)	2.41±0.23	3.08±0.46	<0.001
Hounsfield unit	606.51±192.74	1136.88±289.64	<0.001
Location, n (%)			
Staghorn	25 (65.79)	13 (34.21)	<0.001
Pelvis	86 (97.73)	2 (2.27)	
Upper calyx	31 (96.88)	1 (3.13)	
Middle calyx	100 (100)	0	
Lower calyx	89 (100)	0	

^aResulted from Chi-square and Fisher's exact tests for qualitative data and independent t-test or a Mann-Whitney U-test for quantitative data. AKI=Acute kidney injury; BMI=Body mass index; GFR=Glomerular filtration rate=Hb: Hemoglobin; PCNL=Percutaneous nephrolithotomy

Acute kidney injury prevalence

Various indicators such as GFR, dimercapto succinic acid (DMSA) scan, diethylenetriamine pentaacetate (DTPA) scan, or ultrasonography^[17] have been applied to effectively determine the decline of renal function; however, we opt to conduct the study on the basis of the most recent consensus on the definition and staging of AKI presented by KDIGO Foundation in 2012.^[10] In the current study, among 347 patients who underwent PCNL, 16 (4.61%) were diagnosed with AKI. Although our result is compatible with the prevalence of 4.4% described by Fulla *et al.*,^[18] a review of the literature revealed higher rates of AKI occurrence. A retrospective observational study on 509 consecutive Indian individuals reported that up to 10% of the patients

can develop post-PCNL AKI.^[19] Yu *et al.* conducted a similar study on Korean individuals and reported a prevalence rate of 16.2%.^[20] All of these articles employed the same definition of AKI as in our study; however, the difference in ethnicities, PCNL equipment, and patients' characteristics may explain the inconsistency in the results.

Baseline characteristics

Although a number of studies have reported that obesity, especially a BMI ≥40, could act as an independent risk factor for postoperative AKI,^[19,21] others fail to demonstrate a significant correlation.^[20] A higher amount of adipose tissue and particularly central fat could play a direct pathogenic role in the afferent and efferent arterial vasomotor balance

resulting in an alteration in the renal hemodynamic profile.^[22] We observed that the mean BMI was higher among those who developed AKI.

In our study, hydronephrosis was negatively associated with AKI occurrence. Seventy-five percent of the patients in the AKI group did not have preoperative hydronephrosis while 40.2% of those without AKI suffered from severe hydronephrosis. Data regarding this aspect is very limited. El-Nahas *et al.* provide similar results as in their study hydronephrosis acted as a significant protective factor, which lost significance in multiple variate analyses.^[23] Micoogullari *et al.* found that only severe stages of hydronephrosis were associated with changes in hemoglobin and postoperative blood transfusion, which could explain the protective role of hydronephrosis against AKI in an indirect fashion. The edematous renal parenchyma can reduce the number of PCNL puncture trials due to the wider calyceal mouth and the more evident distribution of the contrast material. This could result in decreased punctural damage and lower operative duration,^[24] lowering the rate of AKI occurrence.

The autonomic neuropathy caused by diabetes mellitus or the vascular damages induced by persistent hypertension could blunt the hemodynamic response during general anesthesia, leading to intraoperative hypotension and renal parenchymal ischemia.^[25] Consequently, the majority of the literature considers diabetes mellitus and hypertension as predisposing factors for AKI occurrence.^[19,20] Nevertheless, we failed to detect a significant association. Our result is supported by Tabibia *et al.*,^[15] who concluded that diabetes and hypertension had no statistically significant associations with the changes in GFR values within the first 2 postoperative days.

In our study, age was comparable between the two groups and did not show significant differences. Although our outcome is compatible with some of the previous data,^[11,18,20,23] the literature is contradictory and inadequate regarding this association. On the one hand, plasma flow rate and renal responses to vasodilating factors are weaker in older patients, reducing the kidney's adaptive capacity to hemodynamic changes.^[26] Pillai *et al.* reported that age, with a cutoff value of 39.5 years, acts as a highly sensitive predictor of post-PCNL AKI.^[19] On the other hand, most of the studies specifically performed on the geriatric population illustrated a maintained renal status on early post-PCNL days.^[11] Therefore, further studies must be carried out to confirm or refute the outcomes.

