Observational Study

Medicine®

OPEN

Risk factors for acute kidney injury after percutaneous nephrolithotomy

Implications of intraoperative hypotension

Jihion Yu, MD[a], Hyung Keun Park, MD, PhD[b], Hyun-Jung Kwon, MD[a], Joonho Lee, MD[a], Jai-Hyun Hwang, MD, PhD[a], Hee Yeong Kim, MD[c,*], Young-Kug Kim, MD, PhD[a,*]

Abstract

Percutaneous nephrolithotomy (PNL) is a minimally invasive technique for renal stone removal but can cause renal parenchymal injury. Renal stones can also affect renal function. We evaluated the risk factors for acute kidney injury (AKI) after PNL.

The study cohort included 662 patients who underwent PNL. Patient characteristics, preoperative laboratory values, intraoperative data, and stone characteristics were collected. Univariate and multivariate logistic regression analyses were performed to identify risk factors for AKI after PNL. Postoperative outcomes such as hospitalization, intensive care unit admission rate and stay duration, and chronic kidney disease were also evaluated.

Of the total study series, there were 107 (16.2%) cases of AKI after PNL (AKI group), and 555 (83.8%) patients who showed no injury (no-AKI group). The risk factors for AKI after PNL were found to be a higher preoperative serum uric acid level [odds ratio (OR) = 1.228; 95% confidence interval (95% CI) = 1.065–1.415; $P = .005$], longer operation time (OR = 1.009; 95% CI = 1.004–1.014; $P < .001$), and intraoperative hypotension (OR = 12.713; 95% CI = 7.762–20.823; $P < .001$). Hospitalization and intensive care unit stay duration were significantly longer in the AKI group (8.7 ± 5.2 vs 6.6 ± 2.8 days, $P < .001$; 0.34 ± 1.74 vs 0.07 ± 0.48 days, $P = .002$, respectively). Chronic kidney disease was also significantly higher in the AKI group (63.6% vs 32.7%, $P = .024$).

As intraoperative hypotension is an important risk factor for AKI after PNL, which leads to poor postoperative outcomes, it should be prevented or managed vigorously during PNL.

Abbreviations: AKI = acute kidney injury, CI = confidence interval, CKD = chronic kidney disease, CKD-EPI = CKD Epidemiology Collaboration, eGFR = estimated glomerular filtration rate, OR = odds ratio, PNL = percutaneous nephrolithotomy, RBC = red blood cell.

Keywords: acute kidney injury, intraoperative hypotension, percutaneous nephrolithotomy

1. Introduction

Percutaneous nephrolithotomy (PNL) is a minimally invasive technique for renal stone removal and is an efficient procedure for large, multiple, and complex stones, particularly staghorn calculi or smaller symptomatic stones that are refractory to extracorporeal shock wave lithotripsy therapy.[1–3] Nevertheless, PNL-related postoperative complications have been reported, including renal hemorrhage, colonic or pleural injury, postoperative pulmonary complications, and septicemia.[4,5] Hence, meticulous anesthetic and surgical management is required during PNL.

Postoperative acute kidney injury (AKI) can lead to poor postoperative outcomes and a longer hospital or intensive care unit stay.[6,7] AKI is a common postoperative complication in urology patients, with an incidence rate of 6.7% to 38.2%.[8–10] The PNL procedure can directly cause renal injury because it involves puncturing and dilating the renal parenchyma to remove the stones. In addition, renal stones can induce obstructive uropathy.[11] Hence, changes in renal function can occur after PNL. However, the incidence, risk factors, and outcomes of AKI after PNL have remained unclear. Furthermore, a definite treatment course for postoperative AKI has not been well established. It is therefore necessary to evaluate the risk factors for AKI after PNL to prevent and minimize its occurrence.

We sought in our current study therefore to identify independent risk factors for AKI after PNL. In addition, we evaluated the postoperative outcomes in patients who have undergone this procedure, including hospitalization, intensive care unit admission rate and stay duration, and chronic kidney disease (CKD).

2. Methods

2.1. Patients

We performed a retrospective cohort study of patients who underwent PNL from January 2005 to December 2015 at Asan

Editor: Helen Gharaei.

No competing financial interests exist and the authors have no conflicts of interest.

[a] Department of Anesthesiology and Pain Medicine, [b] Department of Urology, Asan Medical Center, University of Ulsan College of Medicine, [c] Department of Anesthesiology and Pain Medicine, Hangang Sacred Heart Hospital, Hallym University College of Medicine, Seoul, Republic of Korea.

[*] Correspondence: Young-Kug Kim, Department of Anesthesiology and Pain Medicine, Asan Medical Center, University of Ulsan College of Medicine, 88, Olympic-ro 43-gil, Songpa-gu, Seoul 05505, Republic of Korea (e-mail: kyk@amc.seoul.kr); Hee Yeong Kim, Department of Anesthesiology and Pain Medicine, Hangang Sacred Heart Hospital, Hallym University College of Medicine, 12, Beodeunaru-ro 7-gil, Yeongdeungpo-gu, Seoul 07247, Republic of Korea (e-mail: kamangkebi@naver.com).

