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# Diastolic dysfunction and acute kidney injury in elderly patients with femoral neck fracture

Woori Cho, Tae Yeon Hwang, Yoon Kyung Choi, Ji Hyun Yang, Myung-Gyu Kim, Sang-Kyung Jo, Won Yong Cho, Se Won Oh

Department of Internal Medicine, Korea University Anam Hospital, Korea University College of Medicine, Seoul, Korea

**Background:** Femoral neck fracture is common in the elderly population. Acute kidney injury (AKI) is an important risk factor for mortality in patients who have had such fracture. We evaluated the incidence of AKI in patients who had femoral neck fracture and identified risk factors for AKI and mortality.

**Methods:** This was an observational cohort study including 285 patients who were  $\geq$  65 years of age and who underwent femoral neck fracture surgery between 2013 and 2017.

**Results:** The mean age was 78.63  $\pm$  6.75 years. A total of 67 (23.5%) patients developed AKI during the hospital stay: 57 (85.1%), 5 (7.5%), and 5 (7.5%) patients were classified as having stage 1, 2, and 3 AKI, respectively. Patients with AKI had a lower baseline estimated glomerular filtration rate and higher left atrial dimension, left ventricular mass index, pulmonary artery pressure, and the ratio of early mitral inflow velocity to early diastolic mitral annulus velocity (E/e') and were more likely to have diabetes or hypertension (HTN) (P < 0.05). The presence of HTN (odds ratio [OR], 4.570; 95% confidence interval [CI], 1.632–12.797) higher E/e' (OR, 1.105; 95% CI, 1.019–1.198), and lower hemoglobin (OR, 0.704; 95% CI, 0.528–0.938) were independently associated with a higher risk for developing AKI. Severe AKI (OR, 24.743; 95% CI, 2.822–212.401) was associated with a higher risk of mortality. **Conclusion:** Elderly patients with femoral neck fracture had a high incidence of AKI. Diastolic dysfunction was associated with AKI. Severe AKI was associated with in-hospital mortality.

Keywords: Acute kidney injury, Diastolic heart failure, Femoral neck fractures

# Introduction

Femoral neck fracture is common in the elderly population. A previous study anticipated that the number of

Received July 30, 2018; Revised November 14, 2018; Accepted November 21, 2018 hip fractures occurring worldwide will increase from 1.66 million in 1990 to 6.26 million by 2050 [1]. Elderly patients who have had femoral neck fracture have a lower quality of life and increased morbidity and mortality [2,3]. Acute kidney injury (AKI) is one of the most common complications after surgery, and it is associated with increased hospital costs and mortality [4–6].

The aging kidney shows several structural and functional changes similar to those seen with chronic kidney disease (CKD). Structural changes include arteriosclerosis, glomerulosclerosis, tubular atrophy, and fibrosis. Functional changes include decreased glomerular filtration rate, altered renal sensitivity to vasoconstrictors and vasodilators, and lowered auto-regulatory capacity [7,8]. In addition, the elderly population has shown a higher

Edited by Dong-Ryeol Ryu, Ewha Womans University, Seoul, Korea **Correspondence:** Se Won Oh

Division of Nephrology, Department of Internal Medicine, Korea University Anam Hospital, Korea University College of Medicine, 73 Inchon-ro, Seongbuk-gu, Seoul 02841, Korea. E-mail: hisy81@hanmail.net ORCID: https://orcid.org/0000-0003-3795-9322

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prevalence of left hypertrophy and left ventricular (LV) diastolic dysfunction compared with a younger population [9,10]. Although elderly patients have a high risk of perioperative morbidity, few studies have evaluated orthopedic surgery including femoral fracture in the elderly population.

We evaluated the incidence of AKI along with not only the previously known risk factors, but also echocardiographic findings including peak early trans-mitral flow velocity (E) and early diastolic mitral annular velocity (e') ratio (E/e' ratio). The E/e' ratio indicates the diastolic function that correlates with LV filling pressure. Furthermore, we evaluated the association between AKI and inhospital mortality, and identified risk factors for the development of in-hospital mortality.

# Methods

# Patients

This was a single-center, retrospective cohort study that included 285 patients who were older than 65 years of age and had undergone femoral neck fracture surgery in Korea University Anam Hospital from January 2013 to June 2017. Among 313 patients who had undergone femoral neck fracture surgery, we excluded 20 patients who did not have follow-up creatinine data and 8 patients who had undergone renal replacement therapy. Demographic and laboratory data were collected from electronic medical records.

