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The Correlation between Preoperative and Postoperative Hypoalbuminaemia and the Development of Acute Kidney Injury with Respect to the KDIGO Criteria in the Hip Fracture Surgery in Elderly Patients

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Abstract

Objective: The aim of the present study was to determine the correlation between preoperative and postoperative hypoalbuminaemia and acute kidney injury (AKI) in the hip fracture surgery in elderly patients.

Methods: A total of 160 patients aged ≥65 years were scanned retrospectively. They were grouped into four as the preoperative albumin level of <3.8, preoperative albumin level of >3.8, postoperative day 2 albumin level of <2.9 and postoperative day 2 albumin level of >2.9. In the beginning and 7 days, age, gender, white blood cell, haemoglobin, haematocrit, glucose, blood urea nitrogen, serum creatinine, albumin values, fever, anaesthesia method, presence of blood transfusion, surgical period, hospitalisation durations and expenses in the postoperative period were recorded for all the patients.

Results: In the study, 92 women and 68 men were scanned. AKI was observed in 28 (17.5%) patients, and 16 (57.1%) patients were determined in stage 1. AKI development in Group 1 and Group 3 was significantly high (p<0.05). Advanced age, multiple drug usage, postoperative glucose level and blood product transfusion during the operation were significantly associated with AKI (p<0.05). The hospitalisation period and cost were high in patients with AKI (p<0.05).

Conclusion: It was determined that hypoalbuminaemia was associated with AKI development, and preoperative or postoperative hypoalbuminaemia affected AKI development at similar rates. Advanced age, multiple drug usage, postoperative glucose level and blood product transfusion during the operation were associated with AKI.

Keywords: Acute kidney injury, hip fracture, hypoalbuminaemia, KDIGO criteria

Introduction

Although the biological functions of albumin have not been defined extensively, it has been demonstrated that nutritional status is strongly associated with poor clinical outcomes, particularly infection, and is a potential risk factor and a negative prognostic factor for mortality in acute patients. Therefore, postoperative complications (cardiac, pulmonary, infections, haemorrhage and thromboembolic) are more likely in elderly patients with low albumin levels (1, 2).

For postoperative acute kidney injury (AKI), advanced age, diabetes, general anaesthesia (3), surgery (4), male gender, hypertension, hypoperfusion and blood transfusion (1, 5) are the previously shown risk factors. In addition to all these factors, it has been reported that hypoalbuminaemia is also an independent risk factor for AKI (6). Some studies have revealed that both preoperative hypoalbuminaemia (1, 7) and postoperative hypoalbuminaemia (3, 4, 8) are associated with AKI incidence after various surgeries.

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It has been stated that while postoperative AKI incidence is varying, it is one of the postoperative complications frequently observed after the hip fracture operation, and AKI incidence associated with hip fracture varies between 8% and 24.4% (9-12). Postoperative AKI is associated with prolonged hospitalisation period and increased morbidity and mortality (13, 14).

The aim of the present study was to determine the correlation between preoperative and postoperative hypoalbuminaemia and AKI in the hip fracture surgery in the elderly, identify the period of hypoalbuminaemia that has more contribution on AKI development, determine other factors affecting AKI development and investigate the effect of hypoalbuminaemia on hospitalisation period and cost. When the literature is reviewed, to the best of our knowledge, this is the first study comparing the preoperative and postoperative periods.

Methods

The study was planned as a retrospective descriptive study. The study was approved by the ethics committee of Erzincan Binali YıldırımUniversity (Approval Number: 30/02). Written informed consent was obtained from patients and patients' parents who participated in this study. A total of 160 patients aged ≥65 years who had an American Society of Anesthesiologists I-IV physical status, were below spinal anaesthesia or peripheral nerve block and had hip fracture operation between 01/01/2018 and 01/07/2018 were included in the study (ClinicalTrials.gov Identifier: NCT03675906).

Patients who underwent urgent surgery, had preoperative serum creatinine (sCr) level of >1.5 mg dL⁻¹, had low serum albumin levels in both preoperative and postoperative periods, received preoperative ventilator care, received spinal anaesthesia or peripheral nerve block contraindications (coagulopathies, local infection in puncture location and shock infection) or having non-steroidal anti-inflammatory drug treatment were excluded from the study.

Preoperative management: All the patients' age, gender, number of underlying diseases, number of drugs used, as well as white blood cells (WBCs), haemoglobin (HB), haematocrit (HCT), glucose, blood urea nitrogen (BUN), sCr, albumin values among the laboratory data and the haemodynamic data (blood pressure and fever) from the nurse observations were recorded.

Intraoperative management: The anaesthesia type [spinal anaesthesia or peripheral nerve block (psoas compartment block+parasacral sciatic block)], the presence of blood transfusion and the surgical period were recorded.

