Original article

Hypoalbuminemia Leads to An Increased Risk Of Mortality And Re-Operation Within 3-Months In Patients 75< Years Of Age After Surgery For Hip Fractures

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Summary. *Background:* The focus of this study is to ascertain a baseline nutritional level of adults 75 years old who are hospitalized for hip fracture surgery, and to assess the effects on the mortality rates and post-operative complications that require re-operation within 3 months of the initial surgery. *Material and Methods:* A total of 240 patients having surgery for fractured hips during 2017-2019 were identified. Patients' characteristics, including pre-operative laboratory findings, complications and reoperation rates were assessed. Multivariate logistic regression analysis was used to establish the effect of hypoalbuminemia and total lymphocyte count on the rates of 3-month post-operative complications, re-operation and mortality. *Results:* Among patients studied, 153 had hypoalbuminemia (albumin levels <3.5 g/dL), and 87 showed normal albumin levels (albumin levels ≥3.5 g/dL). Patients in the hypoalbuminemia group were likely to be functionally dependent ($p = 0.002$) and had higher Charlson comorbidity scores ($p = 0.006$) than their counterparts. The American Society of Anesthesiologists score and albumin levels were significant predictors of re-operation ($p = 0.013$, $p = 0.039$). The increase in age by 1 year, albumin level <3.5 g/dL, and lymphocyte count <1500 cells/mm^3 were associated with increased mortality rates ($p = 0.012$, $p = 0.004$, $p = 0.002$). *Conclusion:* Malnutrition is high in patients with hip fractures. In this study, hypoalbuminemia and lymphocyte count (<1500 cells/mm^3) were directly associated with post-operative mortality rates and complications that required re-operation within 3 months of initial surgery.

Key words: hip fractures, hypoalbuminemia, frail elderly

Introduction

Approximately 1.6 million hip fractures (HFs) occur annually worldwide (1). HFs can lead to a reduced quality of life and mortality rates around 20-30% in the first year after surgery (2). Most patients that live beyond the first year have reduced function and require long-term care (3). As a result, HFs are associated with a growing socioeconomic burden, which includes health-care costs (4). Returning patients to their pre-HF functional status within a reasonable timeframe has become paramount, as it may allow them to live independently, reducing the overall toll on the health care systems in countries with aging populations (5).

Malnutrition, common among patients with HFs, has been directly related to an increased risk of pre and post-operative complications and high mortality rates (4). Previous studies have reported malnutrition rates ranging from 31% to 88%, depending on the patient group of interest (6). Trauma due to fracture may exacerbate nutritional deficiency; similarly, a nutritional deficiency may develop in a patient that is already undernourished at the time of the occurrence of such trauma (7). An acute inflammatory response leads to the rapid loss of lean body mass, which is greater if nutritional intake is poor. Inflammation associated with chronic disease such as diabetes or kidney damage can cause a dangerous loss of muscle mass and function over months or years, making post-operative physical therapy and rehabilitation more difficult for affected patients (8).

Malnutrition in patients with HFs is considered the leading cost driver in hospitalized patients (9). Nutritional deficiencies can be improved and thus targeted with interventions aimed at improving post-operative outcomes and reducing recovery time. Moreover, identifying patients at risk of nutritional deficiencies may enable early mediation and suitable follow-up monitoring in the postoperative period (10,11). The goal of this study was determining a baseline nutritional state for adults 75 years of age hospitalized for HF and to assess effects on the rates of post-operative complications requiring reoperation within 3 months of the initial surgery, and overall mortality.

Materials and Methods

This research has been approved by our institutional ethics committee (details redacted for peer review). Among patients 75< years old who had HF surgery between January 2017 and December 2019, a total of 240 eligible patients were analyzed in this retrospective study. Patients were excluded if they developed infection, pathological fracture, polytrauma, or limited life expectancy (6 months), or if they required tube feeding. Preoperative albumin levels were evaluated to divide patients into "normal" (≥3.5 g/dL) or "hypoalbuminemic" (<3.5 g/dL) groups; baseline demographic and clinical characteristics were compared between these groups. All patients were evaluated within the first 48 h of hospital admission but before surgery. Demographic characteristics and body mass index estimates, which were calculated based on each patient's reported height and weight, were extracted. Functional status was then categorized as fully independent, partially dependent (walking with aids and requiring some help with mobility), or dependent (chair- or bed-bound). Medical comorbidities were determined using the Charlson comorbidity index (CCI) (12). Fracture and surgery types were also recorded. Perioperative data collected included American Society of Anesthesiologists (ASA) scores, anesthesia type, and length of post-operative hospital stay (LOS). Preoperative blood parameters including albumin, lymphocyte, and hemoglobin levels were recorded in the acute orthopedic ward. Patients' need for re-operation and fatality status were recorded in the first 3 months after surgery. Where patient records were incomplete, a follow-up assessment was performed over the phone.