The glomerular filtration rate was estimated by the Modification of Diet in Renal Disease Study equation [11]. CKD was defined by baseline estimated glomerular filtration rate (eGFR) < 60 mL/min/1.73 m<sup>2</sup>. The eGFR at admission was defined as the first eGFR after the admission date. Left atrial (LA) dimension, LV mass index, E/A ratio, deceleration time, ejection fraction (EF), E/e', and pulmonary artery (PA) pressure were estimated by echocardiography including tissue Doppler imaging conducted within 6 months prior to surgery. Heart failure with reduced EF (HFrEF) was defined as an EF consistently below 40%. Coronary artery disease (CAD) was defined as a history of myocardial infarction, angina, percutaneous coronary intervention, or coronary artery stenosis of more than 50% of the diameter as documented by coronary angiography. Cerebrovascular accident (CVA) was defined as stroke or transient ischemic accident. The use of nonsteroidal anti-inflammatory drugs, starch, angiotensin-converting-enzyme inhibitor (ACEI)/angiotensin II receptor blocker (ARB), and diuretics was evaluated during one week after the femur neck surgery. The administration of contrast was evaluated within a week before and after the surgery. Transfusion was defined as the administration of blood product within one week after surgery. The incidence of gastrointestinal bleeding, septic shock, mechanical ventilation, cardiac event, and pneumonia was evaluated during admission period after the surgery. A cardiac event was defined by the incidence of angina, myocardial infarction, and aggravation of heart failure during the admission period after the surgery. This study was reviewed and approved by the Institutional Review Board of the Korea University Anam Hospital (IRB number: 2018AN0222). This study was conducted in accordance with the Declaration of Helsinki.

#### Outcomes

AKI was defined by the Kidney Disease Improving Global Outcomes criteria as an increase in serum creatinine of more than 0.3 mg/dL within 48 hours or an increase in serum creatinine of more than 1.5 times baseline within a week [12]. Baseline creatinine value was defined as the creatinine value measured 7 to 365 days before hospitalization [13]. For patients who did not have pre-admission creatinine data, the lowest creatinine concentration during hospitalization was defined as the baseline creatinine [14]. Urine output criteria were not included. AKI was classified into stages 1, 2, and 3: stage 1 was defined as serum creatinine 1.5 to 1.9 times the baseline or  $a \ge 0.3 \text{ mg}/$ dL increase; stage 2 as serum creatinine 2.0 to 2.9 times the baseline; and stage 3 as serum creatinine 3.0 times the baseline, an increase to  $\geq 4.0 \text{ mg/dL}$ , or initiation of renal replacement therapy [12]. Severe AKI was defined as AKI stage 2 or 3. In-hospital mortality was defined as death occurring during the initial hospitalization.

# Statistical analysis

Data were analyzed using IBM SPSS Statistics (version 24.0; IBM Corp., Armonk, NY, USA). Continuous variables are presented as means  $\pm$  standard deviations, and not equally distributed data were presented as medians

and interquartile ranges. Comparisons were made using a Student's *t* test for normally distributed data and a Mann–Whitney *U* test for not normally distributed data. Categorical variables are presented as proportions and were compared with a chi-square test. A two-tailed *P* value of < 0.05 was considered significant. To identify the risk factors for the development of AKI and to identify factors for in-hospital mortality, we initially conducted a univariate logistic regression analysis. Variables that were statistically significant (*P* < 0.1) in this analysis were then included in a multivariate logistic regression analysis. Odds ratios (ORs) and 95% confidence intervals (CIs) were estimated.

# Results

#### Baseline characteristics

The baseline characteristics of the study patients are shown in Table 1. The mean age of the overall population was  $78.63 \pm 6.75$  years and  $80.00 \pm 6.68$  vs.  $78.21 \pm 6.74$ for the AKI and non-AKI groups, respectively, and 75.4% were women. Patients who developed AKI had a higher prevalence of diabetes mellitus (DM) (44.8% vs. 28.0%, P = 0.010) and hypertension (HTN) (79.1% vs. 56.2%, P =0.001). They also had a lower eGFR at baseline (86.55  $\pm$ 32.47 vs.  $100.67 \pm 37.60$ , P = 0.006) and admission ( $63.71 \pm$ 22.82 vs. 79.42  $\pm$  24.87, *P* < 0.001). There was no significant difference between groups in regard to age, sex, blood pressure, body mass index, hemoglobin, erythrocyte sedimentation rate (ESR), C-reactive protein, liver function test, albumin, CKD, CAD, chronic obstructive pulmonary disease, CVA, proteinuria, and hematuria. The length of hospital stay was similar between groups.

The type of femoral neck surgery was evaluated: 66.0% of patients underwent bipolar hemi-arthroplasty, 16.8% was total hip replacement arthroplasty, 6.7% was intramedullary nailing, and 10.5% was screw fixation. The type of surgery was not different between the AKI and non-AKI group. In patients with AKI, the post-operative use of ACEI/ARB and diuretics was significantly higher than non-AKI patients (P = 0.015). Transfusion was more common in patients with AKI, and the higher transfusion volume was administered in AKI patients (P = 0.009) (Table 1).