Postoperative management: 7-day WBC, HB, HCT, glucose, BUN, sCr, albumin, blood pressure, fever, hospitalisation periods and costs were recorded.

After these data were recorded, the patients were divided into four based on their albumin levels as follows:

Group 1: those with preoperative albumin level of <3.8 g dL⁻¹ (1).
Group 2: those with preoperative albumin level of >3.8 g dL⁻¹ (1).
Group 3: those with postoperative day 2 albumin level of <2.9 g dL⁻¹ (4).
Group 4: those with postoperative day 2 albumin level of >2.9 g dL⁻¹ (4).

To prevent Group 1 and Group 3 to get intertwined, patients with low preoperative albumin level and patients whose albumin level were made to return to normal by giving albumin in the postoperative period were included in the study. Since the cause of hypoalbuminaemia could not be reached from the files, all patients who were brought to normal levels with albumin infusion in the postoperative period were included.

The definition of AKI, which was the aim of the study, was done based on the International Kidney Disease: Improving Global, Outcomes (KDIGO) criteria (15). Accordingly, AKI was considered as positive in patients who had an increase of ≥0.3 mg dL⁻¹ in their sCr in 48 h or had an increase of ≥1.5 times than the baseline in their sCr in postoperative day 7, and staging was performed according to these criteria.

The primary outcome of the present study was to determine the correlation between preoperative and postoperative hypoalbuminaemia and AKI in the hip fracture surgeries in the elderly.

Moreover, the secondary outcome was to determine in which period hypoalbuminaemia had more contribution on AKI development, identify other factors affecting AKI development and investigate the effect of hypoalbuminaemia on hospitalisation duration and cost.

Statistical analysis

The power of the study was calculated using 'G-Power' with the hypothesis that AKI incidence, which was found to be 3.5% by Kim et al. (1), may be 8.5% in the present study in which hypoalbuminaemia was obtained in both periods. Accordingly, to provide the power of the study to be 80%, the total sample number was found to be 160. While the results of categorical variables were presented as numbers, the results of continuous variables were presented as mean±standard deviation. Comparison of the groups with respect to the categorical variables was performed using chi-square or

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Fisher's exact test. For comparison of independent continuous variables between the two groups, the Student's t-test or Mann-Whitney U test was used depending on whether the statistical hypotheses were fulfilled or not. The significance level for all tests was considered to be 0.05. Statistical analysis was performed using the IBM Statistical Package for the Social Sciences version 19 package programme (IBM SPSS Corp.; Armonk, NY, USA).

Results

Demographic data
Of the 160 patients included in the study, 92 were female and 68 were male. Without group discrimination, the mean average was found to be 72.0±6.5. One or more comorbid-ities were determined in 116 patients, and 20 of these patients used two or more drugs. A significant difference was not determined between the preoperative creatinine, BUN and postoperative creatinine values of the patients. In the comparison among the groups, a significant difference was observed with respect to preoperative albumin, 48-hour albumin, hospitalisation duration, AKI incidence and AKI stage (p<0.05) (Table 1).

Data on AKI
Without group discrimination, AKI was observed in 28 (17.5%) patients, and 16 (57.1%) patients were determined in stage 1. In the group comparisons of the patients with AKI development, it was observed that it was significantly high in Group 1 and Group 3 (p<0.05) (Table 2).

Table 1. Demographic data and preoperative values **						
	Group 1	**Group 2**	**Group 3**	**Group 4**	**Total**	**p**
Age(year)	72.6±7.2	71.4±5.8	72.4±6.3	71.8±7.0	72.0±6.5	0.843
Sex (F/M)	24/16	25/15	20/20	23/17	92/68	0.698
Surgery time (h)	2.5±0.6	2.5±0.7	2.3±0.7	2.5±0.6		0.433
Anaesthesia management (central/peripheric)	21±19	20±20	20±20	22±18	83/77	0.965
Comorbidity 0	12	12	9	11	44	0.292
1	25	23	24	23	95	
2	3	5	4	6	18	
3	0	0	3	0	3	
Drug (<2/>2)	36/4	34/6	36/4	34/6		0.680
Preop albumin (g dL⁻¹)	2.9±0.4	4.1±0.2	4.1±0.3	4.0±0.2		**0.000**
Preop creatinine (mg dL⁻¹)	0.8±0.3	1.1±1.2	0.8±0.3	0.8±0.3		0.131
Preop BUN (mg dL⁻¹)	19.9±9.7	20.2±10.7	19.0±8.0	19.5±9.4		0.949
48-hour albumin (g dL⁻¹)	4.1±0.2	3.7±0.4	2.4±0.3	3.2±0.2		**0.000**
48-hour creatinine (mg dL⁻¹)	1.0±0.4	1.1±1.2	1.3±1.2	0.9±0.3		0.167
Blood transfusion (−/+)	36/4	37/3	33/7	37/3		0.419
Length of hospital stay (days)	9.0±4.0	7.5±2.7	9.0±4.7	7.2±2.5		**0.044**
Cost (Turkish liras)	4107.6±1772.2	3791.7±1662.3	4167.5±1494.7	3795.2±1440.1		0.598
AKI (occurred/non-occurred)	11/29	4/36	10/30	3/37	**28/132**	**0.010**
AKI stage 1	7	2	6	1	**16**	**0.048**
2	3	1	3	1	8	
3	1	1	1	1	4	