Statistical analysis

The Statistical Package for the Social Sciences (SPSS Inc., IBM Corp., Armonk, NY, USA), Version 23.0. 15.0 for Windows was employed for statistical analysis. For descriptive statistics, category variables were reported as counts and percentages, while continuous variables were reported as means with standard deviations, and medians with ranges, as necessary. Independent comparisons of continuous variables were performed using the Mann-Whitney U test, where the condition of normal distribution was not met. Comparisons for more than two groups were performed with the Kruskal-Wallis test, where the conditions for a parametric test were not met. Subgroup analyses were performed using the Mann-Whitney U test and adjusted with the Bonferroni correction. Relationships between continuous variables were studied using the Spearman correlation analysis, as there was no parametric test condition to be met. Rates were compared between groups using the Chi-square test and risk factors were analyzed using logistic regression. P-values of <0.05 were considered indicative of a statistically significant finding.

Results

A total of 240 patients (160 (66.7%) women) were recruited for this study between January 2017 and December 2019. Patients' mean age was 82.5±5.8 years. The median CCI score was 8 (range, 4–13) points. Before HF, 122 (50.8%), 81 (33.8%), 37 (15.4%) patients were independent, walked with an aid, or were either chair- or bed-bound, respectively.

There were 149 (62.1%) intertrochanteric and 91 (37.9%) femoral neck fractures. Surgery types included a proximal femoral nail and dynamic hip screw insertion, and modular hemiarthroplasty for 134 (55.8%), 15 (6.3%), and 91 (37.9%) patients, respectively. The average LOS was 8±3.1 days. A total of 27 (11.3%) patients underwent reoperation. A total of 153 (63.8%) patients had pre-operative hypoalbuminemia and 87 (36.3%) had normal albumin levels; these patient groups were similar in age and sex (p=0.776 and p=0.113, respectively). Patients with hypoalbuminemia were more likely to be functionally dependent (20.9% vs. 5.7%, p=0.002) and have higher CCI scores (p=0.006) than those with normal serum albumin levels. In addition, the hypoalbuminemic group was connected to a higher likelihood of ASA scores of 4 points (p=0.042) and higher mortality rates (p=0.018) than the normal serum albumin group. Similar anesthesia types were used in both groups (p = 0.786); the LOS was also similar between the groups (p=0.309). The LOS was significantly greater in patients with ASA scores of 3 points than in those with ASA scores of 2 points (p = 0.007).

Comparisons of clinical and functional outcomes among groups are presented in Table 1. Six patients in

Table 1. The analysis of clinical and functional outcomes

		Preoperative albumin level		
		≥3.5 g/dL	**<3,5 g/dL**	***p***
Sex n (%)	Male	30.0 (34.5)	50.0 (32,7)	0.776
	Female	57.0 (65.5)	103.0 (67,3)	
Age Median (min-max)		80.0 (75.0-96.0)	81.0 (68.0-97.0)	0.113
BMI Median (min-max)		26.6 (17.0-42.5)	24.5 (16.0-39.5)	0.003
Obesity, kg/m² n (%)	BMI <30.0	68.0 (78.2)	131.0 (85.6)	0.140
	BMI ≥30.0	19.0 (21.8)	22.0 (14.4)	
Hemoglobin (g/dL) Median (min-max)		11.2 (7.4-16.7)	10.4 (7.0-14.2)	<0.001
Lymphocyte n (%)	⩾1500 cells/mm³	48.0 (55.8)	59.0 (39.1)	0.013
	<1500 cells/mm³	38.0 (44.2)	92.0 (60.9)	
Functional status n (%)	Totally dependent	5.0 (5.7)	32.0 (20.9)	0.002
	Partially dependent	27.0 (31.0)	54.0 (35.3)	
	Independent	55.0 (63.2)	67.0 (43.8)	
CCS Median (min-max)		8.0 (4.0-12.0)	8.0 (4.0-13.0)	0.006
Diagnosis n (%)	CFF	41.0 (47.1)	50.0 (32.7)	0.027
	ITK	46.0 (52.9)	103.0 (67.3)	
Surgery performed n (%)	DHS	2.0 (2.3)	13.0 (8.5)	0.028
	Hemiarthroplasty	41.0 (47.1)	50.0 (32.7)	
	PFN	44.0 (50.6)	90.0 (58.8)	
ASA Score n (%)	2	5.0 (5.7)	13.0 (8.5)	0.042
	3	81.0 (93.1)	127.0 (83.0)	
	4	1.0 (1.1)	13.0 (8.5)	
Anesthesia n (%)	General	2.0 (2.3)	6.0 (3.9)	0.786
	Epidural+Spinal	71.0 (81.6)	124.0 (81.0)	
	Spinal	14.0 (16.1)	23.0 (15.0)	
LOS (Day) Median (min-max)		7.0 (4.0-22.0)	7.0 (4.0-22.0)	0.309
Reoperation n (%)		6.0 (6.9)	21.0 (13.7)	0.108
Mortality n (%)		11.0 (12.6)	39.0 (25.5)	0.018