#### Echocardiographic measurements of study patients

In patients with AKI, the preoperative measurement of LA dimension (37.1 ± 7.0 vs. 34.5 ± 7.2, P = 0.017), LV mass index (96.2 ± 26.5 vs. 86.0 ± 22.1, P = 0.006), and PA pressure (42.7 ± 10.7 vs. 39.1 ± 9.1, P = 0.027) were significantly higher than non-AKI patients (P < 0.05). In addition, LV filling pressure measured by E/e' ratio was significantly higher in patients with AKI (14.5 ± 5.8 vs. 11.6 ± 4.2, P < 0.001). However, EF, the presence of HFrEF, and the presence of valvular disease were not different between AKI and non-AKI patients (Table 2).

# The incidence and risk factors of AKI in elderly patients with femoral neck fracture

Among 285 patients who underwent femoral neck fracture surgery, 67 (23.5%) developed AKI postoperatively during their initial hospitalization: 57 (85.1%), 5 (7.5%), and 5 (7.5%) patients were classified as having AKI stage 1, 2 and 3, respectively. None required renal replacement therapy.

We analyzed factors associated with AKI stages 1 to 3. In the univariate logistic analysis, baseline eGFR (OR, 0.988; 95% CI, 0.980–0.997), E/e' ratio (OR, 1.128; 95% CI, 1.057–1.203), higher LV mass index (OR, 1.018; 95% CI, 1.006–1.030), higher LA dimension (OR, 1.051; 95% CI, 1.004–1.073), DM (OR, 2.087; 95% CI, 1.186–3.672), HTN (OR, 2.948; 95% CI, 1.543–5.631), use of ACEI/ARB, diuretics, and transfusion were significantly associated with AKI (P < 0.05). The presence of chronic obstructive pulmonary disease (OR, 9.571; 95% CI, 1.711–53.539), lower albumin (OR, 0.293; 95% CI, 0.090–0.959), higher LV mass index (OR, 1.032; 95% CI, 1.009–1.055), and lower EF (OR, 0.900; 95% CI, 0.832–0.973) were significantly associated with severe AKI.

The multivariate analysis revealed that the presence of HTN (OR, 4.570; 95% CI, 1.632–12.797), higher E/e' ratio (OR, 1.105; 95% CI, 1.019–1.198), and lower hemoglobin (OR, 0.704; 95% CI, 0.528–0.938) were independently associated with a higher risk for development of AKI (Table 3). In addition, higher mean blood pressure (MBP) (OR, 1.064; 95% CI, 1.006–1.125), higher ESR (OR, 1.047; 95% CI, 1.011–1.083), and lower EF (OR, 0.854; 95% CI, 0.753–0.969) were associated with an increased risk for the de-

Characteristic	AKI (n = 67)	Non-AKI (n = 218)	P value
Age (yr)	80.00 ± 6.68	78.21 ± 6.74	0.057
Sex, male	22 (32.8)	48 (22.0)	0.072
SBP (mmHg)	138.46 ± 21.51	136.20 ± 18.10	0.395
DBP (mmHg)	80.22 ± 10.47	79.84 ± 11.02	0.799
MBP (mmHg)	99.64 ± 13.02	98.63 ± 12.19	0.562
Heart rate (beat/min)	81.49 ± 12.47	82.44 ± 11.00	0.550
Body mass index (kg/m²)	22.88 ± 3.80	22.11 ± 3.59	0.133
Hemoglobin (g/dL)	11.40 ± 1.69	$11.80 \pm 1.61$	0.074
eGFR (mL/min/1.73 m <sup>2</sup> )			
Baseline	86.55 ± 32.48	100.67 ± 37.60	0.006
Admission	63.72 ± 22.82	79.42 ± 24.87	< 0.001
ESR (mm/hr)	28.13 ± 20.36	23.30 ± 18.69	0.071
CRP (mg/L)	14.37 (0.36–187.98)	8.31 (0.15–253.91)	0.154
AST (IU/L)	25.02 ± 7.58	27.89 ± 12.83	0.083
ALT (IU/L)	19.40 ± 15.91	19.72 ± 14.09	0.878
ALP (IU/L)	91.24 ± 29.11	92.64 ± 42.44	0.801
Total bilirubin (mg/dL)	0.74 ± 0.33	0.79 ± 0.34	0.259
Albumin (g/dL)	3.69 ± 0.48	3.78 ± 0.47	0.214
Proteinuria	19 (28.4)	46 (21.1)	0.216
Hematuria	13 (19.4)	46 (21.1)	0.764
Diabetes mellitus	30 (44.8)	61 (28.0)	0.010
Hypertension	53 (79.1)	122 (56.2)	0.001
Chronic kidney disease	12 (17.9)	31(14.2)	0.460
Coronary artery disease	7 (10.4)	15 (6.9)	0.339
COPD	4 (6.0)	5 (2.3)	0.132
Cerebrovascular accident	10 (14.9)	28 (12.8)	0.661
Surgery type			0.390
Total hip replacement arthroplasty	9 (13.4)	39 (17.9)	
Bipolar hemiarthroplasty	50 (74.6)	138 (63.3)	
Intramedullary nailing	3 (4.5)	16 (7.3)	
Screw fixation	5 (7.5)	25 (11.5)	
Contrast	15 (22.4)	59 (27.1)	0.445
NSAIDs	37 (55.2)	146 (67)	0.079
Starch	34 (50.7)	116 (53.2)	0.724
ACEI/ARB	30 (44.8)	63 (28.9)	0.015
Diuretics	57 (85.1)	153 (70.2)	0.015
Transfusion	27 (40.3)	52 (23.9)	0.009
Amount of transfusion (L)	0.50 ± 0.70	0.25 ± 0.52	0.009
Hospital stay (d)	16 (6-70)	15 (4-97)	0.481

