Università di Foggia

PhD Course

"Innovative Sciences and Technologies for Health"

XXXVII Cycle

Title: ***Predicting acute kidney injury after endourological treatment of Kidney stones.***

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Abstract

Introduction and Objective:

Postoperative acute kidney injury (AKI) can occur after Percutaneous Nephrolithotomy (PCNL). This study aimed to assess AKI incidence after standard and mini-PCNL and identify associated risk factors.

Methods:

A retrospective analysis of prospectively collected data from 1,398 patients undergoing PCNL (2005-2024) at a single institution was carried out. Only patients with renal stones into bilaterally anatomically normal kidneys were included. AKI was defined by KDIGO criteria as at least a ≥1.5-fold or ≥0.3 mg/dL increase in baseline serum creatinine (sCr) within 72 hours postoperatively. Multivariable logistic regression analyzed predictors of AKI.

Results:

AKI occurred in 153 (10.9%) patients, classified as stage I, II, and III in 8.0%, 2.0%, and 0.9%, respectively. Major complications increased with AKI severity, notably infections and bleeding requiring angioembolization, leading to AKI patients having a longer postoperative hospital stay. Independent predictors included older age (OR 1.05 per year; 95%CI 1.03–1.07), female gender (OR 1.66; 95%CI 1.14–2.43), baseline eGFR (U-shaped relationship: linear term OR 0.50 per 10-unit increase; 95%CI 0.36–0.68, quadratic term OR 1.06 per 10-unit increase; 95%CI 1.04–1.08), larger tract size >22 Ch (OR 2.29; 95%CI 1.53–3.44), surgical time (OR 1.01 per minute; 95%CI 1.01–1.01), intraoperative hemoglobin loss (OR 1.16 per g/dL; 95%CI 1.05–1.29), minor complications (Clavien grade 1–2, OR 2.29; 95% CI 1.49–3.51), and major complications (Clavien grade≥3, OR 6.08; 95% CI 3.57–10.35).

Conclusion:

AKI following PCNL significantly affects postoperative morbidity and hospitalization. Risk factors include age, gender, baseline renal function, sheath size, surgical time, hemoglobin loss, and postoperative complications. Given the potential negative effects of AKI, urologists should be aware and pay attention to the non-negligible incidence of such event after PCNL, particularly in patients “at risk”

Chapter 1: Introduction

1. Epidemiology of Nephrolithiasis

Nephrolithiasis, or kidney stone disease, is a highly prevalent condition with substantial public health implications worldwide. The prevalence varies by region, ranging from 7–13% in North America, 5–9% in Europe, and 1–5% in Asia [1]. The variation in incidence can be attributed to a complex interplay of environmental, dietary, genetic, and socioeconomic factors. Geography and climate, particularly in hot and arid areas, are strongly associated with dehydration and consequent stone formation. Additionally, lifestyle factors such as inadequate fluid intake, high dietary sodium, protein and oxalate consumption, as well as sedentary behavior, have been shown to increase stone risk.

Genetics also play a notable role, with a positive family history representing a significant risk factor. Certain occupations, especially those involving limited access to hydration or physical inactivity, can further exacerbate this risk. Despite growing awareness and advancements in stone prevention strategies, the disease continues to impose a substantial burden due to its recurrent nature, associated morbidity, and high healthcare costs. Surgical intervention remains a cornerstone of treatment, especially in cases involving larger or symptomatic stones, with endourological techniques offering effective and increasingly less invasive options [2, 3].

1.1. Etiological Classification of Urinary Stones

Urinary stones can be classified according to their underlying etiology, which is essential for guiding treatment and prevention. The major categories include:

- Non-infectious stones: Including calcium oxalate and uric acid stones, the most common types.
- Infectious stones: Typically, struvite stones, associated with urease-producing bacteria (e.g., Proteus, Klebsiella).

- Genetic causes: Such as cystinuria or primary hyperoxaluria, which are often associated with early-onset and recurrent stones [4].
- Drug-induced stones: Resulting from precipitation of poorly soluble medications (e.g., indinavir, triamterene).

Understanding the etiology allows for targeted metabolic evaluation and the implementation of tailored preventive strategies [3].

Table 1.1: Stones classified by aetiology

Non-infection stones
Calcium oxalate
Calcium phosphate
Uric acid
Infection stones
Magnesium ammonium phosphate
Carbonate apatite
Ammonium urate
Genetic causes
Cystine
Xanthine
2,8-Dihydroxyadenine
Drug stones

1.2. Composition of Urinary Stones

Accurate analysis of stone composition is crucial for clinical management, especially for preventing recurrence. Stones often contain multiple components but are generally classified based on their predominant mineral content. The most clinically relevant stone types are presented in Table 1.2

Table 1.2: Stone composition

Chemical name	Mineral name	Chemical formula
Calcium oxalate monohydrate	Whewellite	$CaC_2O_4.H_2O$
Calcium oxalate dihydrate	Wheddelite	$CaC_2O_4.2H_2O$
Basic calcium phosphate	Apatite	$Ca_{10}(PO_4)_6.(OH)_2$
Calcium hydroxyl phosphate	Carbonite apatite	$Ca_5(PO_3)_3(OH)$
b-tricalcium phosphate	Whitlockite	$Ca_3(PO_4)_2$
Carbonate apatite phosphate	Dahllite	$Ca_5(PO_4)_3OH$
Calcium hydrogen phosphate	Brushite	$CaHPO_4.2H_2O$
Calcium carbonate	Aragonite	$CaCO_3$
Octacalcium phosphate		$Ca_8H_2(PO_4)_6.5H_2O$
Uric acid	Uricite	$C_5H_4N_4O_3$
Uric acid dehydrate	Uricite	$C_5H_4O_3.2H_20$
Ammonium urate		$NH_4C_5H_3N_4O_3$
Sodium acic urate monohydrate		$NaC_5H_3N_4O_3.H_2O$
Magnesium ammonium phosphate	Struvite	$MgNH_4PO_4.6H_2O$
Magnesium acid phosphate trihydrate	Newberyite	$MgHPO_4.3H_2O$
Magnesium ammonium phosphate monchydrate	Dittmarite	$MgNH_4(PO_4).H_2O$
Cystine		$[SCH_2CH(NH_2)COOH]_2$
Xanthine		
2,8-Dihydroxyadenine		
Proteins		
Cholesterol		
Calcite		
Potassium urate		
Trimagnesium phosphate		
Melamine		
Matrix		
Drug stones	• Active compounds crystallising in urine • Substances impairing urine composition (Section 4.11)	
Foreign body calculi		

Each type is associated with specific metabolic abnormalities and risk factors, guiding both dietary recommendations and pharmacologic interventions.

1.3. Risk Factors for Stone Formation

The "stone former" status is central to understanding recurrence risk and guiding long-term management. Approximately 50% of patients will have a single recurrence, while more than 10% will develop multiple episodes [5, 6]. Risk factors can be broadly categorized as in Table 1.3. Identification of these risk factors allows for a tailored approach to prevention and management.

Table 1.3: categorization of main risk factors for recurrent kidney stones.