BMI, body mass index; CCS, Charlson comorbidity score; CFF, collum femoris fracture; ITF, intertrochanteric fracture; DHS, dynamic hip screw; PFN, proximal femoral nail; LOS, length of hospital stay; ASA, American Society of Anesthesiologists the normal serum albumin group (2 each with infection, dislocation, and deep wound infection) and 21 patients in the hypoalbuminemia group (3, 2, and 16 with dislocation, fracture, and deep wound infection, respectively) were re-operated on within 90 days of their initial surgery. Patients who required reoperation had lower mean albumin levels and showed a higher likelihood to have lymphocyte levels above 1500 cells/ mm^3 than patients who did not require additional surgery ($p = 0.007$, $p = 0.048$, respectively). Patients with an ASA score of 4 points had a high rate of reoperation ($p = 0.009$).

Through a Univariate Logistic Regression analysis, an increase in albumin levels was seen to lead to a lower risk of re-operation; in contrast, an increase in the ASA score was associated with an increase in the risk of re-operation ($p = 0.004$, $p = 0.002$, respectively). In the Univariate analysis, the ASA score and albumin value were found to be significant statistical factors in the prediction of re-operation in the model formed from variables detected p 0.250 ($p = 0.013$, $p = 0.039$, respectively) (Table 2).

Patients who died were significantly older than those who survived ($p = 0.003$). The mean albumin

Table 2. Factors affecting reoperation

		Reoperation		
		No	**Yes**	***p***
Sex n (%)	Male	73.0 (34.3)	7.0 (25.09)	0.386
	Female	140.0 (65.7)	20.0 (74.1)	
Age Median (min-max)		81.0 (68.0-97.0)	80.0 (75.0-93.0)	0.683
Obesity, kg/m^2 n (%)	BMI <30.0	174.0 (81.7)	25.0 (92.6)	0.186
	BMI ≥30.0	39.0 (18.3)	2.0 (7.4)	
Albumin Median (min-max)		3,2 (2.3-4.6)	3.0 (2.2-3.7)	0.007
Albumin n (%)	≥3.5 g/dL	81.0 (38.0)	6.0 (22.2)	0.108
	<3.5 g/dL	132.0 (62.0)	21.0 (77.8)	
Hemoglobin Median (min-max)		10.8 (7.0-15.7)	10.5 (7.5-16.7)	0.626
Lymphocyte n (%)	≥1500 cells/mm^3	100.0 (47.4)	7.0 (26.9)	0.048
	<1500 cells/mm^3	111.0 (52.6)	19.0 (73,1)	
Functional status n (%)	Totally dependent	31.0 (14.6)	6.0 (22,2)	0.151
	Partially dependent	69.0 (32.4)	12.0 (44.4)	
	Independent	113.0 (53.1)	9.0 (33.3)	
CCS Median (IQR)		8.0 (4.0-13.0)	8.0 (4.0-13.0)	0.155
Diagnosis n (%)	CFF	81.0 (38.0)	10.0 (37.0)	0.920
	ITK	132.0 (62.0)	17.0 (63.0)	
Surgery performed n (%)	DHS	13.0 (6.1)	2.0 (7.4)	0.965
	Hemiarthroplasty	81.0 (38.0)	10.0 (37.0)	
	PFN	119.0 (55.9)	15.0 (55.6)	
ASA Score n (%)	2	18.0 (8.5)	0.0 (0.0)	0.009
	3	186.0 (87.3)	22.0 (81.5)	
	4	9.0 (4.2)	5.0 (18.5)	
Anesthesia n (%)	General	7.0 (3.3)	1.0 (3.7)	0.432
	Epidural+Spinal	175.0 (82.2)	20.0 (74.1)	
	Spinal	31.0 (14.6)	6.0 (22.2)	