Data are presented as mean  $\pm$  standard deviation, number (%), or median (range).

ACEI/ARB, angiotensin-converting-enzyme inhibitor/angiotensin II receptor blockers; AKI, acute kidney injury; ALT, alanine aminotransferase; ALP, alkaline phosphatase; AST, aspartate aminotransferase; COPD, chronic obstructive pulmonary disease; CRP, C-reactive protein; DBP, diastolic blood pressure; eGFR, estimated glomerular filtration rate; ESR, erythrocyte sedimentation rate; MBP, mean blood pressure; NSAIDs, nonsteroidal anti-inflammatory drugs; SBP, systolic blood pressure.

Table 2. Echocardiographic measurements of study patients

Measurement	AKI	Non-AKI	P value
Measurement	(n = 67)	(n = 217)	r value
LA dimension (mm)	37.1 ± 7.0	34.5 ± 7.2	0.017
LV mass index (g/m <sup>2</sup> )	96.2 ± 26.5	86.0 ± 22.1	0.006
E/A ratio	0.7 ± 0.3	0.7 ± 0.2	0.566
Deceleration time (msec)	204.4 ± 56.8	198.5 ± 50.8	0.467
Pulmonary artery pressure <sup>a</sup>	42.7 ± 10.7	39.1 ± 9.1	0.027
HFrEF	0 (0)	4 (1.8)	0.263
Ejection fraction	56.6 ± 4.2	57.1 ± 4.7	0.446
E/e' ratio <sup>b</sup>	14.5 ± 5.8	11.6 ± 4.2	< 0.001
Mitral valve stenosis	0 (0)	0 (0)	
Mitral valve regurgitation	3 (4.5)	5 (2.3)	0.347
Aortic valve stenosis	0 (0)	3 (1.4)	0.333
Aortic valve regurgitation	3 (4.5)	4 (1.8)	0.224
Tricuspid valve regurgitation	5 (7.5)	14 (6.5)	0.772
Tricuspid valve stenosis	0 (0)	0 (0)	

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

AKI, acute kidney injury; E/e', the ratio of mitral peak velocity of early filling to early diastolic mitral annular velocity; HFrEF, heart failure with reduced ejection fraction; LA, left atrial; LV, left ventricular.

<sup>a</sup>Pulmonary artery pressure was measured in 201 patients; <sup>b</sup>the E/e' ratio was measured in 219 patients.

 Table 3. Risk factors associated with acute kidney injury in elderly patients with femoral neck fracture

Risk factor	OR (95% CI)	P value
Hypertension	4.570 (1.632-12.797)	0.004
E/e' ratio	1.105 (1.019-1.198)	0.016
Hemoglobin	0.704 (0.528–0.938)	0.017

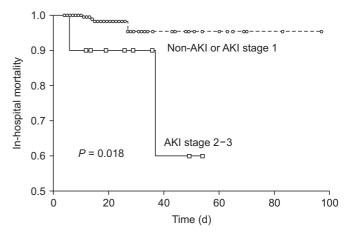
Cl, confidence interval; E/e', ratio of mitral velocity to early diastolic velocity of the mitral annulus; OR, odds ratio.