Risk Factor	Description
Low fluid intake	Concentrated urine promotes crystal formation
Hypercalciuria	Elevated urinary calcium levels
Hyperoxaluria	Excess urinary oxalate, often dietary or genetic
Hyperuricosuria	Increased uric acid excretion
Urinary tract infections	Promote struvite stone formation
Obesity and Metabolic Syndrome	Altered urinary pH and increased lithogenic substances
Anatomic abnormalities	Cause urinary stasis and recurrent infections

Table 1.4. High-risk stone formers

General factors
Early onset of urolithiasis (especially children and teenagers)
Familial stone formation
Brushite-containing stones ($CaHPO_4.2H_2O$)
Uric acid and urate-containing stones
Infection stones
Solitary kidney (the kidney itself does not particularly increase the risk of stone formation, but prevention of stone recurrence is of more importance)
Diseases associated with stone formation
Hyperparathyroidism
Metabolic syndrome
Nephrocalcinosis
Polycystic kidney disease (PKD)
Gastrointestinal diseases (i.e., jejuno-ileal bypass, intestinal resection, Crohn's disease, malabsorptive conditions, enteric hyperoxaluria after urinary diversion) and bariatric surgery
Increased levels of vitamin D
Sarcoidosis
Spinal cord injury, neurogenic bladder
Genetically determined stone formation
Cystinuria (type A, B and AB)
Primary hyperoxaluria (PH)
Renal tubular acidosis (RTA) type I
2,8-Dihydroxyadeninuria
Xanthinuria
Lesch-Nyhan syndrome
Cystic fibrosis
Drug-induced stone formation (see Table 4.11)
Anatomical abnormalities associated with stone formation
Medullary sponge kidney (tubular ectasia)
Ureteropelvic junction (UPJ) obstruction
Calyceal diverticulum, calyceal cyst
Ureteral stricture
Vesico-uretero-renal reflux
Horseshoe kidney
Ureterocele
Environmental factors
High ambient temperatures
Chronic lead and cadmium exposure

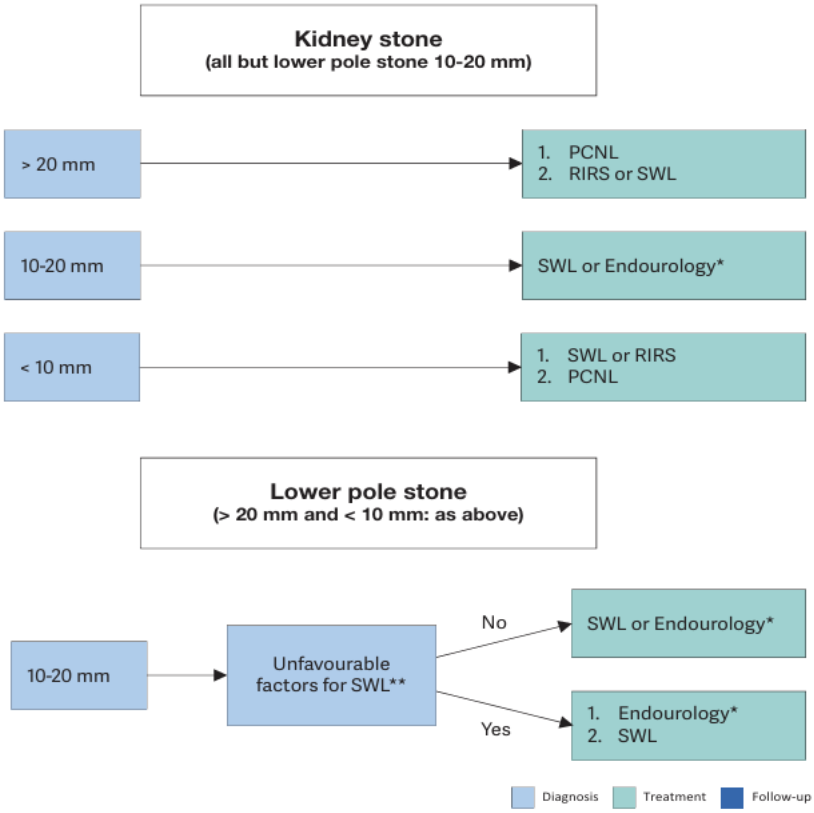
2. Guidelines for the Surgical Management of Urolithiasis

Surgical management of kidney stones has evolved significantly, guided by both technological advancements and evidence-based recommendations. The European Association of Urology (EAU) provides comprehensive guidelines based on stone size, location, composition, and patient factors [3].

For renal stones measuring 1–2 cm, first-line treatments include extracorporeal shock wave lithotripsy (ESWL) and endourological approaches. Endourology encompasses several minimally invasive techniques such as percutaneous nephrolithotripsy (PCNL), ureterorenoscopy (URS), and retrograde intrarenal surgery (RIRS). For stones exceeding 2 cm, PCNL remains the treatment of choice due to its superior stone clearance rates [3].

Patient comorbidities, bleeding risks, anatomic considerations, and surgeon experience all influence the choice of technique. Adherence to these guidelines ensures optimal outcomes while minimizing complications.

Figure 1.1: Treatment algorithm for renal stones (if/when active treatment is indicated)



**The term 'Endourology' encompasses all PCNL and URS interventions.*
PCNL = percutaneous nephrolithotomy; RIRS = retrograde intrarenal surgery; SWL = shock wave lithotripsy; URS = ureteroscopy

2.1. Percutaneous Nephrolithotomy (PCNL)

PCNL is considered the gold standard for managing large (>2 cm) renal calculi. The procedure involves percutaneous access to the renal collecting system, followed by endoscopic fragmentation and extraction of stones. It boasts the highest stone-free rates among all minimally invasive methods.

The miniaturization of PCNL instruments has significantly reduced procedure-related morbidity. Jackman et al. and Helal et al. were pioneers in using smaller tract sizes for pediatric patients in 1997, eventually applying these innovations to adults, achieving reduced complication rates [7, 8].

PCNL variants include:

- Micro-PCNL: 4.8 Fr access sheath
- UltraMini-PCNL (UMP): 11–13 Fr
- Mini-PCNL: 14–20 Fr
- Standard PCNL: >20 Fr

Smaller tract sizes reduce bleeding and renal trauma [9, 10], though they may prolong operative time and reduce visibility [11]. Patients on anticoagulation therapy must discontinue treatment before PCNL due to bleeding risks and require close monitoring [12].

Contraindications to PCNL include:

- Untreated urinary tract infections
- Suspected or confirmed renal malignancy
- Tumors at the access site
- Pregnancy

2.2. Retrograde Intrarenal Surgery (RIRS)

RIRS utilizes flexible ureteroscopes to access and treat intrarenal stones via a retrograde approach. It is indicated for stones between 1 and 2 cm and can be

considered for larger stones in select patients, especially those with contraindications to PCNL, such as bleeding diatheses, obesity, renal anomalies, or solitary kidneys [13].

The EAU guidelines acknowledge both PCNL and RIRS as valid options for mid-sized stones, with the final decision often left to the surgeon’s expertise and institutional resources [3].

3. Kidney Function following endourological treatment for kidney stone

3.1. Acute Kidney Injury (AKI) and Chronic Kidney Disease (CKD)

AKI is a common and serious clinical condition characterized by a rapid decline in kidney function. It affects 7–18% of hospitalized patients and up to 50% of critically ill patients in ICUs [14, 15] . AKI significantly increases the risk of short- and long-term mortality, and survivors face a heightened risk of developing CKD or end stage renal disease, both of which carry substantial health and economic burdens [15]. KDIGO guidelines define AKI as a sudden decrease in kidney function over seven days or less, while CKD involves structural or functional kidney abnormalities lasting more than 90 days [16, 17]. AKI is classified by severity into three stages, typically based on changes in serum creatinine and urine output.

