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Risk Factors for Acute Kidney Injury After Hip Fracture Surgery in the Elderly Individuals

Cagatay Ulucay[1], Zehra Eren[2], Elif Cigdem Kaspar[3], Turhan Ozler[1], Korcan Yuksel[1], Gulcin Kantarci[2], and Faik Altintas[1]

Abstract

Objective: We aimed to evaluate possible risk factors associated with acute kidney injury (AKI) after hip fracture surgery in the elderly individuals. Design: Level II diagnostic study, evidence obtained from prospective cohort study from 1 center with level 2, and 3 patients. Patients: A total of 165 patients (>65 years) with femoral neck fracture were enrolled in this prospective study between 2007 and 2010. Two patients were dropped for inadequate laboratory follow-up data. Patients with kidney failure or renal replacement therapy (RRT) history or AKI at admission were excluded. Intervention: Nephrology consultation was obtained from all patients at admission. All patients had undergone bipolar cemented hip arthroplasty that was performed by the same surgical team in all patients within 24 hours of fracture and admission under the same protocol. Main Outcome Measurements: Serum creatinine (SCr), urine output, and complete blood counts were evaluated at baseline and daily basis thereafter. The AKI was defined based on Acute Kidney Injury Network classification. Hospital charges were converted from Turkish Liras to US dollars and rounded. Results: Among 163 patients, AKI occurred in 25 (15.3%) patients, all within the first 48 postoperative hours. Three (1.8%) patients required RRT. Baseline SCr levels were restored within 4.84 $\pm$ 1.34 days on average (3-8 days). No patient required RRT after discharge. The mean hospital stay was 3 days (2-6 days) longer and the hospital charge was 2500 US$ higher for the patients with AKI. After multivariable adjustment, only lower estimated glomerular filtration rate levels (odds ratio 0.945, 95%confidence interval 0.92-0.96) emerged as an independent predictor for AKI. Conclusion: The AKI represents a frequent complication after hip fracture surgery associated with longer hospital stay and higher treatment costs with increased morbidity. Our results show baseline renal function is an independent predictor of AKI.

Keywords

acute kidney injury (AKI), eGFR, hip fracture, surgery, trauma

Introduction

Advances in technology and medicine have made major contributions to increased life expectancy of humans[1] resulting in an aging population vulnerable to osteoporotic fractures including the fracture of the femoral neck. Femoral neck fractures in the elderly individuals can be debilitating or even fatal.[2,3] Several assessment tools including the Barthel Index, Charlson Comorbidity Index, and American Society of Anesthesiologists score help to evaluate the risk factors (eg, chronic mental or physical diseases and organ failure) associated with increased morbidity and mortality in patients with femoral neck fractures.[4-6] In this group of patients, acute kidney injury (AKI), previously referred to as acute renal failure, during the perioperative period is one of such risk factors associated with prolonged hospital stay, increased morbidity, mortality, and poor outcome.[7-9] Three mechanisms held responsible for the development of AKI include prerenal, renal (intrinsic), and postrenal (postobstructive) failure.

Femoral neck surgery in the elderly individuals is usually associated with the former 2 mechanisms. Prerenal AKI may result from hypovolemia especially with acute tubular necrosis (prolonged dehydration or hemorrhage at perioperative period), pulmonary embolism, acute myocardial infarction, hearth failure, anesthetics, and sepsis, while renal AKI may be due to renal artery occlusion (embolism or thrombus), drugs

[1] Orthopaedics and Traumatology Department, Yeditepe Medical Faculty, Ankara Cad no 102 Kozyatagi Istanbul PK, Turkey
[2] Nephrology Department, Yeditepe Medical Faculty, Ankara Cad no 102 Kozyatagi Istanbul PK, Turkey
[3] Biostatistics Department, Yeditepe Medical Faculty, Ankara Cad no 102 Kozyatagi Istanbul PK, Turkey

Corresponding Author:
Cagatay Ulucay, Orthopaedics and Traumatology Department, Yeditepe Medical Faculty, Ankara Cad no 102 Kozyatagi, Istanbul PK 34578, Turkey.
Email: culucay@tnn.net