Medicine (2018) 97:30(e11580)

Received: 21 February 2018 / Accepted: 19 June 2018

http://dx.doi.org/10.1097/MD.0000000000011580

Medical Center, a tertiary care hospital in Seoul, Republic of Korea. Our study protocol was approved by the Institutional Review Board of Asan Medical Center (approval number: 2016-0432). For patients who underwent more than 1 PNL procedure, we analyzed the AKI incidence and postoperative outcomes after their first surgery. We excluded patients under the age of 18 years and those with a known CKD.

2.2. Anesthetic and surgical techniques

Anesthetic techniques for PNL were performed in accordance with our institutional standards. Briefly, anesthesia was induced by propofol, rocuronium, and sevoflurane, and maintained using a 1.5 to 2.5 vol% sevoflurane and a 50% O_2/air mixture with supplemental rocuronium. The radial artery was cannulated for continuous arterial blood pressure monitoring. Mechanical ventilation was performed with a tidal volume of 8 to 10 mL/kg at a respiratory rate of 10 to 14 breaths/min to maintain an end-tidal carbon dioxide concentration at 35 to 40 mm Hg. Fluid was administered according to our institutional protocol with a guidance of mean arterial blood pressure, heart rate, and blood loss. Crystalloid [lactated Ringer solution or Plasma solution A (CJ Pharmaceutical, Seoul, Korea)] was administrated at a rate of 2 to 4 mL/kg/h, and colloid (Voluven, 6% hydroxyethyl starch 130/0.4) was administered when estimated blood loss >500 mL occurred during PNL. Mean arterial blood pressure was maintained at > 70 mm Hg. If the mean arterial blood pressure was not maintained at >70 mm Hg, additional fluids or drugs such as ephedrine, phenylephrine, and norepinephrine were administered. Transfusion of red blood cells (RBCs) was performed when the hemoglobin concentration decreased to <8 g/dL during surgery.

PNL procedures were performed using standard techniques at our institution.[12] Briefly, the patient was placed in the lithotomy position and a ureteral catheter was placed using cystoscopy. After placement of the patient in a prone position, the ureteral catheter position was confirmed by fluoroscopy, and a renal puncture was performed using an intercostal or subcostal approach. After inserting the guide wire, the track was dilated using a balloon and a 34-French working sheath was inserted. The stone was broken using an ultrasonic lithotripter, a ballistic lithotripter, or a holmium: YAG laser, and then removed using a grasp. Finally, a 14-French malecot nephrostomy tube was placed in the renal pelvis to allow the urine to drain.

2.3. Data collection

The following data were collected: patient characteristics, preoperative laboratory values, intraoperative data, stone characteristics, and postoperative outcomes. Patient characteristics included age, gender, body mass index, American Society of Anesthesiologists physical status, comorbidities (hypertension and diabetes mellitus), preoperative beta-blocker use (atenolol, carvedilol, propranolol, or disoprolol), preoperative calcium channel blocker use (amlodipine, felodipine, nifedipine, diltiazem, or nicardipine), preoperative angiotensin converting-enzyme inhibitor or angiotensin II receptor blocker use (captopril, losartan, valsartan, or candesartan), and preoperative nonsteroidal anti-inflammatory drug use (aspirin, ibuprofen, or aceclofenac). Preoperative laboratory values included serum hemoglobin, platelet, prothrombin time, uric acid, albumin, blood urea nitrogen, creatinine, sodium, and potassium. Intraoperative data included operation time, RBC transfusion, amounts of total fluid administered, amounts of crystalloid administered, amounts of colloid administered, estimated blood loss, intraoperative lowest hematocrit, intraoperative hypotension, hydronephrosis, and surgical approach (intercostal or subcostal). Estimated blood loss was calculated by the following formula: Estimated blood loss (mL) = patient's estimated blood volume (mL) × [preoperative hematocrit (%) - postoperative hematocrit (%)] + (transfused RBC in units × 213 mL × 70%); in this formula, the patient's estimated blood volume was 75 mL/kg for males and 65 mL/kg for females, the average volume of RBC was 213 mL, and the average hematocrit of RBC was 70%.[13,14] Stone characteristics included number, location, size, analysis, and staghorn stone. Postoperative outcomes included hospitalization, intensive care unit admission rate and stay duration, and CKD at 12 months after PNL.

2.4. Definitions

Intraoperative hypotension was defined as a mean arterial blood pressure of <70 mm Hg for >5 minutes recorded in the intraoperative anesthesia records.[15] Postoperative AKI was defined by applying the Kidney Disease: Improving Global Outcomes criteria, that is, an increase in the serum creatinine level by ≥0.3 mg/dL within 2 days after surgery or an increase in the serum creatinine level to ≥1.5 times the baseline value within 7 days after surgery.[16] CKD was evaluated at 12 months after the PNL procedure and was defined by an estimated glomerular filtration rate (eGFR) of <60 mL/min/1.73 m^2.[17] eGFRs were calculated using the CKD Epidemiology Collaboration (CKD-EPI) equation: $eGFR_{CKD\text{-}EPI} = 141 \times [\text{minimum of standardized serum creatinine (mg/dL)}/\kappa \text{ or } 1]^{\alpha} \times [\text{maximum of standardized serum creatinine (mg/dL)}/\kappa \text{ or } 1]^{-1.209} \times 0.993^{age} \times (1.018 \text{ if female}) \times (1.159 \text{ if black})$, where κ is 0.7 for women and 0.9 for men and α is −0.329 for women and -0.411 for men.[18]