Table 1.5: KDIGO Criteria for AKI Staging Based on Serum Creatinine[17]

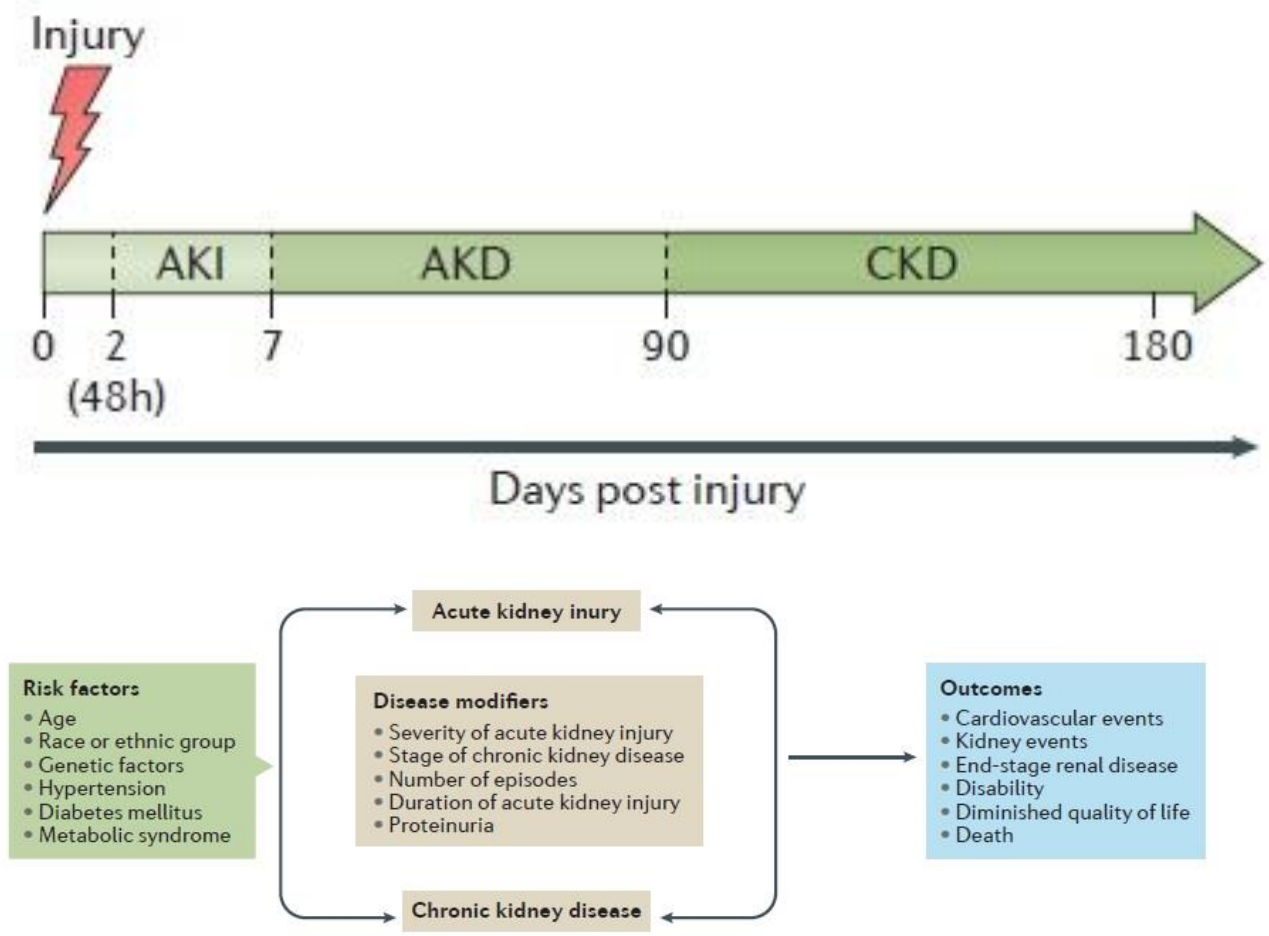
Stage	Serum Creatinine Criteria
1	- 1.5–1.9 times baseline OR - Increase ≥0.3 mg/dL (≥26.5 µmol/L)
2	- 2.0–2.9 times baseline
3	- 3.0 times baseline OR - Increase in serum creatinine to ≥4.0 mg/dL (≥353.6 µmol/L) OR - Initiation of renal replacement therapy OR - In patients <18 years, decrease in eGFR to <35 mL/min/1.73 m²

The term Acute Kidney Disease (AKD) has been introduced to bridge the gap between AKI and CKD. AKD encompasses kidney dysfunction lasting from 7 to 90 days following an AKI event. In 2012, KDIGO proposed that AKD includes:

- eGFR <60 ml/min/1.73 m²
- ↓ GFR >35%
- ↑ serum creatinine >50%
- Renal damage <3 months in duration

While AKI and CKD are well-characterized, AKD remains poorly understood and represents a critical therapeutic window. Patients with preexisting CKD who experience AKD are at particularly high risk for progression to ESRD.

Figure 1.2: Disease continuum from AKI to AKD and CKD



3.2. Methods for Assessing Renal Function and Recovery

A major limitation in AKI management is the lack of accurate tools to assess renal function in real time. Gold standard techniques such as inulin clearance, 51Cr-EDTA, or iohexol clearance are impractical for routine use. Current eGFR equations, while reliable in CKD, are inaccurate in the setting of acute changes (evidence level: 4).

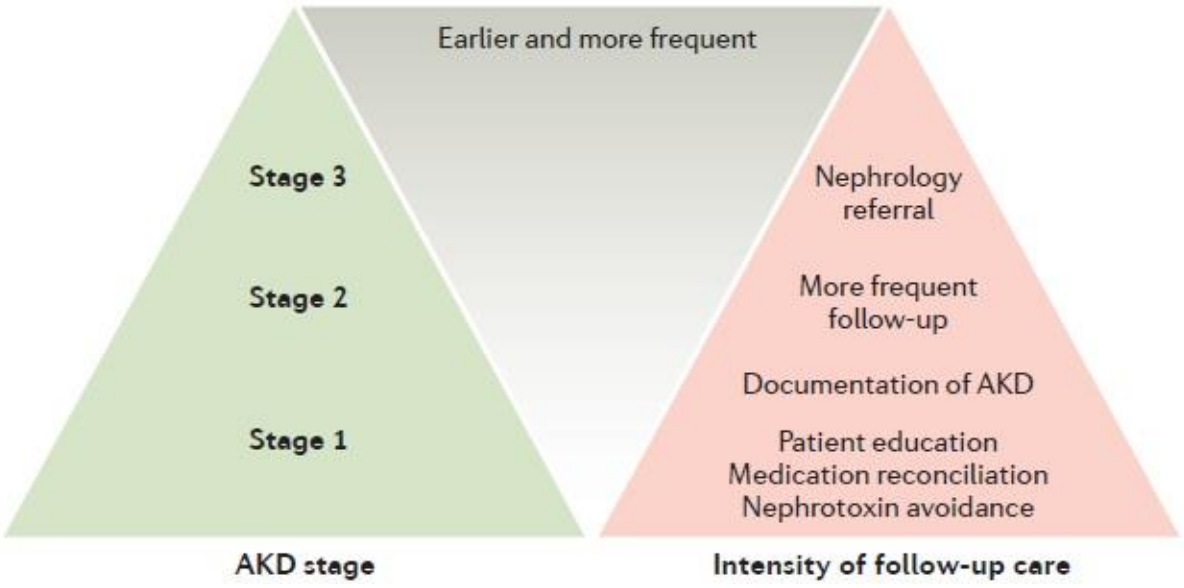
Serum creatinine, although widely used, does not always reflect true renal recovery. Studies show that apparent normalization may mask underlying damage and increased CKD risk [16, 18] . Cystatin C and other filtration markers show promise but require further validation [19]. There is an urgent need for better biomarkers, clinical scores, and imaging tools to identify patients at risk of persistent AKI.