(aminoglycosides, amphotericin B, nonsteroidal anti-inflammatory drugs (NSAIDs), proton-pump inhibitors, radiocontrast agents), and pyelonephritis.[10]

The Acute Dialysis Quality Initiative Working group encompassing nephrology and critical care medicine specialists have established a consensus definition for AKI referred to as the "RIFLE" criteria, the acronym is Risk, Injury, Failure, Loss, and End-stage Kidney Disease.[11] The RIFLE, which proposes 3 different grades of AKI according to criteria for serum creatinine (SCr) and urine output (UOCr), was redefined and revised by the Acute Kidney Initiative Network (AKIN) group.[12] In this revised definition, a > 0.3 mg/dL increase in SCr is diagnosed as AKI, therefore placing less emphasis on basal SCr at admission and requiring a minimum of 2 SCr measurements within the first 48 hours. Staging of the kidney injury is based on hourly measurement of urine output.[12]

In the present study, etiology, incidence, and clinical predictors of kidney injury were examined in order to define independent predictors for AKI, which could enable us to pinpoint patients with a high risk of AKI before its occurrence.

Patients and Methods

Patients over 65 years of age with femur neck fracture were enrolled in this prospective study conducted between 2007 and 2010 at our medical faculty. The clinical and ethical research review board of our medical university approved the study protocol. Standard medical and surgical treatment and follow-up protocols were done in all patients.

Patient Population

A total of 165 patients over 65 years of age with femoral neck fracture and without any AKI criteria were enrolled in this prospective study conducted between 2007 and 2010 at the Department of Orthopaedics and Traumatology of our university. All patients were consulted and evaluated by nephrology specialists at admission as a protocol. Cemented bipolar hip arthroplasty was performed under general anesthesia in all patients by the same surgical team within 24 hours of fracture and admission. Patients with a history of kidney failure or renal replacement therapy (RRT) or had AKI at admission were excluded from the study.

Baseline and daily SCr levels, urine output, and standard hematological tests were monitored in all patients. The AKI was defined according to AKIN classification.

Clinical and Laboratory Data Collection

Data were retrieved from the Hospital Information System Software and verified against the original printed copy for each patient. Standard demographic, clinical, and physiological data that were collected included the following: age, sex, height (cm), weight (kg), body mass index (BMI), length of hospital stay, primary diagnosis, comorbidities (diabetes mellitus , hypertension [HT], previous cerebrovascular accidents, previous myocardial infarction, or previous coronary revascularization), and smoking status (Table 1). These data were enrolled for investigating correlation between patients with AKI and patients without AKI. Baseline, daily, and discharge SCr levels, blood urea nitrogen (BUN), urine output, and complete blood counts were determined in all the patients. Serum sodium, potassium, and chlorine measurements were also performed at admission and discharge, if required more frequently. Duration of operation, intraoperative hemodynamics (baseline, peak, trough, final measurements), and intraoperative urinary outflow were recorded. Urinary output was recorded using silicone Foley urinary catheter with UnoMeter Safeti Plus (Denmark) kit for all the patients. This catheter was placed at the time of admission and removed at the discharge day. Hemodynamic parameters at follow-up (systolic and diastolic blood pressure and heart rate [HR]; Table 2) and daily uses of medications were recorded.

Table 1. Baseline Characteristics of the Patients With Femoral Neck Fracture.

Variable	AKI, n = 25 (15.3%)	No AKI, n = 138 (84.7%)	*P* value
Demographic characteristics			
Age, years (mean ± SD)	77.20 ± 11.32	83.96 ± 7.84	.005
Male sex, n (%)	31 (73.8%)	11 (26.2%)	.044
Height, cm	161.72 ± 9.59	163.20 ± 8.52	.473
Weight, kg	67.07 ± 16.28	67.44 ± 11.10	.915
BMI	25.44 ± 4.80	25.33 ± 3.86	.917
Comorbidities n (%)			
Hypertension	102 (82.9%)	21 (17.1%)	.325
Diabetes Mellitus	27 (75%)	9 (25%)	.112
Previous CVA	10 (71.4%)	4 (28.6%)	.234
Previous MI	9 (81.8%)	2 (18.2%)	.677
Previous coronary revascularization	11 (91.7%)	1 (8.3%)	.694
Smoking history	22 (91.7%)	2 (8.3%)	.538
Length of hospital stay (days)	7.08 ± 2.98	4.36 ± 1.30	<.0001
Blood transfusion	105 (76.1%)	21 (84.0%)	.387