2.5. Statistical analysis

All data were expressed as the mean ± standard deviation and number (percentage). The Student *t* test or Mann–Whitney *U* test was used for continuous variables. The Chi-square test or Fisher exact test was used for categorical variables. Univariate logistic regression analysis was performed to identify risk factors for AKI after PNL. All variables that had *P* value <.05 on univariate logistic regression analysis were entered into stepwise multivariate logistic regression analysis. All variables for logistic regression analysis were checked for multicollinearity, and only the variables with variance inflation factors <10 were used. In addition, univariate and multivariate logistic regression analyses were performed to evaluate the variables associated with intraoperative hypotension during PNL. *P* values <.05 were considered to be statistically significant. All statistical analyses were performed using SPSS version 22.0 (IBM, Armonk, NY).

3. Results

A total of 662 patients who underwent PNL at our hospital during the study period were included (Fig. 1). Table 1 presents the demographic characteristics of the study patients. Of the 662 study patients, 107 (16.2%) experienced AKI after PNL. Preoperative beta-blocker and nonsteroidal anti-inflammatory drug uses were significantly higher in the AKI cases. The preoperative serum uric acid and creatinine levels were also significantly higher in the AKI group. Table 2 lists the

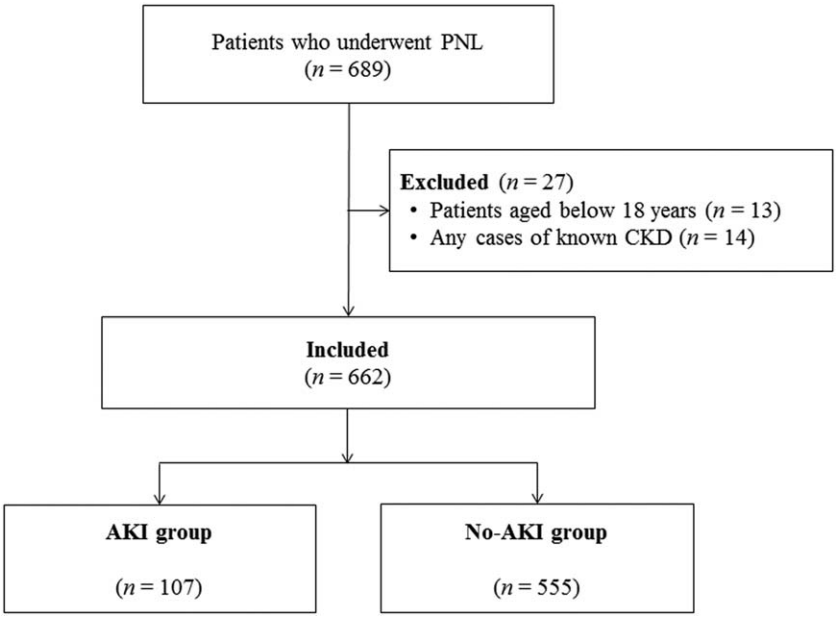

Figure 1. Study flow chart. AKI = acute kidney injury, CKD = chronic kidney disease, PNL = percutaneous nephrolithotomy.

intraoperative data and stone characteristics. Operation time was significantly longer in the AKI group; RBC transfusion, amount of total fluid administered, amount of colloid administered, estimated blood loss, and intraoperative lowest hematocrit were significantly higher in the AKI group as well. Intraoperative hypotension was also significantly higher in the AKI group cases. The stone characteristics did not differ significantly between the 2 groups.

The results of univariate logistic regression analysis indicated that the preoperative beta-blocker use, preoperative nonsteroidal anti-inflammatory drug use, preoperative serum uric acid level, preoperative serum creatinine level, operation time, RBC transfusion, amounts of colloid administered, estimated blood loss, intraoperative lowest hematocrit, and intraoperative hypotension were significantly associated with AKI after PNL (Table 3). Multivariate logistic regression analysis further

Table 1

Patient characteristics and preoperative laboratory values.