Perioperative data and laboratory values

Multiple access tracts could be directly attributed to an increased surface area of parenchymal violation, increasing

AKI occurrence.^[23,27] A multi-tract approach may result in a higher complication rate, blood loss volume, and significant drop in postoperative hemoglobin level, which could imply a rather indirect role in provoking other predictive factors of AKI occurrence than a simple direct association.^[28] An interesting porcine study conducted by Handa *et al.* revealed that besides the marked decline in the ipsilateral renal function, the establishment of multiple tracts also imposes a greater impact on the untreated contralateral kidney leading to a significant drop in GFR level.^[29]

Based on our results, a longer PCNL duration was observed among those who developed AKI. It could be interpreted by the complex interplay that exists between PCNL duration and various influential factors of AKI occurrence implying that surgical duration plays a rather indirect part in AKI development. Moreover, a two-sided relation further explains the outcomes. Not only prolonged operation increase the rate of complications and, therefore, AKI occurrence,^[28] but also, a longer period is required to carry out the operation on more complicated patients with predisposing problems for AKI such as higher BMI.^[30]

Data regarding the association between blood loss volume and AKI occurrence is scarce and only one study of the kind has evaluated this feature.^[20] We observed that the estimated blood loss volume was 1581.25 ml in the AKI group compared to the 1058.61 ml among those who did not develop AKI. El-Nahas *et al.* described the need for blood transfusion as an independent risk factor for AKI.^[23] This could be explained due to the hemodynamic instability caused by excessive bleeding, which leads to prerenal AKI. Besides, Oner *et al.* described that the volume of blood loss is associated with larger stone size, PCNL duration, and the number of access tracts, playing an additional indirect role in the development of AKI.^[28]

We noted that those who had a lower preoperative hemoglobin level were more susceptible to developing AKI. Fulla *et al.* proposed the cutoff point of 10.6 g/dL as a predictor of post-PCNL AKI.^[18] Anemia has been previously demonstrated as an independent risk factor for AKI occurrence, regardless of the type of surgery.^[31]

In our study, the period of hospitalization was significantly longer in the AKI group as compared to those without AKI. Most of the literature revealed that AKI was associated with a longer hospitalization period,^[18,20,32] which is rationally expected as thorough management of patients with AKI commonly requires lengthier periods of medical care.

Stone features

We concluded that the mean stone size and Hounsfield values

were significantly higher in the AKI group. Besides, 81.25% of those with AKI had staghorn calculi, whereas the prevalence of staghorn calculi among patients without AKI was 7.55%. All of the aforementioned features seem to increase the complexity of the PCNL procedure, operative duration, risk of perioperative bleeding, and infective complications; thus, predisposing the patient to AKI.^[19,23] Balasar *et al.* reported a positive correlation between renal stone size and the values of kidney injury molecule-1, which is an ischemic biomarker for predicting and diagnosing AKI.^[33] Moreover, the disintegration process of larger and denser calculi is more difficult and combined with an elevated likelihood of small fragments remaining after the procedure.

Having said all that, AKI is an important complication of the PCNL procedure. Although complete improvement in renal function is commonly achieved after 6–12 months,^[34] it is important to identify high-risk individuals so that we are able to provide timely relevant management. A thorough interdisciplinary cooperation between urology and nephrology, avoidance of nephrotoxic drugs, and appropriate fluid resuscitation are key to avoiding further damage to the kidney.

Limitations and strengths

Despite the insights that the current study may have provided, it contains certain limitations. First, the data are restricted to people of Persian ancestry referring to two of the tertiary medical centers in Isfahan, Iran; therefore, results might not be capable of being generalized to other ethnicities, and studies on more diverse samples are required to establish better comprehensive conclusions. Second, the nature of the study fails to provide a cause-and-effect relationship between AKI occurrence and the presented associated factors. Third, certain predisposing factors such as intraoperative hypotension, preexisting CKD, or patients' pharmaceutical regimen including nonsteroidal anti-inflammatory drug consumption, were not included in this study. Fourth, although the two different urologists conducting the surgical procedures interacted closely with each other and used the same methods and instruments, technique bias was inevitable.

CONCLUSION

In summary, the prevalence of post-PCNL AKI was 4.61% in the present study. We concluded that the mean BMI, preoperative hemoglobin level, PCNL duration, intraoperative blood loss volume, and hospitalization period were significantly higher among patients who developed AKI. Moreover, those with AKI had significantly larger stones with higher Hounsfield units and more frequently of staghorn type. Patients' age, gender, and comorbidities (hypertension and diabetes mellitus) were not statistically different between the groups.

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Conflicts of interest

There are no conflicts of interest.

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