The risk factors were adjusted by age, sex, mean blood pressure, body mass index, presence of hypertension, diabetes mellitus status, baseline estimated glomerular filtration rate, E/e' ratio, aspartate aminotransferase, hemoglobin, erythrocyte sedimentation rate, transfusion, left atrial dimension, left ventricular mass index, pulmonary artery pressure, use of nonsteroidal anti-inflammatory drugs, use of diuretics, and use of angiotensin-converting-enzyme inhibitor/ angiotensin II receptor blocker drugs.

velopment of severe AKI.

## Risk factors predicting in-hospital mortality

Six patients died during hospitalization: 3 (4.5%) in the AKI group and 3 (1.4%) in the non-AKI group. In the AKI group, 2 (3.0%) patients who developed severe AKI died. Development of AKI stages 1 to 3 did not show a significant association with in-hospital mortality. However, a



**Figure 1.** In-hospital mortality for the presence of severe AKI. A Kaplan—Meier curve for in-hospital mortality based on acute kidney injury (AKI) shows that patients with AKI 2 or 3 had a significantly increased risk for in-hospital mortality compared with those having stage 1 AKI or non-AKI (log rank test, P = 0.018).

Kaplan–Meier curve for in-hospital mortality based on AKI showed that patients with AKI 2 or 3 had a significantly increased risk for in-hospital mortality compared with stage 1 AKI or no AKI (log rank test, P = 0.018) (Fig. 1).

In the univariate analysis, higher age, higher MBP, lower serum albumin, lower baseline eGFR, higher E/e' ratio, lower EF, higher LV mass index, presence of HFrEF, CAD, incidence of gastrointestinal bleeding, septic shock, mechanical ventilation, cardiac event, pneumonia, transfusion, and severe AKI were significantly associated with in-hospital mortality (P < 0.05) (Table 4). In the multivariate analysis, lower serum albumin (OR, 0.114; 95% CI, 0.011–1.165) was significantly associated with in-hospital mortality. Severe AKI showed a 24.743-fold higher risk for the development of in-hospital mortality (95% CI, 2.822–212.401) (Table 5).

# Discussion

AKI is a common complication after surgery and is associated with higher hospital cost, prolonged hospital stay, morbidity, and mortality [15–17]. Patients who have undergone AKI are at a higher risk of developing CKD, cardiovascular events, and stroke [15,18].

In our study, 23.5% developed AKI, which is higher than the incidence of up to approximately 10% associated with other non-cardiac surgeries in previous studies [15,16,19–21]. The reports of incidence of AKI have

Risk factor	Non-survivor	Survivor	P value	
	(n = 6)	(n = 279)		
Age (yr)	88.0 ± 7.0	78.4 ± 6.6	0.001	
Male	3 (50.0)	67 (24.0)	0.143	
MBP (mmHg)	111.2 ± 15.0	98.6 ± 12.2	0.014	
BMI (kg/m <sup>2</sup> )	21.9 ± 2.6	22.3 ± 3.7	0.797	
Hemoglobin (g/dL)	11.4 ± 1.4	11.7 ± 1.6	0.679	
ESR (mm/hr)	13.5 ± 6.5	24.7 ± 19.3	0.158	
CRP (mg/L)	24.4 ± 33.2	28.1 ± 40.5	0.826	
Albumin	3.3 ± 0.3	3.8 ± 0.5	0.022	
Baseline eGFR (mL/ min/1.73 m <sup>2</sup> )	134.6 ± 94.3	96.6 ± 34.6	0.012	
PA pressure (mmHg)	38.3 ± 3.0	40.0 ± 9.7	0.719	
E/e' ratio	17.8±2.3	12.3±4.7	0.044	
Ejection fraction	51.2 ± 12.0	57.1 ± 4.3	0.002	
HFrEF	2 (33.3)	2 (0.7)	< 0.001	
LA dimension (mm)	39.1 ± 5.2	35.0 ± 7.3	0.266	
LV mass index (g/m²)	114.9 ± 34.8	88.0 ± 23.2	0.023	
Diabetes mellitus	2 (33.3)	89 (31.9)	0.941	
Hypertension	3 (50.0)	172 (61.9)	0.554	
Chronic kidney disease	1 (16.7)	42 (15.1)	0.913	
Coronary artery disease	2 (33.3)	20 (7.2)	0.018	
Gastrointestinal bleeding	2 (33.3)	1(0.4)	< 0.001	
Septic shock	2 (33.3)	1 (0.4)	< 0.001	
Mechanical ventilation	3 (50.0)	5 (1.8)	< 0.001	
Cardiac event	2 (33.3)	9 (3.2)	< 0.001	
Pneumonia	3 (50.0)	23 (8.2)	< 0.001	
Transfusion	4 (66.7)	75 (26.9)	0.031	
Amount of transfusion (L)	0.79 ± 1.07	0.30 ± 0.56	0.040	
Severe AKI (stage 2 or 3)	2 (33.3)	8 (2.9)	< 0.001	