Variables	All patients (n = 662)	AKI group (n = 107)	No-AKI group (n = 555)	P*
Age, y	54.8 ± 12.5	55.9 ± 12.6	54.5 ± 12.5	.297
Gender (male)	409 (61.8)	75 (70.1)	334 (60.2)	.053
Body mass index, kg/m^2	24.98 ± 4.12	24.86 ± 4.38	25.00 ± 4.06	.755
ASA physical status				.732
≤ 2	646 (97.6)	104 (97.2)	542 (97.7)	
3	16 (2.4)	3 (2.8)	13 (2.3)	
Hypertension	278 (42.0)	53 (49.5)	225 (40.5)	.084
Diabetes mellitus	122 (18.4)	19 (17.8)	103 (18.6)	.845
Preoperative beta-blocker	49 (7.4)	14 (13.1)	35 (6.3)	.018
Preoperative CCB	176 (26.6)	29 (27.1)	147 (26.5)	.905
Preoperative ACEi/ARB	52 (7.9)	9 (8.4)	43 (7.7)	.844
Preoperative NSAID	52 (7.9)	14 (13.1)	38 (6.8)	.028
Preoperative laboratory test				
Hemoglobin, g/dL	13.8 ± 1.8	13.7 ± 1.8	13.8 ± 1.8	.435
Platelet, $10^3/\mu L$	245.5 ± 67.8	237.3 ± 69.7	247.1 ± 67.3	.168
Prothrombin time (INR)	0.98 ± 0.07	0.98 ± 0.11	0.97 ± 0.06	.165
Uric acid, mg/dL	5.8 ± 1.7	6.3 ± 1.8	5.7 ± 1.6	.002
Albumin, g/dL	4.03 ± 0.37	3.98 ± 0.36	4.04 ± 0.37	.113
BUN, mg/dL	15.7 ± 5.3	16.6 ± 6.1	15.6 ± 5.1	.074
Creatinine, mg/dL	1.01 ± 0.38	1.08 ± 0.48	0.99 ± 0.36	.026
Na^+, mmol/L	140.8 ± 2.5	140.5 ± 2.5	140.8 ± 2.5	.178
K^+, mmol/L	4.18 ± 0.36	4.19 ± 0.33	4.18 ± 0.36	.691

Data are presented as the mean ± standard deviation or number (%).

ACEi/ARB = angiotensin-converting enzyme inhibitor or angiotensin II receptor blocker, AKI = acute kidney injury, ASA = American Society of Anesthesiologist, BUN = blood urea nitrogen, CCB = calcium channel blocker, INR = international normalized ratio, NSAID = nonsteroidal anti-inflammatory drug.

* Comparison between the AKI group and no-AKI group.

Table 2

Intraoperative data and stone characteristics.

Variables	All patients (n = 662)	AKI group (n = 107)	No-AKI group (n = 555)	P*
Operation time, min	89.4 ± 45.2	106.4 ± 56.4	86.1 ± 42.0	<.001
RBC transfusion	28 (4.2)	14 (13.1)	14 (2.5)	<.001
Total fluid administered, mL	1358.3 ± 792.8	1578.0 ± 1068.1	1315.9 ± 721.5	.002
Crystalloid administered, mL	1286.1 ± 689.7	1381.2 ± 749.1	1267.6 ± 676.8	.113
Colloid administered, mL	68.2 ± 232.5	179.1 ± 426.4	46.7 ± 163.3	<.001
Estimated blood loss, mL	173.8 ± 234.6	258.9 ± 382.6	157.4 ± 189.7	<.001
Intraoperative lowest hematocrit (%)	38.0 ± 5.4	36.9 ± 6.6	38.2 ± 5.2	.018
Intraoperative hypotension	176 (26.6)	78 (72.9)	98 (17.7)	<.001
Hydronephrosis	458 (69.2)	79 (73.8)	379 (68.3)	.255
Surgical approach (intercostal)	341 (51.5)	58 (54.2)	283 (51.0)	.542
Stone number (multiple)	496 (74.9)	81 (75.7)	415 (74.8)	.840
Stone location				.924
Diverticulum	13 (2.0)	2 (1.9)	11 (2.0)	
Calyx	218 (32.9)	37 (34.6)	181 (32.6)	
Pelvis	431 (65.1)	68 (63.6)	363 (65.4)	
Largest stone size, mm	26.1 ± 12.4	27.3 ± 13.3	25.9 ± 12.2	.294
Stone analysis				.234
Mixed stone	282 (42.6)	46 (43.0)	236 (42.5)	
Uric acid	129 (19.5)	22 (20.6)	107 (19.3)	
Calcium oxalate monohydrate	113 (17.1)	20 (18.7)	93 (16.8)	
Carbonate apatite	63 (9.5)	4 (3.7)	59 (10.6)	
Others†	75 (11.3)	15 (14.0)	60 (10.8)	
Staghorn stone	250 (37.8)	46 (43.0)	204 (36.8)	.223

Data are presented as the mean ± standard deviation or number (%).

AKI = acute kidney injury, RBC = red blood cell.

* Comparison between the AKI group and no-AKI group.

† Others include struvite, brushite, cystine, ammonium urate, and cholesterol stones.

Table 3

Univariate and multivariate logistic regression analyses for predictors of acute kidney injury after percutaneous nephrolithotomy.