3.3. Follow-Up and Treatment

Recovery from AKI lacks a standardized definition. In practice, improvement is typically inferred from a downstaging of AKI (e.g., from stage 3 to stage 1). While no specific therapy has been conclusively shown to reduce AKI morbidity and mortality, observational studies suggest that early nephrology referral may improve outcomes [20, 21].

Despite this, the majority of AKI survivors do not receive specialized follow-up [22, 23]. Current KDIGO recommendations emphasize that follow-up intensity should be risk-adjusted, but evidence on optimal frequency and intervention strategies remains limited.

Figure 1.3: Proposed follow-up care according to AKD stages.



Chapter 2: Clinical Study

1. Introduction

Percutaneous nephrolithotomy (PCNL) is the recommended treatment option for large or otherwise complex renal or proximal ureteral stones [3]. The procedure involves creating a percutaneous access to the kidney to allow endoscopic stone disintegration and removal of the stone fragments.

Though effective, standard PCNL, i.e. performed with a sheath diameter >22 F, has been considered challenging as major and even lethal complications may occur [24]. Among potential complications there is the risk of loss of nephrons that may result from the trauma caused by puncturing and dilating the renal parenchyma, as well as by the high intrapelvic pressures that may occur during stone fragmentation. High intrarenal pressure may indeed lead to renal damage due to the pressure itself as well as to pyelovenous passage of bacteria released into the bloodstream during stone fragmentation [25]. Such acute postoperative kidney damage may convert into acute renal failure and is currently known as acute kidney injury (AKI).

AKI is diagnosed by calculating the changes in serum creatinine (sCr) from preoperative (baseline) to early (24 to 72 hours after the procedure) postoperative period, and involves at least a >1.5-fold or ≥0.3 mg/dL increase in baseline sCr [17]. Available literature clearly suggest that AKI may lead to postoperative complications and prolonged hospital stay [26]. Additionally, patients who experience AKI are at increased risk of developing chronic kidney disease (CKD), a condition that carries a high economic, social, and personal burden and the risk of increased mortality [27]. This may be particularly relevant in patients with a solitary kidney and/or preexisting CKD.

So far, few studies explored changes in renal function after PCNL. The findings of these studies are controversial as some showed an improvement [28, 29], others showed stable values [30, 31], and others showed a deterioration of renal function [32-35]. Moreover, among those studies reporting renal function deterioration, the incidence of AKI ranged widely from 4.4% to 25% [35]

This study aimed to assess the incidence of post-PCNL AKI and identify risk factors associated with its incidence in patients with renal stone(s).

2. Material and methods

2.1. Study population

Data from patients who underwent percutaneous nephrolithotomy (PCNL) at our department between January 2005 and December 2024 were prospectively entered into an Internal Review Board-approved database. For the present study, only adult patients with renal stones within bilaterally anatomically normal renal kidneys were included. Exclusion criteria comprised children, the presence of a solitary kidney (either functional or anatomical), concomitant ureteral stones, malignant tumors in the treated kidney, and stones located within a calyceal diverticulum.

2.2. Preoperative evaluation

Preoperatively, all patients underwent an abdominal computed tomography (CT) scan to assess stone size, number, and location. Stone size was measured by gathering the longest diameter of the stone or the sum of their longest diameters in the case of multiple stones. A preoperative midstream urine culture was taken to evaluate urinary infections. According to current recommendations [36], patients with positive urine cultures received a single course of sensitivity-based antibiotic therapy. Patients with persistently positive urine culture further received another course of sensitivity-based antibiotics starting 3 days before the procedure and continued until discharge. All patients with a negative urine culture received intravenous antibiotic prophylaxis with 2 g cefazolin and 400mg ciprofloxacin or 300 mg netilmicin at anesthesia induction and 1 g ceftriaxone per day intravenously until discharge if no infectious complications occurred.

2.3. Surgical procedures and follow-up

All procedures were performed with the patient in either the supine anterolateral position or the Galdakao-modified supine position [37, 38]. General anesthesia was routinely used until the end of 2014 and spinal anesthesia became the standard approach since then. Access to the renal collecting system was primarily obtained under fluoroscopic guidance, although ultrasound (US) guidance and the endovision technique were

employed when appropriate. The choice of target calyx was based on stone location and the anatomical configuration of the collecting system.

Between January 2005 and September 2014, the standard PCNL technique was employed, thus using a tract dilation of 26–30 Ch. Tract access was achieved with the Amplatz Type Renal Sheath Set (Boston Scientific, Marlborough, MA, USA). Specifically, following the placement of the 8/10 Ch dilator sheath over the guidewire, a one-step dilation was performed to insert a 17-cm long 26–30 Ch Amplatz sheath. Standard PCNL was conducted using an 8-mm rigid nephroscope (Karl Storz), and lithotripsy was performed with the EMS Swiss Lithoclast Master.

Since September 2014, a gradual transition to mini-PCNL (17.5 Ch) began, with this procedure becoming the routine approach by the end of 2015. Mini-PCNL was performed using the MIP system (Karl Storz, Tuttlingen, Germany). After passing the 11 Ch metallic dilator, a one-step dilation was carried out to insert a 17.5 Ch, 18-cm long “supine” Amplatz sheath. A 4-mm rigid nephroscope (Karl Storz) was used for mini-PCNL, with lithotripsy performed using the holmium laser (Lumenis, Yokneam, Israel) and, more recently, the thulium fiber laser (Quanta, Varese, Italy). Regardless of the laser type used, energy settings were adapted to achieve a combination of dusting (with particles passing around the nephroscope) and the production of 1–3 mm fragments that could be easily evacuated through the sheath via the Venturi effect during nephroscope retraction. At the end of lithotripsy, flexible ureteroscopy and/or flexible nephroscopy were routinely performed to inspect for residual fragments.

The preferred exit strategy was a tubeless approach with the placement of a single-J ureteral catheter or a double-J stent. In cases of standard PCNL, Tachosil was often applied to seal the tract [38]. Nevertheless, nephrostomy tubes were placed when clinically indicated, particularly in cases of significant bleeding or high risk of sepsis.

2.4. Variable definitions

Perioperative complications were classified using the Clavien–Dindo system, as adapted for PCNL procedures [24]. Renal function was assessed via serum creatinine (sCr), measured preoperatively (baseline), and at 24 and 72 hours postoperatively. The

baseline estimated glomerular filtration rate (eGFR) was calculated using the Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) formula [19].
AKI was defined and staged according to the KDIGO criteria [17]: Stage 1, a >1.5-fold or ≥0.3 mg/dL increase in baseline sCr; Stage 2, a ≥2-fold increase; and Stage 3, a ≥3-fold increase or an absolute rise in sCr of ≥4 mg/dL, or the initiation of renal replacement therapy.