Bold: The mean difference is significant at the 0.05 level. Data are given as mean±SD. **Multiple comparisons. AKI: Acute Kidney Injury

Table 2. Incidence and stages of AKI**						
	Group 1	**Group 2**	**Group 3**	**Group 4**	**Total**	**p**
AKI (occurred)	11	4	10	3	28	**0.010**
(non-occurred)	29	36	30	37	132	
AKI stage 1	7	2	6	1	**16**	**0.048**
2	3	1	3	1	8	
3	1	1	1	1	4	

Bold: The mean difference is significant at the 0.05 level. Dataare given as n (patient number).**Multiple comparisons. AKI: Acute Kidney Injury.

Table 3. Hypoalbuminaemia and AKI development between the groups**						
	Groups 1 and 2	Groups 1 and 3	Groups 1 and 4	Groups 2 and 3	Groups 2 and 4	Groups 3 and 4
AKI (occurred)	11 and 4	11 and 10	11 and 3	4 and 10	4 and 3	10 and 3
p	**0.009**	0.856	**0.032**	**0.009**	0.632	**0.032**

Bold: The mean difference is significant at the 0.05 level. Data are given as n (patient number).**Multiple comparisons. AKI: Acute Kidney Injury.

Table 4. Factors affecting AKI development**			
	AKI+	AKI−	p
Age(year)	81.71±7.2	79.8±6.1	**0.001**
Sex (F/M)	16/12	76/46	0.108
Surgery time (h)	2.46±0.693	2.50±0.677	0.413
Anaesthesia management (central/peripheric)	13/11	70/66	0.126
Comorbidity 0	6	38	0.250
1	17	78	
2	4	14	
3	1	2	
Drug (>2/<2)	22/6	118/14	**0.014**
Preop WBC/HB/HCT	9.6±4.5/11.4±1.7/35.2±5.2	9.3±3.1/11.4±1.6/34.9±4.9	0.611/0.958/0.706
Preop glucose/BUN	130.2±42.7/20.0±9.6	142.1±50.9/19.5±9.3	0.141/0.734
Preop creatinine (mg dL^{-1})	0.8±0.3	0.9±0.8	0.363
Preop MAP (mmHg)	89.4±16.7	90±14.2	0.379
Postop MAP (mmHg)	67.4±11.9	69.2±14.7	0.617
48-hourglucose (mg dL^{-1})	149.4±53.0	131.2±44.4	**0.022**
Blood transfusion (unit)	12	5	**0.002**
Length of hospital stay (days)	11.5±3.9	6.4±1.8	**0.000**
Cost (Turkish liras)	5119.6±1142.1	3344.0±1450.1	**0.000**

Bold: The mean difference is significant at the 0.05 level. Data are given as n (patient number).**Chi-square tests. AKI: Acute Kidney Injury.

In the groups with hypoalbuminaemia in the preoperative or postoperative periods, AKI incidence was significantly higher than the other groups (p<0.05) (Table 3).

When the factors affecting AKI development were examined, it was determined that advanced age, multiple drug use, postoperative glucose level and blood product transfusion during operation had a significant correlation with AKI development (p<0.05) (Table 4). In addition, it was observed that hospitalisation duration and cost in patients with AKI development were higher than those in patients without AKI development (p<0.05) (Table 4).

Discussion

In the present study in which hypoalbuminaemia and postoperative AKI incidence and the factors contributing to AKI development were examined, AKI incidence was determined to be 17.5% based on the KDIGO criteria. In addition, in the present study, it was determined that preoperative or postoper-

ative hypoalbuminaemia affected AKI development at similar rates, and advanced age, multiple drug usage, postoperative glucose level and blood product transfusion during the operation were significantly associated with AKI development.