	Univariate analysis		Multivariate analysis	
	OR (95% CI)	P	OR (95% CI)	P
Age	1.009 (0.992–1.026)	.297		
Gender (male/female)	0.645 (0.412–1.009)	.055		
Body mass index	1.921 (0.600–6.149)	.272		
Hypertension	1.440 (0.950–2.180)	.085		
Diabetes mellitus	0.961 (0.593–1.555)	.870		
ASA physical status	1.203 (0.337–4.294)	.776		
Preoperative beta blocker	2.237 (1.158–4.318)	.016		
Preoperative CCB	1.032 (0.647–1.645)	.895		
Preoperative ACEi/ARB	1.093 (0.516–2.316)	.815		
Preoperative NSAID	2.048 (1.068–3.928)	.031		
Uric acid	1.217 (1.075–1.377)	.002	1.228 (1.065–1.415)	.005
Creatinine	1.666 (1.047–2.650)	.031		
Operation time	1.009 (1.005–1.013)	<.001	1.009 (1.004–1.014)	<.001
RBC transfusion	5.817 (2.686–12.599)	<.001		
Crystalloid administered	1.000 (1.000–1.000)	.108		
Colloid administered	1.002 (1.001–1.003)	<.001		
Estimated blood loss	1.001 (1.001–1.002)	<.001		
Intraoperative lowest hematocrit	0.956 (0.922–0.993)	.019		
Intraoperative hypotension	12.543 (7.770–20.247)	<.001	12.713 (7.762–20.823)	<.001
Stone number (multiple/single)	1.051 (0.649–1.701)	.840		
Largest stone size	1.009 (0.993–1.025)	.294		
Hydronephrosis	1.310 (0.822–2.089)	.256		
Staghorn stone	1.297 (0.853–1.974)	.224		
Surgical approach (intercostal/subcostal)	0.887 (0.581–1.356)	.580		

ACEi/ARB = angiotensin-converting enzyme inhibitor or angiotensin II receptor blocker, ASA = American Society of Anesthesiologists, CCB = calcium channel blocker, CI = confidence interval, NSAID = nonsteroidal anti-inflammatory drug, OR = odds ratio, RBC = red blood cell.

Table 4

Univariate and multivariate logistic regression analyses for variables associated with intraoperative hypotension during percutaneous nephrolithotomy.

Variables	Univariate analysis		Multivariate analysis	
	OR (95% CI)	P	OR (95% CI)	P
Age	1.031 (1.013–1.047)	<.001	1.024 (1.008–1.040)	.004
Gender (male/female)	0.869 (0.607–1.242)	.440		
Body mass index	1.006 (0.961–1.053)	.805		
ASA physical status	0.919 (0.292–2.887)	.884		
Hypertension	1.418 (1.002–2.006)	.049		
Diabetes mellitus	3.149 (2.162–4.587)	<.001	2.755 (1.864–4.072)	<.001
Preoperative beta blocker	2.216 (1.223–4.015)	.009		
Preoperative CCB	0.931 (0.628–1.380)	.721		
Preoperative ACEi/ARB	2.171 (1.216–3.877)	.009	1.893 (1.022–3.506)	.042
Preoperative NSAID	2.171 (1.216–3.877)	.009		
Hematocrit	0.976 (0.942–1.012)	.184		
Operation time	1.003 (0.999–1.007)	.115		
RBC transfusion	5.423 (2.452–11.993)	<.001	5.073 (2.223–11.576)	<.001
Crystalloid administered	1.000 (1.000–1.000)	.072		
Colloid administered	1.002 (1.001–1.002)	<.001		
Estimated blood loss	1.001 (1.001–1.002)	.001		
Intraoperative lowest hematocrit	0.945 (0.916–0.976)	.001		
Stone number (multiple/single)	1.048 (0.702–1.564)	.818		
Largest stone size	1.004 (0.990–1.018)	.589		
Hydronephrosis	0.973 (0.670–1.412)	.884		
Staghorn stone	1.198 (0.842–1.704)	.315		
Surgical approach (intercostal/subcostal)	0.940 (0.662–1.335)	.729		

ACEi/ARB = angiotensin-converting enzyme inhibitor or angiotensin II receptor blocker, ASA = American Society of Anesthesiologists, CCB = calcium channel blocker, CI = confidence interval, NSAID = nonsteroidal anti-inflammatory drug, OR = odds ratio, RBC = red blood cell.

revealed that preoperative serum uric acid level [odds ratio (OR) = 1.228; 95% confidence interval (95% CI) = 1.065–1.415; $P = .005$], operation time (OR = 1.009; 95% CI = 1.004–1.014; $P < .001$), and intraoperative hypotension (OR = 12.713; 95% CI = 7.762–20.823; $P < .001$) were independent risk factors for AKI after PNL (Table 3).

In addition, intraoperative hypotension during PNL was associated with age (OR = 1.024; 95% CI = 1.008–1.040; $P = .004$), diabetes mellitus (OR = 2.755; 95% CI = 1.864–4.072; $P < .001$), preoperative angiotensin converting-enzyme inhibitor or angiotensin II receptor blocker use (OR = 1.893; 95% CI = 1.022–3.506; $P = .042$), and RBC transfusion (OR = 5.073; 95% CI = 2.223–11.576; $P < .001$) (Table 4).

The duration of hospitalization and intensive care unit stay were significantly longer in the AKI group (8.7 ± 5.2 vs 6.6 ± 2.8 days, $P < .001$; 0.34 ± 1.74 vs 0.07 ± 0.48 days, $P = .002$, respectively; Table 5). CKD was evaluated in 101 patients at 12 months after PNL and found to be significantly higher in the AKI group than in the patients in the no-AKI group (63.6% vs 36.7%, $P = .024$; Table 5).