BMI, body mass index; CCS, Charlson comorbidity score; CFF, collum femoris fracture; ITF, intertrochanteric fracture; DHS, dynamic hip screw; PFN, proximal femoral nail; ASA, American Society of Anesthesiologists and hemoglobin levels were significantly lower among patients who died than among surviving patients (p 0.001, p = 0.037, respectively). In univariate logistic regression analysis, an increase in age of 1 year, albumin level of <3.5 g/dL, and lymphocyte count <1500 cells/mm3 were associated with increased mortality rate (p = 0.012, p = 0.004, p = 0.002, respectively) (Table 3).

Discussion

At the time of writing, there is no consensus on guidelines for the diagnosis of protein-energy malnutrition. Malnutrition has been previously defined using serologic laboratory values, anthropometric measurements and standardized nutrition scoring tools (13). A previous study examined the prevalence

Table 3. Factors affecting mortality

		Mortality		
		Alive	**Dead**	***p***
Sex n (%)	Male	67.0 (35.3)	13.0 (26.0)	0.216
	Female	123.0 (64.7)	37.0 (74.0)	
Age Median (min-max)		80.0 (75.0-96.0)	85.5 (68.0-97.0)	0.003
BMI Median (min-max)		25.3 (16.0-42.5)	22.9 (17.0-32.0)	0.012
Obesity, kg/m^2 n (%)	BMI <30	153.0 (80.5)	46.0 (92.0)	0.055
	BMI ≥30	37.0 (19.5)	4.0 (8.0)	
Albumin Median (min-max)		3.3 (2.2-4.6)	3.0 (2.3-3.8)	<0.001
Albumin n (%)	≥3.5 g/dL	76.0 (40.0)	11.0 (22.0)	0.018
	<3.5 g/dL	114.0 (60.0)	39.0 (78.0)	
Hemoglobin Median (min-max)		10.9 (7.2-16.7)	10.25 (7.0-13.5)	0.037
Lymphocyte Median (min-max)		1.40 (0.35-4.25)	1.21 (0.47-3.11)	0.021
Lymphocyte n (%)	≥1500	92.0 (49.2)	15.0 (30.0)	0.015
	<1500	95.0 (50.8)	35.0 (70.0)	
Functional status n (%)	1	25.0 (13.2)	12.0 (24.0)	0.067
	2	62.0 (32.6)	19.0 (38.0)	
	3	103.0 (54.2)	19.0 (38.0)	
Charlson comorbidity score Median (IQR)		8.0 (4.0-13.0)	8.0 (4.0-13.0)	0.324
Diagnosis n (%)	CFF	75.0 (39.5)	16.0 (32.0)	0.332
	ITK	115.0 (60.5)	34.0 (68.0)	
Surgery performed n (%)	DHS	7.0 (3.7)	8.0 (16.0)	0.006
	Hemiarthroplasty	75.0 (39.5)	16.0 (32.0)	
	PFN	108.0 (56.8)	26.0 (52.0)	
ASA Score n (%)	2	15.0 (7.9)	3.0 (6.0)	0.337
	3	166.0 (87.4)	42.0 (84.0)	
	4	9.0 (4.7)	5.0 (10.0)	
Anesthesia n (%)	General	5.0 (2.6)	3.0 (6.0)	0.401
	Epidural+Spinal	154.0 (81.1)	41.0 (82.0)	
	Spinal	31.0 (16.3)	6.0 (12.0)	
LOS (Day) Median (min-max)		7.0 (4.0-22.0)	8.0 (4.0-22.0)	0.019

BMI, body mass index; CCS, Charlson comorbidity score; CFF, collum femoris fracture; ITF, intertrochanteric fracture; DHS, dynamic hip screw; PFN, proximal femoral nail; LOS, length of hospital stay; ASA, American Society of Anesthesiologists of malnutrition among patients with HFs reported at a rate of 13-55%, depending on the diagnostic instrument used (14). The most common serology-based definitions of malnutrition are total lymphocyte count of <1,500 cells/mm^3 and a serum albumin concentration of <3.5 g/dL (6,10,13,15).