2.5. Statistical analysis

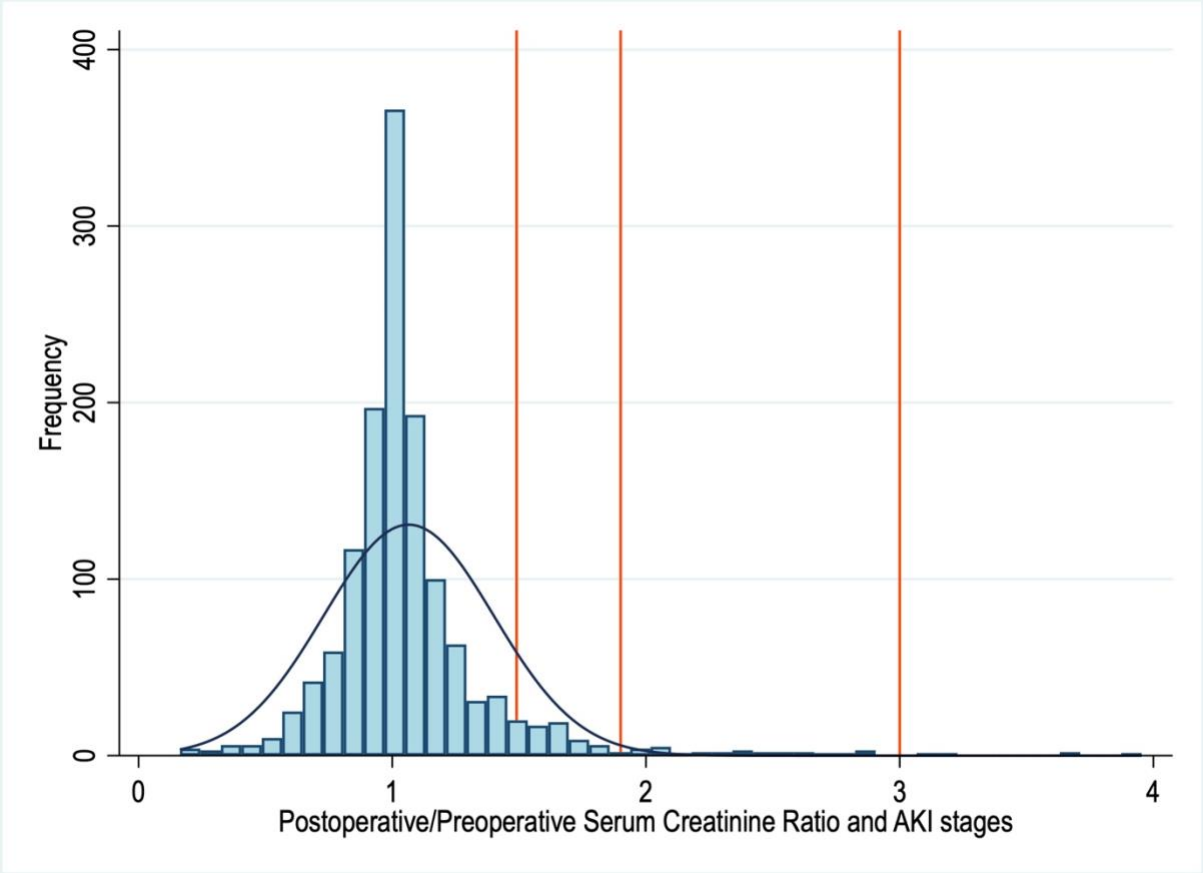
Kidney function changes and AKI stages were graphically presented using a histogram of the Post-operative/Pre-operative sCr ratio. Descriptive statistics were performed for the overall population and stratified according to the presence or absence of AKI after PCNL.
Continuous variables were reported as median and interquartile range and compared by the Kruskal-Wallis test. Categorical variables were reported as frequencies and percentages and were compared using Fisher's exact test or chi-square test, as appropriate. Multivariable binary logistic regression was used to evaluate predictors of any stage AKI using a priori selected variables according to the literature. Baseline eGFR was included in the model as a quadratic term to account for its non-linear association with AKI.
Statistical analyses were conducted using Stata 14. A p-value less than 0.05 was used for evaluating statistical significance.

3. Results

3.1. Post-operative/pre-operative sCr ratio and changes in kidney function after PCNL

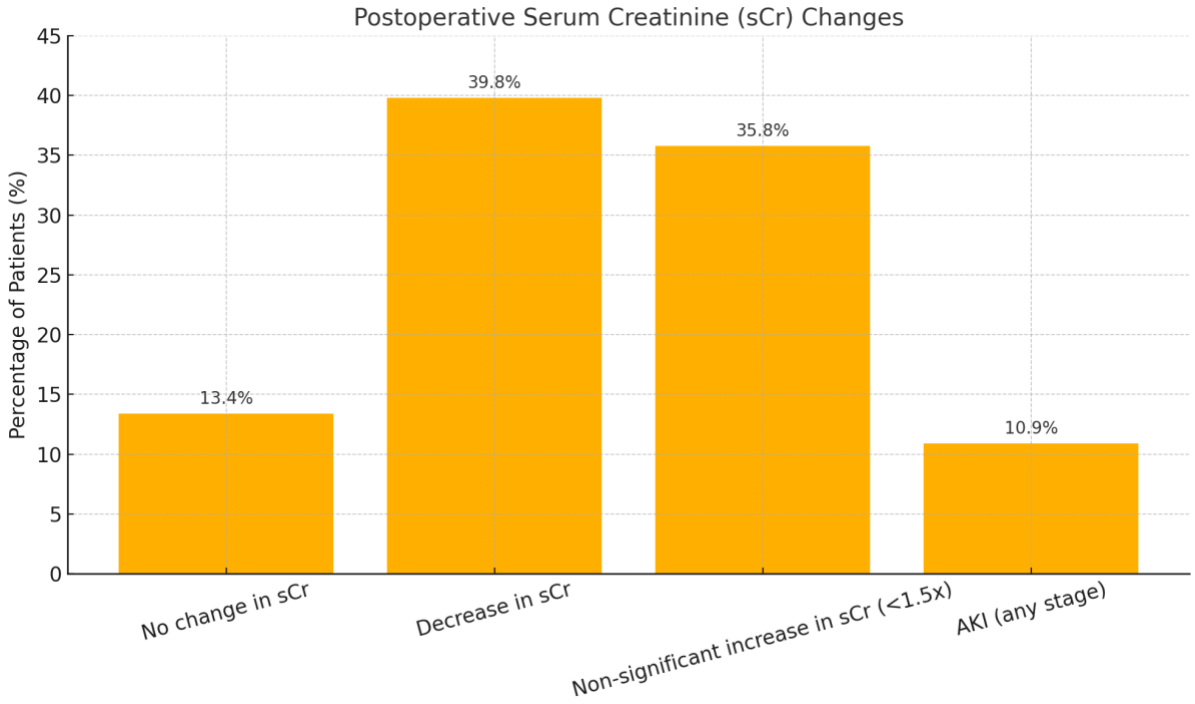
Overall, 1508 patients underwent PCNL at our institution during the study period. Ultimately, 1398 patients were considered eligible for the present study. A histogram showing the post-operative/pre-operative sCr ratio and AKI stages after PCNL in our population is presented in **Figure 2.1**.