Table 5

Postoperative outcomes.

Variables	AKI group (n = 107)	No-AKI group (n = 555)	P
Hospitalization, d	8.7 ± 5.2	6.6 ± 2.8	<.001
Intensive care unit admission rate	7 (6.5)	14 (2.5)	.062
Intensive care unit stay duration, d	0.34 ± 1.74	0.07 ± 0.48	.002
Chronic kidney disease*	14 (63.6)	29 (36.7)	.024

Data are presented as the mean ± standard deviation or number (%).

AKI = acute kidney injury.

* Chronic kidney disease was evaluated in 101 patients at 12 months after percutaneous nephrolithotomy.

4. Discussion

Our present analysis has indicated that 16.2% of the patients in our study cohort experienced AKI after a PNL procedure. A high preoperative serum uric acid level, long operation time, and a high incidence of intraoperative hypotension were identified as risk factors for postoperative AKI. Intraoperative hypotension was significantly associated with old age, diabetes mellitus, angiotensin converting-enzyme inhibitor or angiotensin II receptor blocker use, and RBC transfusion. In addition, patients who experienced AKI after PNL showed significantly prolonged hospitalization and intensive care unit stay, and a higher incidence of CKD.

Our current study findings demonstrate that intraoperative hypotension is a significant risk factor for AKI after a PNL procedure. The definition of intraoperative hypotension varies widely in the published literature[15] but in our present study was defined as a reduction of the mean arterial blood pressure of <70 mm Hg for more than 5 minutes.[19] Intraoperative hypotension is known to cause cardiac complications such as myocardial injury and rhythm abnormality, and ischemic stroke, resulting in increased mortality, morbidity, and health care costs.[19–21] Renal blood flow is maintained between a mean arterial pressure of 75 and 170 mm Hg and is known to be dependent on an arterial pressure beyond this range. Intraoperative hypotension may therefore lead to a decrease in the glomerular filtration rate and renal perfusion, which subsequently increases the risk of postoperative AKI. Most instances of perioperative AKI are caused by prerenal azotemia or acute tubular necrosis due to renal hypoperfusion.[22,23] Hence, intraoperative hypotension-related renal hypoperfusion is a suggested cause of adverse outcomes such as renal ischemic injury.

In our current study, intraoperative hypotension was significantly associated with old age, diabetes mellitus, preoperative

angiotensin-converting enzyme inhibitor or angiotensin II receptor blocker use, and RBC transfusion. Association between old age and intraoperative hypotension has been reported in previous studies,[24–27] and elderly patients have reduced plasma volume, which increases the risk of intraoperative hypotension.[24] It has been also reported that age-related cardiac dysfunction and neuronal impairment are associated with intraoperative hypotension.[27] Thus, elderly patients require meticulous anesthetic managements. It is known that autonomic neuropathy-related diabetes mellitus damages the parasympathetic and sympathetic nerve fibers of the cardiovascular system. Therefore, diabetes mellitus is a significant risk factor for hypotension, tachycardia, and silent ischemia. Autonomic neuropathy, a complication of diabetes mellitus, can also lead to hypotension by blunting the hemodynamic response during general anesthesia.[28,29] Patients with diabetes mellitus should therefore be made aware that hypotension is a common occurrence during surgery. In addition, angiotensin-converting enzyme inhibitors and angiotensin II receptor blockers have also been reported to cause intraoperative hypotension by impairing the responsiveness and actions of catecholamine in the renin-angiotensin system in patients undergoing general anesthesia. Indeed, it has been recommended to withhold these drugs on the day of surgery.[30,31] In our present study patients, we performed a RBC transfusion if the hemoglobin was less than 8 g/dL. We consider that patients who underwent a transfusion during surgery were more likely to develop intraoperative hypotension.

In line with the results of previous studies,[8,32] our present findings indicated that a high preoperative uric acid level is also a risk factor for AKI after PNL. Hyperuricemia causes endothelial dysfunction and oxidative stress. This in turn activates the renin-angiotensin system and the development of renal vasoconstriction.[33] In addition, uric acid induces proinflammatory responses that interfere with endothelial cell proliferation and alter renal autoregulation.[34,35] Through these mechanisms, hyperuricemia exerts negative effects on renal hemodynamics and can thereby cause subsequent AKI.

Prolonged operation times can lead to complications such as hemorrhaging that require blood transfusions or hemo-pneumothorax during a PNL procedure.[36] We observed in our present study that a prolonged surgery duration increased the risk of postoperative AKI following PNL. This is because longer PNL operations typically require more complex surgical procedures and increase the chance of directly or indirectly damaging the kidney during the perioperative period.

Previous studies have reported that surgical factors such as approach method and stone characteristics affect the occurrence of perioperative bleeding and blood transfusion, postoperative pulmonary complications, colon perforation, and renal artery fistula.[36,37] In contrast, our current findings suggest that surgical factors and stone characteristics do not significantly affect the occurrence of postoperative AKI. This is, at least in part, likely due to the considerable experience of our surgical team.