Abbreviations: CVA, cerebrovascular accident; MI, myocardial infarction; BMI, body mass index; SD, standard deviation.

Assessment of kidney function

The AKI was classified based on the change in SCr levels as suggested by AKIN criteria (Table 3)[7] that propose 3 different severity stages for AKI. In this classification scheme, stage 1, 2, and 3 AKI are defined as follows using the serial measurements in the first 48 hours: (1) stage 1: patients showing a sudden increase in SCr of $\geq$0.3 mg/dL or an increase up to $\geq$150% to 200% (1.5- to 2-fold) from baseline SCr or urine output <0.5 mL/kg per hour for >6 hours; (2) stage 2: $\geq$2-fold increase in SCr from baseline level or urine output <0.5 mL/kg/hour for >12 hours; (3) stage 3: $\geq$3-fold increase in SCr from baseline

Table 2. Baseline Laboratory and Hemodynamic Characteristics of the Patients.

Variables	AKI, n = 25 (15.3%)	No AKI, n = 138 (84.7%)	*P* value
BUN, mg/dL	31.92 ± 17.10	19.92 ± 7.41	**<.0001**
Creatinine, mg/dL	1.58 ± 1.32	0.98 ± 1.57	.771
eGFR, mL/min per 1.73 m^2	49.40 ± 20.01	78.84 ± 24.37	**<.0001**
Sodium, mg/dL	138.36 ± 2.95	138.95 ± 2.73	.323
Potassium, mg/dL	4.47 ± 0.50	4.105 ± 0.56	**.002**
Hemoglobin, g/dL	11.75 ± 1.33	11.75 ± 1.67	.990
White blood cells	13.21 ± 3.55	12.08 ± 2.90	.089
Systemic blood pressure, mm Hg			
Systolic	126.52 ± 15.63	125.51 ± 17.34	.786
Diastolic	71.20 ± 11.54	75.26 ± 58.20	.729

Abbreviations: BUN, blood urea nitrogen; eGFR, estimated glomerular filtration rate; AKI, acute kidney injury.

level with a sudden increase in SCr of ≥0.5 mg/dL, an increase in SCr ≥ 4.0 mg/dL, urine output <0.3 mL/kg/hour for 24 hours or anuria for 12 hours.

Chronic kidney disease was diagnosed in patients with an estimated glomerular filtration rate (eGFR) of <60 mL/min per 1.73 m^2 for >3 months, according to the guidelines of the National Kidney Foundation.[13] Baseline GFR was estimated using the 4-component (ie, age, race, sex, and SCr levels) Modification of the diet in renal disease equation: $eGFR = 186 \times (\text{SCr level in mg/dL})^{-1.154} \times (\text{age in years})^{-0.203}$.

Health Economics

All patients paid their charges by themselves without any government or insurance support or discount. The nephrology specialist's consultancy to all patients at admission was free of cost. The total cost includes everything such as operation, x-rays, consultations, hospital stay, medications, blood tests, and RRT. The total sums were converted from Turkish Liras (TL) to US dollars and rounded.

Statistical Analyses

Continuous variables are expressed as mean ± standard deviation and discrete variables as frequencies and percentages. Independent sample *t* tests were applied to evaluate the differences in means between the 2 groups. Chi-square test was used to compare frequencies between the groups.

Multiple logistic regression analysis was used to identify the independent predictors of AKI. Parameters having a *P* value less than .05 in univariate analysis were included in the model.