Figure 2.1: Histogram showing Post-operative/Pre-operative serum creatinine ratio and AKI stages in patients undergoing PCNL.



In 188 (13.4%) patients, baseline sCr did not change after surgery; 557 (39.8%) patients had a decrease in sCr, while 500 (35.8%) had an increase in sCr of less than <1.5-fold (**Figure 2.2**). According to KDIGO criteria, 153 (10.9%) patients developed any stage of AKI after surgery, with stage I, II, and III being found in 112 (8.0%), 28 (2.0%), and 13 (0.9%) patients, respectively.

Figure 2.2: Postoperative Serum Creatinine (sCr) Changes in patients undergoing PCNL.



3.2. Acute kidney injury after PCNL: pattern of presentations.

Patients who developed postoperative AKI differed significantly from those who did not in several demographic, clinical, and perioperative parameters (**Table 2.1**). Age and BMI were comparable between groups, while female sex was more prevalent among patients with AKI (58.8% vs 49.1%, p=0.023). The prevalence of hypertension, diabetes, and history of previous PCNL did not differ significantly. Baseline hemoglobin was lower in the AKI group (13.1 vs 13.7 g/dL, p=0.011). Baseline eGFR was higher in AKI patients (92.5 vs 86.9 mL/min/1.73m², p=0.001), and baseline serum creatinine was lower (0.7 vs 0.9 mg/dL, p<0.0001). The proportion of staghorn calculi was higher among patients with AKI (25.5% vs 20.6%, p=0.038), and ASA scores were significantly higher in the AKI group (p<0.0001).

Table 2.1. Patients' characteristics according to post-operative AKI

	No AKI N=1245	**AKI** N=153	**P Value**
Age, years	56.0 (47.0, 65.3)	57.0 (44.4, 68.1)	0.6
Gender, n (%)			
Male	634 (50.9%)	63 (41.2%)	**0.023**
Female	611 (49.1%)	90 (58.8%)	
BMI	26.0 (24.0, 29.3)	26.0 (24.0, 31.0)	0.7
Hypertension, n (%)			
Absent	770 (61.8%)	101 (66.0%)	0.3
Present	475 (38.2%)	52 (34.0%)	
Diabetes mellitus, n (%)			
Absent	1061 (85.2%)	133 (86.9%)	0.6
Present	184 (14.8%)	20 (13.1%)	
Baseline Hb	13.7 (12.5, 15.0)	13.1 (12.2, 14.3)	**0.011**
Baseline GFR	86.9 (71.3, 99.0)	92.5 (75.4, 108.3)	**0.001**
Baseline Cr	0.9 (0.8, 1.0)	0.7 (0.6, 0.9)	**<0.0001**
History of previous PCNL, n (%)			
No	1003 (80.6%)	122 (79.7%)	0.8
Yes	242 (19.4%)	31 (20.3%)	
Preop. Urine culture, n (%)			
Negative	1118 (89.8%)	139 (90.8%)	0.7
Positive	127 (10.2%)	14 (9.2%)	
Stone size', mm	23.0 (18.0, 30.0)	25.0 (19.0, 30.0)	**0.038**
Stone features, n (%)			
Single	567 (45.5%)	66 (43.1%)	0.4
Multiple	422 (33.9%)	48 (31.4%)	
Staghorn	256 (20.6%)	39 (25.5%)	
ASA Score, n (%)			
1	412 (33.1%)	24 (15.7%)	**<0.0001**
2	723 (58.1%)	110 (71.9%)	
3	110 (8.8%)	19 (12.4%)	

Peri-operative and Post-operative outcomes are presented in **Table 2.2**. AKI was more frequent in patients having undergone standard PCNL (>22 Ch: 39.9% vs 20.2%, p<0.0001) and in those who had longer surgical times (80 vs 60 minutes, p<0.0001). Postoperative complications were more common among patients with AKI, including both minor (Clavien 1–2: 32.0% vs 18.9%) and major complications (Clavien ≥3: 20.3%

vs 5.4%, p<0.0001). Major (Clavien grade ≥3) infectious complications occurred in 11.1% of AKI patients compared to 5% without AKI (p<0.0001). Hemoglobin loss was higher (1.5 vs 1.2 g/dL, p=0.010), and transfusion rates were increased (8% vs 3%, p=0.001) in the AKI group. Median postoperative hospital stay was longer in the AKI group (3.0 (2.0, 6.0) days vs 3.0 (2.0, 4.0) days, p=0.011).

Table 2.2. Perioperative characteristics and complications according to post-operative AKI

	No AKI N=1245	**AKI** N=153	**P Value**
Amplatz sheath, n (%)			
<22	994 (79.8%)	92 (60.1%)	**<0.0001**
>22	251 (20.2%)	61 (39.9%)	
Surgical time, min	60.0 (50.0, 90.0)	80.0 (65.0, 120.0)	**<0.0001**
Clavien, n (%)			
No Complications	943 (75.7%)	73 (47.7%)	**<0.0001**
1	175 (14.1%)	39 (25.5%)	
2	60 (4.8%)	10 (6.5%)	
3a	62 (5.0%)	23 (15.0%)	
3b	5 (0.4%)	4 (2.6%)	
4a	0 (0.0%)	2 (1.3%)	
5	0 (0.0%)	2 (1.3%)	
Complications, n (%)			
None	943 (75.7%)	73 (47.7%)	**<0.0001**
Clavien 1-2	235 (18.9%)	49 (32.0%)	
Clavien ≥3	67 (5.4%)	31 (20.3%)	
Mean Postop. Hosp Stay, Days	3.0 (2.0, 4.0)	3.0 (2.0, 6.0)	**0.011**
Infectious complications, n (%)			
None	1110 (89.2%)	122 (79.7%)	**<0.0001**
Clavien 1-2	73 (5.9%)	11 (7.2%)	
Clavien≥3	62 (5.0%)	20 (11.1%)	
Hb Loss, g/dl	1.2 (0.3, 2.0)	1.5 (0.4, 2.8)	**0.010**
Blood Transfusion, n (%)			
No	1212 (97%)	141 (92%)	**0.001**
Yes	33 (3%)	12 (8%)	

The distribution of major complications varied significantly according to the presence and severity of AKI **(Table 2.3).** Among patients without AKI (n=1245), the most frequent Clavien grade 3a complication was febrile UTI or suspected sepsis without organ failure requiring supportive therapy and enhanced monitoring (4.1%), followed by issues related to stent or nephrostomy displacement. In contrast, infectious complications became increasingly prevalent with higher AKI severity, occurring in 11.6% of patients with stage 1 AKI, 17.9% in stage 2, and 23.1% in stage 3. Serious events requiring angioembolization for bleeding (Clavien grade 3b) also increased with AKI severity—from 0.3% in patients without AKI to 7.7% in those with stage 3. Clavien grade 4 events, such as postoperative tetany or combined colon perforation and bleeding requiring nephrectomy and colostomy, were rare and occurred only in patients with AKI. Notably, both deaths (Clavien 5) occurred in patients with stage 3 AKI and were attributed to infectious complications. These findings highlight a clear association between increasing AKI severity and the risk and complexity of postoperative complications.