It is notable that we observed an adverse impact of AKI on postoperative outcomes. Postoperative AKI extended the duration of hospitalization and intensive care unit stay, which is in line with previous studies.[38,39] Moreover, we found in our current cohort that postoperative AKI was associated with a higher incidence of CKD, which was not unexpected because AKI has been reported to directly induce end-stage renal disease, increase the risk of developing incident CKD, and aggravate underlying CKD.[40,41]

This study had several limitations of note. First, our retrospective observational design may have introduced a selection bias, which would have influenced our results. However, we evaluated almost all of the possible factors that were likely to influence the postoperative renal function following PNL. Hence, we believe that we effectively minimized the possibility of selection bias in our current analysis. Second, we could not follow-up the serum creatinine level at 12 months after PNL in all patients. Thus, we were only able to evaluate CKD development in 101 cases in our study.

In conclusion, a high preoperative serum uric acid level, long operation duration, and intraoperative hypotension are independent risk factors for postoperative AKI following PNL. In addition, postoperative AKI is associated with prolonged hospitalization and intensive care unit stay, and a higher incidence of CKD. Therefore, it is essential to minimize the risk of intraoperative hypotension with meticulous anesthetic and surgical management in patients undergoing PNL.

Acknowledgment

We thank Dr Joon Seo Lim from the Scientific Publications Team at Asan Medical Center for his editorial assistance in preparing this manuscript.

Author contributions

Conceptualization: Hee Yeong Kim, Young-Kug Kim.
Data curation: Jihion Yu, Hyung Keun Park, Hyun-Jung Kwon, Joonho Lee.
Formal analysis: Jihion Yu, Hee Yeong Kim, Young-Kug Kim.
Methodology: Jihion Yu, Hyung Keun Park, Hyun-Jung Kwon, Jai-Hyun Hwang, Hee Yeong Kim, Young-Kug Kim.
Project administration: Hee Yeong Kim, Young-Kug Kim.
Supervision: Jai-Hyun Hwang, Hee Yeong Kim, Young-Kug Kim.
Validation: Jihion Yu, Hyung Keun Park, Hyun-Jung Kwon, Joonho Lee, Jai-Hyun Hwang, Hee Yeong Kim, Young-Kug Kim.
Writing – original draft: Jihion Yu.
Writing – review & editing: Hyung Keun Park, Hee Yeong Kim, Young-Kug Kim.

References

[1] Fernstrom I, Johansson B. Percutaneous pyelolithotomy. A new extraction technique. Scand J Urol Nephrol 1976;10:257–9.
[2] Olbert PJ, Hegele A, Schrader AJ, et al. Pre- and perioperative predictors of short-term clinical outcomes in patients undergoing percutaneous nephrolitholapaxy. Urol Res 2007;35:225–30.
[3] Miller NL, Lingeman JE. Management of kidney stones. Bmj 2007; 334:468–72.
[4] Michel MS, Trojan L, Rassweiler JJ. Complications in percutaneous nephrolithotomy. Eur Urol 2007;51:899–906. discussion 906.
[5] Yu J, Choi JM, Lee J, et al. Risk factors for pulmonary complications after percutaneous nephrolithotomy: a retrospective observational analysis. Medicine (Baltimore) 2016;95:e4513.
[6] Chertow GM, Burdick E, Honour M, et al. Acute kidney injury, mortality, length of stay, and costs in hospitalized patients. J Am Soc Nephrol 2005;16:3365–70.
[7] Hobson C, Ozrazgat-Baslanti T, Kuxhausen A, et al. Cost and mortality associated with postoperative acute kidney injury. Ann Surg 2015; 261:1207–14.
[8] Joung KW, Choi SS, Kong YG, et al. Incidence and risk factors of acute kidney injury after radical cystectomy: importance of preoperative serum uric acid level. Int J Med Sci 2015;12:599–604.
[9] Caddeo G, Williams ST, McIntyre CW, et al. Acute kidney injury in urology patients: incidence, causes and outcomes. Nephrourol Mon 2013;5:955–61.