The model fit was evaluated by Hosmer-Lemoshow goodness-of-fit test. Two-tailed *P* values less than .05 were considered statistically significant. Statistical analyses were performed using SPSS version 19.0 (SPSS Inc., Chicago, Illinois)

Results

Baseline Characteristics

Two patients were dropped from the study due to inadequate laboratory follow-up data. Demographic and clinical characteristics including laboratory parameters are presented in Tables 1 and 2. Patients who developed AKI at follow-up were older ($P = .005$), had significantly higher mean BUN ($P < .0001$) and potassium levels ($P = .002$), and lower mean eGFR values ($P < .0001$) at admission.

Intraoperative Characteristics of Patients

No significant differences were found at follow-up in terms of the duration of operation, intraoperative hemodynamic parameters (blood pressure and HR [baseline, peak, trough, and final measurements]) between patients with and without AKI. The only exception was the significantly lower urinary output in AKI patients (107.40 ± 91.19 mL/hour) than in patients without AKI (266.41 ± 186.34/hour; $P = .041$).

The AKI Incidence

The AKI developed in 25 (15.3%) patients. The mean time from operation to the occurrence of AKI was 1.20 ± 0.66 days (range: 0-2 days). Of these, 17 (10.4%), 5 (3.1%), and 3 (1.8%) had stage 1, 2, and 3 AKI according to AKIN classification scheme, respectively. The SCr returned to baseline in 4.84 ± 1.34 days (3-8 days) in all patients with AKI. Three (1.8%) patients required RRT. There were no patients requiring RRT after discharge.

Health Economics

Cemented bipolar hip arthroplasty comprises the standard treatment protocol for elderly patients with femoral neck fracture in our unit and requires an average of 4 days of hospital stay with an overall cost of approximately 6300 US$ per patient. The mean length of hospital stay was 3 days or longer (2-6 days) and the overall cost was 2500 US$ (1200-5100 US$) or higher ($P < .0001$) in patients with AKI when compared to patients not developing AKI. Major contributors to increased medical costs were extra laboratory tests, longer duration of hospital stay, and RRT.

Predictors of AKI

In univariate analysis, age per year increase (odds ratio [OR] 1.07; 95% confidence interval [CI] 1.21-1.13), male gender (OR for female 0.36, 95%CI 0.15-0.89), previous coronary revascularization history (OR 2.13, 95%CI 1.33-3.40), increasing number of comorbidities (OR 2.13, 95%CI 1.33-3.40), and lower eGFR levels (OR 0.945, 95%CI 0.92-0.96) were significantly associated with AKI (Table 5), whereas after multivariable adjustment, lower eGFR levels (OR 0.97, 95%CI 0.93-1.007) remained as the only independent predictor of AKI (Table 5).

Table 3. Classification/Staging System for Acute Kidney Injury According to AKIN.

Stage	Serum creatinine criteria	Urine output criteria
1	Increase in serum creatinine more than or equal to 0.3 mg/dL (≥26.4 μmol/L) or increase to more than or equal to 150%-200% (1.5- to 2-fold) from baseline	Less than 0.5 mL/kg per hour for more than 6 hours
2	Increase in serum creatinine to more than 200%-300% (>2- to 3-fold) from baseline	Less than 0.5 mL/kg per hour for more than 12 hours
3	Increase in serum creatinine to more than 300% (>3-fold) from baseline (or serum creatinine of more than or equal to 4.0 mg/dL [≥354 μmol/L] with an acute increase of at least 0.5 mg/dL [44 μmol/L])	Less than 0.3 mL/kg per hour for 24 hours or anuria for 12 hours

Abbreviation: AKIN, Acute Kidney Injury Network.

Table 4. Intraoperative Characteristics of Patients.