Table 2.3. Categorization of Complications according to Clavien Score and presence and stages of AKI

Major Complications	**No AKI** (N=1245)	**AKI Stage 1** (N=112)	**AKI Stage 2** (N=28)	**AKI Stage 3** (N=13)
Clavien 3a				
Bleeding managed by postoperative ureteric stenting	1 (0.1%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Displaced mono-J stent managed by ureteric stenting	2 (0.2%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Displaced nephrostomy requiring ureteric stenting	3 (0.2%)	1 (0.9%)	0 (0.0%)	0 (0.0%)
Hemothorax managed by intercostal draining	1 (0.1%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Febrile UTI or suspected sepsis without organ failure	51 (4.1%)	13 (11.6%)	5 (17.9%)	3 (23.1%)
Perirenal abscess managed by percutaneous drainage	0 (0.0%)	0 (0.0%)	1 (3.6%)	0 (0.0%)
Urine leakage managed by ureteric stenting	4 (0.3%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Clavien 3b				
Bleeding managed by Angio embolization	4 (0.3%)	2 (1.8%)	1 (3.6%)	1 (7.7%)
Colon Perforation managed by colostomy	1 (0.1%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Clavien 4				
Postoperative tetany managed in ICU	0 (0.0%)	0 (0.0%)	1 (3.6%)	0 (0.0%)
Colon Perforation and Bleeding managed by nephrectomy and colostomy	0 (0.0%)	1 (0.9%)	0 (0.0%)	0 (0.0%)
Clavien 5				
Death due to infective complication	0 (0.0%)	0 (0.0%)	0 (0.0%)	2 (15.4%)

3.3. Predictors of AKI after PCNL

Multivariable logistic regression identified several independent predictors of AKI following PCNL (**Table 2.4**). Increasing age was associated with higher odds of AKI (OR 1.05 per year; 95% CI 1.03–1.07; $p<0.001$), as was the female gender (OR 1.66; 95% CI 1.14–2.43; $p=0.008$). In this model, the linear term for baseline eGFR was inversely associated with AKI (OR 0.50 per 10-unit increase; 95% CI 0.36–0.68; $p<0.001$), while the quadratic term showed a positive association (OR 1.06 per 10-unit increase; 95% CI 1.04–1.08; $p<0.001$), indicating a U-shaped relationship.

Standard PCNL (>22 Ch) was significantly associated with increased odds of AKI (OR 2.29; 95% CI 1.53–3.44; $p<0.001$), as was surgical time (OR 1.01 per minute; 95% CI 1.01–1.01; $p<0.001$). Postoperative complications were also strongly predictive: Clavien grade 1–2 complications conferred a more than twofold increase in risk (OR 2.29; 95% CI 1.49–3.51; $p<0.001$), while Clavien grade ≥3 complications were associated with markedly higher odds of AKI (OR 6.08; 95% CI 3.57–10.35; $p<0.001$). Hemoglobin loss emerged as an additional independent predictor (OR 1.16 per g/dL; 95% CI 1.05–1.29; $p=0.006$).

Table 2.4. Multivariable Analysis predicting AKI after PCNL Including preoperative eGFR levels

Covariate	OR	95% CI	P-value
Age, per year	1.05	1.03 - 1.07	**<0.001**
Gender			
Male	Ref.		
Female	1.66	1.14 - 2.43	**0.008**
Baseline eGFR, per 10 unit	0.50	0.36 - 0.68	**<0.001**
Baseline eGFR ^{2}, per 10 unit	1.06	1.04 - 1.08	**<0.001**
Amplatz sheath size			
Mini (<22)	Ref.		
Standard (≥22)	2.29	1.53 - 3.44	**<0.001**
Surgical time, per minute	1.01	1.01 - 1.01	**<0.001**
Complications			
None	Ref.		
Clavien 1-2	2.29	1.49 - 3.51	**<0.001**
Clavien≥3	6.08	3.57 - 10.35	**<0.001**
Hb loss, per g/dl	1.16	1.05 - 1.29	**0.006**

The association between eGFR and AKI is graphically presented in **Figure 2.3** with patients at low and high eGFR having higher risk of AKI.
Similarly, we further evaluated the association between Amplatz sheath size, surgical time, and the risk of AKI (**Figure 2.4**).

Figure 2.3. Association of eGFR and risk of AKI after PCNL

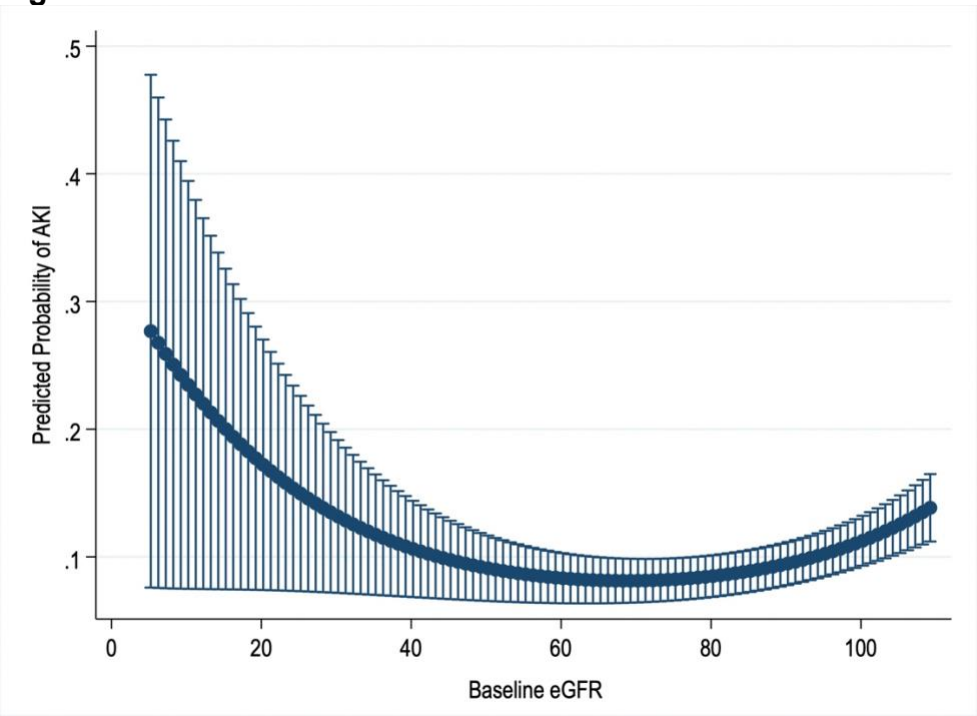
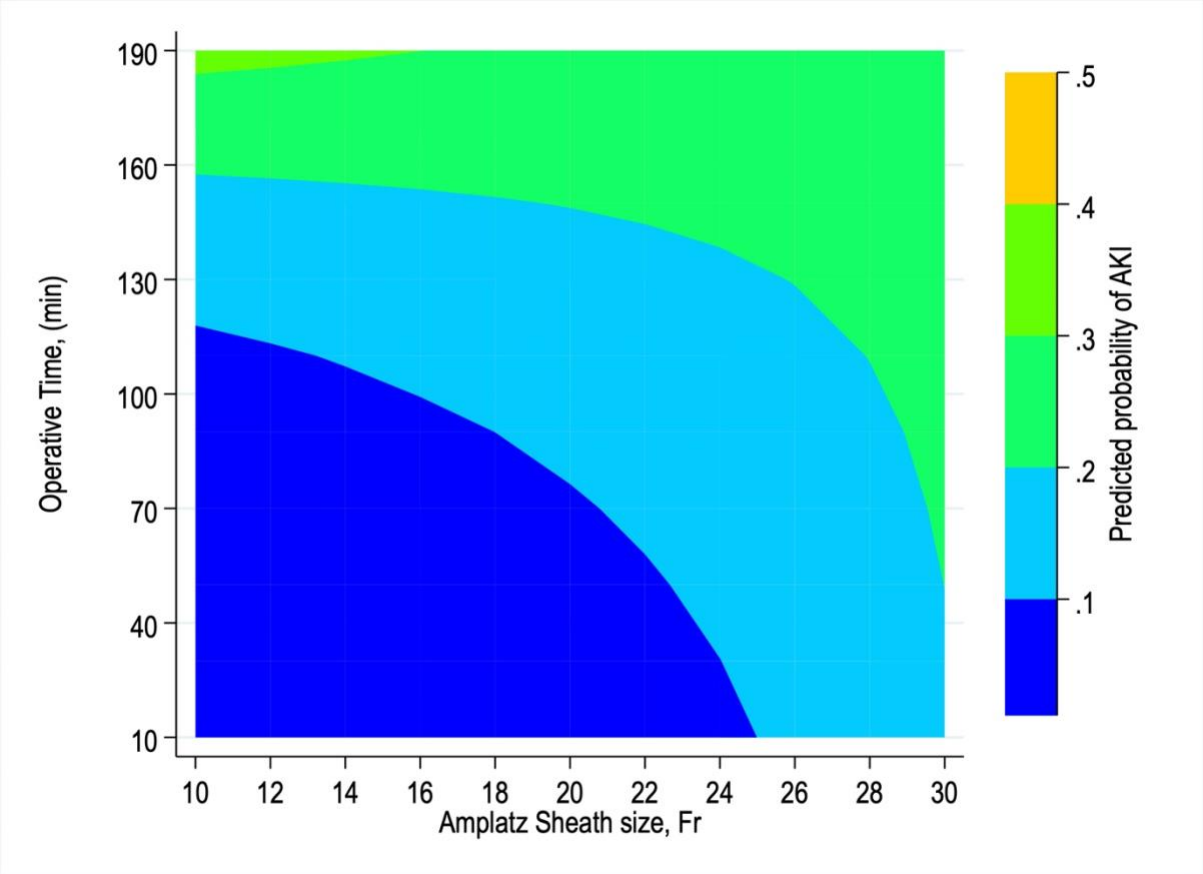