In the present study, the prevalence of hypoalbuminemia in a companion of older adults with HF was 63.7%. This group of patients was at increased risk of mortality and re-operation due to post-operative complications. Previously, different rates of hypoalbuminemia have been reported among patients with HF; in comparison, the present rate is high. Koval et al. (2) in their retrospective study, reviewed 490 patients with hip fracture and found that 18% of patients had hypoalbuminemia (16). Newman et al. reported that the incidence as 34% in 1667 HF patients (10). Bohl et al. found that the prevalence of hypoalbuminemia was 45.9% in their study of 17.651 patients (17). One of the possible reasons for the present rate being higher than those previously reported is that this study included patients aged 75 years and above, with the average age of 80 years. In fact, previous studies have shown a direct relationship between the mean age of a study population and the observed rate of hypoalbuminemia (4,6,10,18).

Consistent with previous studies, this study shows that patients with hypoalbuminemia and HF were likely to be older and have higher CCI and ASA scores than did their counterparts with normal serum album levels. This can be explained by age-related physiological, pathological and socio-economic changes (18). The association of malnutrition and lower functioning has been discussed at length in the past few years. In their study of more than 10,000 elderly people, Guigoz et al. found a prevalence of malnutrition in 1%-5% of elderly people (19). In another study, malnutrition was connected to lower cognitive and physical function during the rehabilitation of geriatric patients (20). The association between preoperative albumin levels and outcomes of HF surgery is well established (4,13,21-28). Three previous studies have used the combination of pre-operative albumin levels and total lymphocyte count as indicators of nutritional status, showing a strong association between these parameters and postoperative outcomes (26,27,28). Chung et al. evaluated postoperative complications in two groups as major and minor, and showed their relationship with the severity of hypoalbuminemia in a study of 12373 patients. The authors found that the rates of both major and minor complications increased in direct proportion to a decrease in albumin levels (4). In our study, we evaluated only serious orthopedic complications that required re-operation. Alongside hypoalbuminemia, an increase 3 in the ASA score and lymphocyte count of <1500 cells/mm^3 were associated with increased reoperation rate. Hypoalbuminemia has been previously associated with increased mortality rate after HF surgery (29-31). O'Daly et al. evaluated 415 HF patients, showing nutritional status and serum albumin levels to be independently associated with mortality risk in these patients (32). In our study, alongside hypoalbuminemia, an increase in age by 1 year and lymphocyte count of <1500 cells/mm^3 were associated with an increased mortality rate. There are several limitations to our study, including its retrospective design. In addition, although serum albumin level was used to determine nutritional status, it is not the most sensitive marker. Nevertheless, the present study did not involve other laboratory measurements, for example, serum transferrin, muscle circumference measurements, or other nutritional indices (33). Concurrently, the strength of our study relies on accounting for three different surgical options for treating HF, the most used methods in the treatment of most hip fractures.

The prevalence of malnutrition in patients with HF remains high. In the present study, the hypoalbuminemia and lymphocyte count of <1500 cells/mm^3 was associated with increased rates of post-operative mortality and complications that required re-operation within 3 months of the index surgery. Based on our findings, we propose that the assessment of hypoalbuminemia and total lymphocyte count become part of the standard pre-operative evaluation of older adult patients admitted for HF surgery. Given the high occurrence of malnutrition and its impact on outcomes, prevention and early intervention are essential. Further, diagnosis and treatment of malnutrition prior to surgery may decrease surgical costs and the rate of post-operative complications. As HF surgery tends to be performed as part of emergency care, it precludes pre-operative correction of malnutrition, suggesting that albumin levels should be addressed as soon as possible post-operatively.

Conclusion

- Malnutrition is prevalent among patients with hip fractures, and it affects postoperative outcomes.
- Albumin levels and lymphocyte count may be used as measures of malnutrition and should be included in pre-surgical assessment of patients.
- Treatment of malnutrition may improve the outcomes of patients with hip fractures, reducing the associated socio-economic cost.

Ethics Committee Approval: Ethics committee approval was received for this study from the Committee of Sakarya University Training and Research Hospital (number: 2020-604927).

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