Variables	AKI, n = 25 (15.3%)	No AKI, n = 138 (84.7%)	*P* value
Duration of anesthesia, min	111.40 ± 29.84	121.92 ± 29.11	.100
Systemic pressure at the beginning, mm Hg			
Systolic	135.00 ± 25.49	138.54 ± 23.38	.494
Diastolic	73.36 ± 15.52	74.83 ± 14.32	.643
Systemic pressure at the end, mm Hg			
Systolic	116.40 ± 26.90	113.53 ± 21.04	.549
Diastolic	64.40 ± 15.02	63.75 ± 11.98	.810
The highest systemic pressure, mm Hg			
Systolic	142.40 ± 22.78	144.18 ± 21.88	.710
Diastolic	79.36 ± 14.10	80.30 ± 13.10	.744
The lowest systemic pressure, mm Hg			
Systolic	91.60 ± 24.26	92.28 ± 19.06	.875
Diastolic	51.40 ± 14.25	54.39 ± 11.73	.259
The highest MBP, mm Hg	100.49 ± 14.77	101.31 ± 14.08	.790
The lowest MBP, mm Hg	64.53 ± 17.15	67.28 ± 12.46	.442
Heart rate at the beginning, bpm	76.08 ± 13.66	78.52 ± 12.86	.388
Heart rate at the end, bpm	73.76 ± 16.42	70.35 ± 13.54	.264
The fastest heart rate, bpm	81.04 ± 15.04	82.80 ± 14.21	.572
The slowest heart rate, bpm	63.00 ± 13.58	62.69 ± 10.83	.899
Urinary output, mL/h	107.40 ± 91.17	266.41 ± 186.34	**.041**

Abbreviations: MBP, mean blood pressure; bpm, beats per minute; AKI, acute kidney injury.

Discussion

The previously reported incidence of AKI among elderly patients undergoing arthroplasty for femoral neck fractures varies between 16% and 24.44%[8,14]; these figures are consistent with our findings (ie, 15.3%). The somewhat lower figure in our study might be related to shorter duration of preoperative hospitalization as well as the protocol-required nephrology consultation that could have provided effective identification and management of patients carrying higher risk of AKI.

Heterogeneous ethnic or geographic populations undergoing different treatment strategies and preoperative care practices in these studies might have caused the significant variability in reported incidences. In our study, the population was rather homogenous according to age, treatment type, preoperative preparation time, and nephrology consultation at the time of admission.

Several studies have evaluated a number of factors with a predictive value for AKI in noncardiac patients and patients who underwent cardiac surgery, [15,16] where age, diabetes, BMI, HT, peripheral vascular occlusive disease, chronic obstructive pulmonary disease, emergency surgery, congestive heart disease, and chronic kidney disease emerged as independent predictors of AKI in different studies among surgically treated patients.[15,17-19] In our study, age, male gender, history of chronic kidney disease, previous coronary revascularization, and increasing number of comorbidities were significantly associated with an increased risk of AKI, whereas after multivariable adjustment, only lower eGFR level remained as an independent predictor, similar to some other previous studies.[20-23] In our view, despite this finding, previous identification of other risk factors apart from low eGFR warrants further studies with different patient populations to better delineate the role of lower eGFR as a sole predictor of AKI.

Table 5. Univariate and Multivariate Logistic Regression Analysis for Predictors of AKI.

	Univariate			Multivariate		
Predictors	OR	95% CI	*P* value	OR	95%CI	*P* value
Age, years	1.077	1.021-1.136	**.007**	1.049	0.984-1.118	.140
Gender (female)	0.369	0.152-0.894	**.027**	2.643	0.909-7.686	.074
BMI	0.995	0.908-1.091	.916			
Diabetes mellitus	2.312	0.923-5.795	.074			
Hypertension	1.853	0.596-5.763	.287			
Previous CVA	2.438	0.700-8.493	.162			
Previous MI	1.246	0.253-6.143	.787			
Previous coronary revascularization	2.134	1.338-3.403	**.001**			
Smoking status	2.181	0.479-9.923	.313			
Comorbidities	2.134	1.338-3.403	**.001**			
Systolic blood pressure	1.003	0.979-1.028	.784			
Diastolic blood pressure	0.998	0.983-1.013	.749			
Heart rate, bpm	0.985	0.952-1.020	.406			
Hemoglobin, g/dL	1.002	0.770-1.303	.990			
Potassium, mg/dL	3.402	1.487-7.783	.004	1.688	0.693-4.110	.249
Sodium, mg/dL	0.924	0.791-1.080	.321			
eGFR, mL/kg per 1.73 m^2	0.931	0.923-0.945	**<.0001**	0.945	0.921-0.963	**<.0001**

Abbreviations: BMI, body mass index; CVA, cerebrovascular accident; MI, myocardial infarction; EF, ejection fraction; eGFR, estimated glomerular filtration rate; CI, confidence interval; OR, odds ratio; bpm, beats per minute.