Figure 2.4. Contour Plot showing the association of Operative time and Amplatz sheath size with AKI.



4. Discussion

In this study, we evaluated the incidence, clinical presentation, and predictors of AKI following standard and mini PCNL in patients harboring kidney stone into bilaterally anatomically normal kidneys. Although overall renal function was not adversely affected in most cases, AKI occurred in 10.9% of patients, with 2.9% experiencing AKI stage 2 or 3. Significant predictors of AKI included increasing age, female gender, and baseline renal function (exhibiting a U-shaped relationship with eGFR). Additionally, intraoperative factors such as prolonged surgical time, standard PCNL (Amplatz sheath >22 Ch), and increased hemoglobin loss were associated with an elevated risk. Furthermore, postoperative complications, both minor and major, were strongly correlated with AKI development.

These findings support the hypothesis that both patient-related and procedural factors contribute to renal injury following PCNL. Although injury mechanisms may vary among individuals, potential contributors include mechanical trauma to renal parenchyma from tract dilation, elevated intrapelvic pressures causing pyelovenous backflow, ischemic insults from significant blood loss or hypotension, and infectious complications.

Our findings align with previous research demonstrating varied outcomes concerning renal function after PCNL [28, 29, 32-35, 39]. In our cohort, 42.9% experienced postoperative improvement in serum creatinine, likely reflecting obstruction relief, as previously described by Pérez-Fentes et al. [40]. Conversely, 35.8% had a modest rise in serum creatinine without meeting AKI criteria, while only a small subgroup of patients (2.9%) developed moderate-to-severe AKI.

Notably, surgical time and Amplatz sheath size emerged as primary determinants of AKI risk following PCNL. This supports the rationale for using smaller tract sizes whenever possible, given that mini-PCNL reduces renal parenchymal trauma and the subsequent damage, and emphasizes the importance of minimizing operative duration to reduce exposure to high intrapelvic pressures. It is worth mentioning that in our experience mini-PCNL was not associated with longer surgical time nor lower stone-free rates even in complex populations such as the obese patients [41].

Studies comparing standard-PCNL, mini-PCNL and retrograde intrarenal surgery (RIRS) primarily focused on stone-free rates, procedural metrics, and postoperative

complications [42], whereas the impact of these procedures on renal function has been less extensively evaluated [25]. Memmos et al [43] recently published the first randomized clinical trial comparing standard PCNL, mini-PCNL, and retrograde intrarenal surgery (25 patients in each arm) by assessing urinary biomarkers indicative of tubular injury, such as neutrophil gelatinase-associated lipocalin (NGAL), kidney injury molecule-1 (KIM-1), and interleukin-18 (IL-18). Their findings revealed significant increases in these biomarkers across all three procedures shortly after surgery, suggesting mild and transient tubular injury. No significant differences were observed between the procedures regarding these biomarkers but the study was not powered to test differences between the three arms [43].

The correlation between AKI severity and postoperative complications is particularly noteworthy as demonstrated by our findings. The incidence of infectious complications, bleeding requiring angioembolization and blood transfusion, and mortality were significantly higher in patients who developed AKI, particularly stage 3 AKI. Thus, AKI may represent not only a marker of intraoperative stress but also an indicator of a more complicated postoperative course. This also highlights the need for patient-tailored postoperative management, i.e. balancing fluids and avoiding drugs associated with kidney damage and hypotension, in those developing major postoperative complications.

Although AKI is commonly considered reversible [44], its occurrence has been linked to CKD progression, particularly in vulnerable populations. While our study focused primarily on early postoperative outcomes, future research should include mid- and long-term follow-up to fully elucidate the potential for long-lasting renal impairment.

Several limitations warrant consideration. First, AKI was defined solely by serum creatinine changes, potentially overlooking subclinical or tubular injury. Incorporating novel biomarkers such as NGAL or KIM-1 in future studies could enhance diagnostic sensitivity. Second, systematic long-term renal follow-up data were unavailable in our study. Third, as a single-center retrospective study, our findings may be subject to unmeasured confounding factors, necessitating external validation.

Despite these limitations, the large sample size, prospective data collection methodology, and comprehensive multivariable analysis reinforce the reliability of our conclusions.

Our data indicate that evaluating PCNL safety should extend beyond traditional outcomes such as stone-free rates and bleeding complications to include renal function assessments. This approach is especially crucial for patients at heightened risk of renal impairment, emphasizing the importance of minimizing renal parenchymal injury.

5. Conclusion

AKI is a relatively common complication following PCNL, occurring in over 10% of patients, and contributes significantly to postoperative morbidity, prolonged hospitalization, and also death. Independent predictors of AKI identified in this study include increased age, female gender, baseline renal function, surgical time, larger tract sizes, intraoperative hemoglobin loss, and postoperative complications. Given the potential negative effects of AKI, urologists should be aware and pay attention to the non-negligible incidence of such event after PCNL, particularly in patients “at risk”. Future investigations should confirm the long-term renal consequences of PCNL-related AKI and explore strategies that could mitigate its adverse outcomes.

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