 Table 4. The association of risk factors with in-hospital mortality in elderly patients with femoral neck fracture

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

AKI, acute kidney injury; BMI, body mass index; CRP, C-reactive protein; E/e', ratio of mitral velocity to early diastolic velocity of the mitral annulus; eGFR, estimated glomerular filtration rate; ESR, erythrocyte sedimentation rate; LA, left atrial; LV, left ventricular; HFrEF, heart failure with reduced ejection fraction; MBP, mean blood pressure; PA, pulmonary artery.

varied by up to 40%, according to the type of surgery [3,15,16,19–22]. Orthopedic surgery was the second most frequent type of surgery associated with AKI in a major surgical setting, following cardiovascular surgery in patients in the intensive care unit [19]. However, most studies have involved critically ill patients or those who have undergone cardiac surgery, and few studies have evaluated AKI in patients who had orthopedic surgery. Previous studies have evaluated the incidence and the risk factors of AKI as a major complication after hip frac-

# Table 5. Risk factors for the prediction of in-hospital mortality in elderly patients with femoral neck fracture

Risk factor	OR (95% CI)	P value
Albumin	0.114 (0.011-1.165)	0.067
Severe AKI	24.743 (2.822–212.401)	0.003

AKI, acute kidney injury; CI, confidence interval; OR, odds ratio. The risk factors are adjusted by age, sex, mean blood pressure, body mass index, albumin, coronary artery disease, heart failure with reduced ejection fraction, left ventricular mass index, baseline estimated glomerular filtration rate, gastrointestinal bleeding, septic shock, mechanical ventilation, cardiac event, pneumonia, transfusion, and severe AKI.

ture. The incidence of AKI was similar in our study [23,24]. Also consistent with previous studies, use of ACEI/ARB, transfusion, and baseline eGFR were associated with AKI in univariate analysis [23,24]. However, our study showed that E/e' ratio, hemoglobin, and hypertension were independent risk factors after the adjustment. Our study is meaningful because we showed the relationship of the echocardiographic parameters to AKI.

Multiple factors are associated with postoperative AKI, including neuroendocrine responses; hemodynamic changes such as bleeding, volume imbalance, and systemic inflammation; and nephrotoxic agents that cause tubular injury [22]. In previous studies, multiple factors such as older age, obesity, CKD, HTN, DM, cardiovas-cular disease, chronic obstructive pulmonary disease, peripheral vascular disease, hypoalbuminemia, use of nephrotoxic agents, and emergency surgery were associated with perioperative AKI [16,19,25–27]. In our study, hypertension, lower hemoglobin, and higher E/e' ratio were associated with perioperative AKI. These factors, except the E/e' ratio, are consistent with the classic predictors revealed in the previous studies.

Heart failure with preserved EF is manifested by diastolic function disorder, which is characterized by an increase of the stiffness of the left ventricle and a decrease in the left ventricle [28]. The E/e' ratio indicates the diastolic function, which correlates well with LV filling pressure [29]. Ventricular hypertrophy can lead to diastolic dysfunction, which in turn leads to impaired distensibility of the myocardium and decreased cardiac output [30]. The reduced cardiac output then decreases renal perfusion and increases the activation of the renin-angiotensin-aldosterone and sympathetic systems, which triggers salt and water retention, which in turn causes venous congestion. The result is an increase in renal venous and intra-abdominal pressure, which worsens renal function [30,31]. A higher E/e' ratio is an independent predictor of AKI occurring after cardiac surgery [32,33]. An E/e' ratio > 15 is associated with AKI among patients with ST-segment elevation myocardial infarction [34].

Elderly patients have more severe LV hypertrophy and LV diastolic dysfunction than younger patients [9,10]. The average age of patients with proximal femur fracture has been increasing, so it is meaningful to focus on diastolic function in patients who have experienced femur fracture [35]. We evaluated the echocardiographic parameters associated with diastolic function such as LA dimension, LV mass index, and PA pressure [36-38]. Patients who developed postoperative AKI, preoperative measurements of LA dimension, LV mass index, PA pressure, and E/e' ratio were significantly higher than non-AKI patients. However, only E/e' ratio was significant after the adjustment. E/e' ratio was known to be closely associated with fluid overload [39]. Preoperative volume overload status could be associated the development of AKI after surgery. Careful volume control is needed before and after the surgery, especially in elderly patients.