Postoperative AKI is often multifactorial and may be caused by pre-, peri-, and postoperative factors and complications[17,24,25] including longer preoperative preparation time and operation, dehydration, malnutrition, nephrotoxic drug use (including NSAID), and the choice of surgical procedure.[9,15,24,26-28] With respect to operative factors, while no association between AKI and the duration of anesthesia and hemodynamic parameters was found, urinary output was significantly lower in patients who had AKI at follow-up. Therefore, lower operative urinary output might be considered as an important warning sign for the development of AKI necessitating very close monitoring of these patients postoperatively. In our study, urinary output was determined using silicone Foley urinary catheter with UnoMeter Safeti Plus (Denmark) kit for all patients starting from the time of admission until discharge day. This device allows accurate monitoring of hourly urine output. Although this silicone catheter stayed up to 10 days, no urinary tract infection was diagnosed. A change in SCr is often not detectable until 48 hours after deterioration in kidney functions; in this regard, urine output may represent quicker assessment of renal physiology that also allows bedside measurement.[29] Monitoring hourly urine output (which is less than 0.5 mL/kg per hour for more than 6 hours is the first threshold for AKI) can also provide a means for earlier diagnosis of AKI.[29]

Increase in life expectancy has developed a large population who are vulnerable to osteoporotic femoral neck fractures. This pathology is treated surgically and is associated with a significant societal and personal burden.[30,31] A recent study from Turkey showed that annual number of elderly patients undergoing surgical treatment for hip fractures is around 15 500 with an associated cost of nearly 65 million US$.[32] This figure does not take into account the indirect costs such as RRT for AKI. Early intervention for AKI undoubtedly is less costly, shortens the duration of hospital stay, and gives a better treatment outcome.[8,33,34] Thus, our findings suggest that a predictive role of eGFR for AKI may help identification of high-risk patients for earlier diagnosis and treatment with less cost, shortened hospital stay, and a better outcome. The AKI is associated with an increased postoperative mortality[8,26,35] that may reach up to 20% during early postoperative period following femoral neck fractures. In our study, no deaths were recorded probably in connection with a relatively lower rate with early identification of AKI and fewer patients were drawn with severe comorbidity.

One of the limitations of our study is the absence of long-term follow-up for mortality after discharge. In addition, the contribution of each nephrotoxic medication to the development of AKI was not studied because the patients' daily medications and intraoperative drugs given could not be grouped because of high heterogeneity. During the course of the study, pharmacological treatments were modified according to clinical status and renal function of the patient. As a matter of fact, polypharmacy was very common among our patients including angiostein converting enzyme inhibitors, aminoglycosides (used as standard preoperative prophylactic antibiotic for arthroplasty with urinary catheter), and NSAIDs that are known to be associated with nephrotoxic effects. However, it was not possible to determine individual contribution of these medications due to the multiplicity of combinations.

In conclusion, AKI is a mostly transient but frequent complication after hip fracture surgery that is associated with increased length of hospital stay, treatment cost, mortality, and morbidity. Our findings suggest that baseline renal function is an independent predictor for the development of AKI. It may be prudent to request a nephrology consultation at the time of admission for patients at high risk of AKI. This consultation

makes you know the patients at risk of AKI and may reduce the risk of RRT and chronic kidney disease.

Authors' Note

The clinical and ethical research review board of Yeditepe Medical University approved the study protocol. Standard medical and surgical treatment protocols were followed in all patients. All authors agree to license Sage Publications for publishing all written materials and tables.

Declaration of Conflicting Interests

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

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