[10] Kwon T, Jeong IG, Lee C, et al. Acute kidney injury after radical cystectomy for bladder cancer is associated with chronic kidney disease and mortality. Ann Surg Oncol 2016;23:686–93.
[11] Lameire NH, Bagga A, Cruz D, et al. Acute kidney injury: an increasing global concern. Lancet 2013;382:170–9.
[12] Shim M, Park M, Park HK. Effects of continuous peritubal local anesthetic instillation on postoperative pain after percutaneous nephrolithotomy: a prospective, randomized three-arm study. J Endourol 2016;30:504–9.
[13] Bang SR, Ahn HJ, Kim GS, et al. Predictors of high intraoperative blood loss derived by simple and objective method in adult living donor liver transplantation. Transplant Proc 2010;42:4148–50.
[14] Furman EB, Roman DG, Lemmer LA, et al. Specific therapy in water, electrolyte and blood-volume replacement during pediatric surgery. Anesthesiology 1975;42:187–93.
[15] Bijker JB, van Klei WA, Kappen TH, et al. Incidence of intraoperative hypotension as a function of the chosen definition literature definitions applied to a retrospective cohort using automated data collection. Anesthesiology 2007;107:213–20.
[16] Okusa MD, Davenport A. Reading between the (guide)lines: the KDIGO practice guideline on acute kidney injury in the individual patient. Kidney Int 2014;85:39–48.
[17] Matsushita K, Selvin E, Bash LD, et al. Risk implications of the new CKD Epidemiology Collaboration (CKD-EPI) equation compared with the MDRD Study equation for estimated GFR: the Atherosclerosis Risk in Communities (ARIC) Study. Am J Kidney Dis 2010;55:648–59.
[18] Levey AS, Stevens LA, Schmid CH, et al. A new equation to estimate glomerular filtration rate. Ann Intern Med 2009;150:604–12.
[19] Sun LY, Wijeysundera DN, Tait GA, et al. Association of intraoperative hypotension with acute kidney injury after elective noncardiac surgery. Anesthesiology 2015;123:515–23.
[20] Sposato LA, Suarez A, Jauregui A, et al. Intraoperative hypotension, new onset atrial fibrillation, and adverse outcome after carotid endarterectomy. J Neurol Sci 2011;309:5–8.
[21] Bijker MD, Jilles B, Persoon MDS, et al. Intraoperative hypotension and perioperative ischemic stroke after general surgery: a nested case-control study. Anesthesiology 2012;116:658–64.
[22] Lameire N. The pathophysiology of acute renal failure. Crit Care Clin 2005;21:197–210.
[23] Schrier RW, Wang W, Poole B, et al. Acute renal failure: definitions, diagnosis, pathogenesis, and therapy. J Clin Invest 2004;114:5–14.
[24] Charlson ME, MacKenzie CR, Gold JP, et al. Preoperative characteristics predicting intraoperative hypotension and hypertension among hypertensives and diabetics undergoing noncardiac surgery. Ann Surg 1990;212:66–81.
[25] Hallqvist L, Granath F, Huldt E, et al. Intraoperative hypotension is associated with acute kidney injury in noncardiac surgery: an observational study. Eur J Anaesthesiol 2018;35:273–9.
[26] Cheung CC, Martyn A, Campbell N, et al. Predictors of intraoperative hypotension and bradycardia. Am J Med 2015;128:532–8.
[27] Lin PH, Zhou W, Kougias P, et al. Factors associated with hypotension and bradycardia after carotid angioplasty and stenting. J Vasc Surg 2007;46:846–53. discussion 853–844.
[28] Rehman H-u, Mohammed K. Perioperative management of diabetic patients. Curr Surg 2003;60:607–11.
[29] Oakley I, Emond L. Diabetic cardiac autonomic neuropathy and anesthetic management: review of the literature. AANA J 2011;79: 473–9.
[30] Comfere T, Sprung J, Kumar MM, et al. Angiotensin system inhibitors in a general surgical population. Anesth Analg 2005;100:636–44. table of contents.
[31] Kheterpal S, Khodaparast O, Shanks A, et al. Chronic angiotensin-converting enzyme inhibitor or angiotensin receptor blocker therapy combined with diuretic therapy is associated with increased episodes of hypotension in noncardiac surgery. J Cardiothorac Vasc Anesth 2008; 22:180–6.
[32] Ejaz AA, Beaver TM, Shimada M, et al. Uric acid: a novel risk factor for acute kidney injury in high-risk cardiac surgery patients? Am J Nephrol 2009;30:425–9.
[33] Sanchez-Lozada LG, Tapia E, Santamaria J, et al. Mild hyperuricemia induces vasoconstriction and maintains glomerular hypertension in normal and remnant kidney rats. Kidney Int 2005;67:237–47.
[34] Kang DH, Park SK, Lee IK, et al. Uric acid-induced C-reactive protein expression: implication on cell proliferation and nitric oxide production of human vascular cells. J Am Soc Nephrol 2005;16:3553–62.
[35] Kono H, Chen CJ, Ontiveros F, et al. Uric acid promotes an acute inflammatory response to sterile cell death in mice. J Clin Invest 2010;120:1939–49.
[36] Oner S, Okumus MM, Demirbas M, et al. Factors influencing complications of percutaneous nephrolithotomy: a single-center study. Urol J 2015;12:2317–23.
[37] de la Rosette JJ, Zuazu JR, Tsakiris P, et al. Prognostic factors and percutaneous nephrolithotomy morbidity: a multivariate analysis of a contemporary series using the Clavien classification. J Urol 2008; 180:2489–93.
[38] Abelha FJ, Botelho M, Fernandes V, et al. Determinants of postoperative acute kidney injury. Crit Care 2009;13:R79.
[39] Borthwick E, Ferguson A. Perioperative acute kidney injury: risk factors, recognition, management, and outcomes. BMJ 2010;341: c3365.
[40] Chawla LS, Kimmel PL. Acute kidney injury and chronic kidney disease: an integrated clinical syndrome. Kidney Int 2012;82:516–24.
[41] Venkatachalam MA, Griffin KA, Lan R, et al. Acute kidney injury: a springboard for progression in chronic kidney disease. Am J Physiol Renal Physiol 2010;298:F1078–94.