Unlike stage 1 AKI, EF was an independent risk factor for the development AKI above stage 2. Severe AKI was significantly associated with in-hospital mortality. In univariate analysis, preoperative E/e' ratio was higher in non-survivors (P = 0.044). However, we could not evaluate the risk of E/e' ratio for the incidence of mortality in multivariate analysis because the E/e' ratio was calculated only in 3 (50%) non-survivors. Malnutrition and the presence of severe AKI were significant risk factors for inhospital mortality. We observed only in-hospital mortality, and the incidence was low (2.1%). To better evaluate the association between the E/e' ratio and mortality, a long-term follow-up study is needed.

This study has several limitations. First, this study is retrospective in nature. Second, the correct baseline renal function was not known in some of the patients. For patients who did not have creatinine laboratory data from 7 to 365 days prior to the study, we defined the baseline creatinine value as the lowest creatinine concentration during the hospitalization. Therefore, the incidence of AKI could have been overestimated. Third, we did not include urine output criteria in the definition of AKI. Finally, the observation period for the development of mortality was short. In conclusion, this study showed an association between diastolic dysfunction and AKI in elderly patients who underwent surgery for femoral neck fracture. Echocardiography and strict volume management can be helpful for improving perioperative outcomes in these patients. In conclusion, elderly patients with femoral neck fracture had a high incidence of AKI. HTN, lower hemoglobin, and higher E/e' ratio were all associated with AKI, and severe AKI was associated with in-hospital mortality. Therefore, careful management is necessary for high-risk patients after they undergo femoral neck surgery.

# **Conflicts of interest**

All authors have no conflicts of interest to declare.

#### References

- Cooper C, Campion G, Melton LJ 3rd. Hip fractures in the elderly: a world-wide projection. *Osteoporos Int* 1992;2: 285-289.
- [2] Hailer NP, Garland A, Rogmark C, Garellick G, Kärrholm J. Early mortality and morbidity after total hip arthroplasty in patients with femoral neck fracture. *Acta Orthop* 2016;87: 560-566.
- [3] Griffin XL, Parsons N, Achten J, Fernandez M, Costa ML. Recovery of health-related quality of life in a United Kingdom hip fracture population. The Warwick Hip Trauma Evaluation: a prospective cohort study. *Bone Joint J* 2015; 97-B:372-382.
- [4] Hobson C, Ozrazgat-Baslanti T, Kuxhausen A, et al. Cost and mortality associated with postoperative acute kidney injury. *Ann Surg* 2015;261:1207-1214.
- [5] Coca SG, Yusuf B, Shlipak MG, Garg AX, Parikh CR. Longterm risk of mortality and other adverse outcomes after acute kidney injury: a systematic review and meta-analysis. *Am J Kidney Dis* 2009;53:961-973.
- [6] Lafrance JP, Miller DR. Acute kidney injury associates with increased long-term mortality. J Am Soc Nephrol 2010;21: 345-352.
- [7] Anderson S, Eldadah B, Halter JB, et al. Acute kidney injury in older adults. *J Am Soc Nephrol* 2011;22:28-38.
- [8] Denic A, Glassock RJ, Rule AD. Structural and functional changes with the aging kidney. *Adv Chronic Kidney Dis* 2016; 23:19-28.

- [9] Villari B, Vassalli G, Schneider J, Chiariello M, Hess OM. Age dependency of left ventricular diastolic function in pressure overload hypertrophy. *J Am Coll Cardiol* 1997;29: 181-186.
- [10] Burlew BS. Diastolic dysfunction in the elderly--the interstitial issue. *Am J Geriatr Cardiol* 2004;13:29-38.
- [11] Levey AS, Bosch JP, Lewis JB, Greene T, Rogers N, Roth D. A more accurate method to estimate glomerular filtration rate from serum creatinine: a new prediction equation. Modification of Diet in Renal Disease Study Group. Ann Intern Med 1999;130:461-470.
- [12] Thomas ME, Blaine C, Dawnay A, et al. The definition of acute kidney injury and its use in practice. *Kidney Int* 2015; 87:62-73.
- [13] Siew ED, Ikizler TA, Matheny ME, et al. Estimating baseline kidney function in hospitalized patients with impaired kidney function. *Clin J Am Soc Nephrol* 2012;7:712-719.
- [14] Siew ED, Matheny ME. Choice of reference serum creatinine in defining acute kidney injury. *Nephron* 2015;131: 107-112.
- [15] Biteker M, Dayan A, Tekkeşin Aİ, et al. Incidence, risk factors, and outcomes of perioperative acute kidney injury in noncardiac and nonvascular surgery. *Am J Surg* 2014;207: 53-59.
- [16] Kheterpal S, Tremper KK, Heung M, et al. Development and validation of an acute kidney injury risk index for patients undergoing general surgery: results from a national data set. *Anesthesiology* 2009;110:505-515.
- [17] Cho EJ, Cha IH, Yoon KC, et al. Clinical characteristics and outcomes of septic acute kidney injury in critically ill patients. *Kidney Res Clin Pract* 2011;30:253-259.
- [18] Shiao CC, Wu PC, Huang TM, et al; National Taiwan University Hospital Study Group on Acute Renal Failure (NSARF) and the Taiwan Consortium for Acute Kidney Injury and Renal Diseases (CAKs). Long-term remote organ consequences following acute kidney injury. *Crit Care* 2015;19:438.
- [19] Thakar CV. Perioperative acute kidney injury. Adv Chronic Kidney Dis 2013;20:67-75.
- [20] Sun LY, Wijeysundera DN, Tait GA, Beattie WS. Association of intraoperative hypotension with acute kidney injury after elective noncardiac surgery. *Anesthesiology* 2015;123:515-523.
- [21] Lim SY, Lee JY, Yang JH, et al. Predictive factors of acute kidney injury in patients undergoing rectal surgery. *Kidney Res Clin Pract* 2016;35:160-164.