Elderly patients with a hip fracture need special care as they have had an acute attack that represents a chronic process that generally develops slowly and often triggers serious complications and disabilities. The malnutrition prevalence in these patients varies to a large extent among the reviewed articles, and it reaches to 50% in most of them (2). Two of the long-term results of inadequate calorie and protein intake are osteoporosis and loss of strength, causing fractures due to the decrease of bone resistance against impact. Therefore, in elderly patients with low albumin levels, the possibility of having postoperative complications (cardiac, pulmonary, infectious, haemorrhagic and thromboembolic) is higher (16).

The disorder, which was known as acute kidney failure in previous years, has become the diagnosis of AKI after the KDI-

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GO criteria has combined the Risk, Injury, Failure, Loss and End-stage kidney disease and Acute Kidney Injury Network criteria (15). AKI, which has been described again based on the KDIGO criteria, is characterised by the situation in which there is an increase of ≥ 0.3 mg dL^{-1} than the baseline level in sCr in 48 h or there is an increase of ≥ 1.5 times in serum creatinine level than the baseline level in postoperative day 7 or the urine volume of 6 h is <0.5 mL kg^{-1} h^{-1} (15). It is observed in 5%-7% of all the patients hospitalised in the clinics or surgical hospitals. While its incidence in the postoperative period varies between 0.1% and 30% due to the detection criteria and the operation type, it is known that AKI incidence associated with the hip fracture is between 8% and 24% (9-12). This was consistent with the incidence determined to be 17.5% for postoperative AKI in patients who underwent an operation for proximal hip intertrochanteric fracture.

Although the mechanism is not known exactly, studies have revealed that albumin has a renoprotective effect (17-19). The data obtained so far suggest that albumin protects the colloid osmotic pressure, increases the effective circulation volume, increases the renal blood flow and protects renal function. In addition, albumin, renal perfusion, glomerular filtration and maintain medullary fluid reabsorption (20). Moreover, albumin activates phosphoinositide 3-kinase and stimulates the proliferation of renal tubular cells (3). Especially it is known that the endothelial glycocalyx layer, which is rich with respect to albumin made of glycosaminoglycans, is very important for endothelial barrier, and the deterioration of the glycocalyx layer is associated with protein extravasation, tissue oedema and accelerated inflammation (21). It has been reported that both preoperative hypoalbuminaemia (1, 7) and early postoperative hypoalbuminaemia (3, 4, 8) are independent risk factors for AKI (6, 7). In addition, similarly in the present study, it was determined that preoperative and postoperative hypoalbuminaemia was a risk factor for AKI. Although we could not emphasise the effects of hypoalbuminaemia on AKI, we attributed postoperative AKI, together with hypoalbuminaemia, to the endothelial glycocalyx layers, and that the above-mentioned protective effects of albumin were damaged. We wanted to perform the risk comparison of the two periods themselves in the present study with respect to AKI development because we think that early detection of the risk factors for AKI may be useful perioperative treatment and improve the clinical outcomes (13, 14).

There are many factors affecting AKI development other than hypoalbuminaemia. It has been shown that there are multiple risk factors, such as male gender (22), perioperative hypotension, advanced age, diabetes mellitus (7), high body mass index (BMI), urgent surgery, vasopressor infusion usage, blood products transfusion (1, 5) and diuretic application in various environments (3). Collaterally, in addition to the pres-ent study, it was determined that advanced age, multiple drug use, postoperative glucose level and blood product transfusion during operation had a significant correlation with AKI development ($p < 0.05$) (Table 4).

Postoperative AKI is associated with prolonged hospitalisation duration and increased morbidity and mortality after heart surgery (13, 14). The postoperative mortality rate may vary between 20% and 80% depending on comorbid diseases (11). Furthermore, it was similarly determined in the present study that hospitalisation duration and cost were higher in patients with AKI development than in those without AKI development.

There are some limitations in the present study. We conducted the present study as retrospective and descriptive. Although we tried to consider the surprising factors and decrease the bias, it is impossible to exclude the effect of the hidden factors. Although it was known that one of the most important factors in AKI development was hypoperfusion, only systolic and diastolic arterial pressure and transfusion information could be obtained from intraoperative perfusion data. Owing to the current opportunities of our hospital, the BMIs of the patients could not be reached. In addition, general mortality was excluded in these patients.

Conclusion

In the present study investigating AKI incidence and the effects contributing to AKI development with respect to hypoalbuminaemia and the postoperative KDIGO criteria, it was determined that hypoalbuminaemia was associated with AKI development, preoperative or postoperative hypoalbuminaemia affected the AKI development at similar rates and advanced age, multiple drug usage, postoperative glucose level and blood product transfusion during the operation were significantly associated with AKI development. We think that hypoalbuminaemia is a condition that should not be ignored for the elderly people, regardless of its cause and onset time.

Conflict of Interest: The authors have no conflicts of interest to declare.

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