- [22] Goren O, Matot I. Perioperative acute kidney injury. *Br J Anaesth* 2015;115 Suppl 2:ii3-ii14.
- [23] Hong SE, Kim TY, Yoo JH, et al. Acute kidney injury can predict in-hospital and long-term mortality in elderly patients undergoing hip fracture surgery. *PLoS One* 2017;12: e0176259.
- [24] Ulucay C, Eren Z, Kaspar EC, et al. Risk factors for acute kidney injury after hip fracture surgery in the elderly individuals. *Geriatr Orthop Surg Rehabil* 2012;3:150-156.
- [25] Golden D, Corbett J, Forni LG. Peri-operative renal dysfunction: prevention and management. *Anaesthesia* 2016; 71 Suppl 1:51-57.
- [26] McKinlay J, Tyson E, Forni LG. Renal complications of anaesthesia. *Anaesthesia* 2018;73 Suppl 1:85-94.
- [27] Abelha FJ, Botelho M, Fernandes V, Barros H. Determinants of postoperative acute kidney injury. *Crit Care* 2009;13:R79.
- [28] Redfield MM. Heart failure with preserved ejection fraction. *N Engl J Med* 2016;375:1868-1877.
- [29] Nagueh SF, Appleton CP, Gillebert TC, et al. Recommendations for the evaluation of left ventricular diastolic function by echocardiography. J Am Soc Echocardiogr 2009;22:107-133.
- [30] O'Rouke RA, Hurst JW. Hurst's the heart: Manual of cardiology. 10th ed. New York: McGraw-Hill; 2001. p. 658-660.
- [31] Anand IS. Cardiorenal syndrome: a cardiologist's perspective of pathophysiology. *Clin J Am Soc Nephrol* 2013;8: 1800-1807.
- [32] Han SS, Park S, Kang SH, et al. Usefulness of preoperative echocardiography to predict acute kidney injury and longterm mortality after coronary artery bypass grafting. *Am J Cardiol* 2017;119:231-236.
- [33] Hur M, Nam K, Jo WY, Kim G, Kim WH, Bahk JH. Association between elevated echocardiographic index of left ventricular filling pressure and acute kidney injury after offpump coronary artery surgery. *Circ J* 2018;82:857-865.
- [34] Flint N, Kaufman N, Gal-Oz A, et al. Echocardiographic correlates of left ventricular filling pressures and acute cardio-renal syndrome in ST segment elevation myocardial infarction patients. *Clin Res Cardiol* 2017;106:120-126.
- [35] Muhm M, Amann M, Hofmann A, Ruffing T. [Changes in the patient population with proximal femur fractures over the last decade : incidence, age, comorbidities, and length of stay]. Unfallchirurg 2018;121:649-656. German.
- [36] Neuman Y, Kotliroff A, Bental T, Siegel RJ, David D, Lishner M. Pulmonary artery pressure and diastolic dysfunction in normal left ventricular systolic function. *Int J Cardiol* 2008;

127:174-178.

- [37] Teo SG, Yang H, Chai P, Yeo TC. Impact of left ventricular diastolic dysfunction on left atrial volume and function: a volumetric analysis. *Eur J Echocardiogr* 2010;11:38-43.
- [38] Kimura H, Takeda K, Tsuruya K, et al. Left ventricular mass index is an independent determinant of diastolic dysfunc-

tion in patients on chronic hemodialysis: a tissue Doppler imaging study. *Nephron Clin Pract* 2011;117:c67-c73.

[39] Kim JS, Yang JW, Yoo JS, Choi SO, Han BG. Association between E/e' ratio and fluid overload in patients with predialysis chronic kidney disease. *PLoS One* 2017;12:e0184764.