# Association of preoperative C-reactive protein to albumin ratio and mortality in elderly patients with hip fractures: A cross-sectional study

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# ABSTRACT

**BACKGROUND:** Hip fractures in the elderly have a significant impact, both in terms of human suffering and healthcare costs. Little is known about preoperative markers that may predict mortality following geriatric hip fracture surgery. This study aimed to investigate potential risk factors, including the C-reactive protein to albumin ratio (CAR), for mortality in elderly patients undergoing surgery for hip fracture.

**METHODS:** A total of 180 elderly patients with hip fractures were included in this cross-sectional study. The patients were divided into two groups: the survival group and the deceased group. Serum levels of C-reactive protein (CRP) and albumin, as well as the CAR, were compared between the two groups to determine whether CAR is a predictor of mortality in elderly patients undergoing hip fracture surgery. The Mini Nutritional Assessment-Short Form was used to evaluate the nutrition status of the patients.

**RESULTS:** The mean age of the 180 participants was 78 years, and 53.3% were female. A statistically significant difference was observed between the two groups in terms of the duration of hospital and intensive care unit stay (p<0.05). According to the receiver operating characteristic (ROC) analysis, with a cutoff value of >0.15, CAR could predict mortality after geriatric hip fracture surgery with a sensitivity of 74% and a specificity of 53%. The area under the ROC curve (AUC) for CAR was 0.67 (95% confidence interval [CI]: 0.57-0.76, p<0.001). CAR and the time between fracture and surgery were found to be independent predictors of mortality (p=0.003, odds ratio [OR]=1.37 and p=0.044, OR=1.33, respectively).

**CONCLUSION:** An elevated preoperative CAR is associated with a significantly increased risk of mortality in elderly patients undergoing hip fracture surgery. Additionally, a shorter time to surgery was associated with lower mortality in these patients.

Keywords: C-reactive protein (CRP) to albumin ratio; elderly patients; hip fracture; Mini Nutritional Assessment-Short Form; mortality.

# INTRODUCTION

Geriatric hip fractures are a significant public health issue that has become an epidemic in recent years. The current increase in life expectancy, coupled with a decline in bone quality, has contributed to a rise in geriatric hip fractures. While approximately 1.6 million hip fractures occurred annually in the 2000s, this number is projected to reach 6.3 million by 2050.<sup>[1]</sup> Hip fracture surgery in the elderly carries substantial risk and is prone to numerous complications. Following hip fracture surgeries in patients over the age of 65, mortality rates of 10% within one month and between 8% and 36% within one year have been observed.<sup>[2,3]</sup> The primary factors influencing mortality include advanced age, the American Society of Anesthesiologists (ASA) score, dementia, anemia, time to surgery, and the surgical procedure. Furthermore, the incidence

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of postoperative lung and heart failure complications increases mortality.<sup>[3]</sup> Over the past two decades, the most significant factors contributing to the reduction in mortality from hip fractures have been standardized care protocols and the early performance of surgeries in conjunction with established algorithms.<sup>[4]</sup>

Serum C-reactive protein (CRP) is synthesized in the liver and serves as a prognostic factor in the inflammatory pathway.<sup>[5]</sup> Malnutrition is a critical geriatric syndrome that can lead to increased mortality and rehabilitation problems in patients with hip fractures during the geriatric period.<sup>[1]</sup> While serum albumin provides important information about nutritional status and liver function, impaired albumin levels have been associated with increased postoperative complications.<sup>[6]</sup> Serum albumin levels are considered a prognostic factor in geriatric hip fractures, while CRP levels are regarded as a prognostic indicator for survival following hip fractures.<sup>[7,8]</sup> In previous studies, advanced age, cardiovascular disease, respiratory disease, and a history of stroke were identified as risk factors for postoperative complications.<sup>[9]</sup>

While it is known that preoperative CRP and albumin levels influence mortality in the postoperative period in geriatric patients with hip fractures, studies evaluating the CRP and albumin ratio in relation to prognosis have only recently emerged, yet they are limited in number. Furthermore, these studies have not thoroughly examined nutritional status, anemia, and other laboratory parameters that may affect mortality following hip fractures.<sup>[10-13]</sup>

In our study, we aimed to assess the impact of the preoperative CRP and albumin ratio on the length of hospitalization, duration of stay in intensive care, and mortality in the geriatric population after hip fracture surgery, while also identifying additional risk factors.

# MATERIALS AND METHODS

Our study was designed as a cross-sectional study. Ethical approval was obtained from the Local Ethics Committee (2022/223). The study sample comprised 180 patients who met the inclusion and exclusion criteria. Patients over 65 years of age with intracapsular or extracapsular proximal femur fractures, who were hospitalized in the orthopedic ward between January 2020 and January 2022, were included in this cross-sectional study. Subtrochanteric and diaphyseal femur fractures were excluded. Fracture classification was performed using the AO Foundation/Orthopedic Trauma Association (AO/OTA) classification. Patients were followed up for at least one year or until death. Mortality data were retrieved from the National Death Notification System. Inclusion criteria included patients over 65 years old with proximal femur fractures caused by low-energy trauma. Exclusion criteria included patients whose medical records could not be fully accessed, those followed for less than one year, patients treated for hypoalbuminemia, patients with cancer or severe inflammatory diseases, those who developed bacterial infection, sepsis, or systemic infection during hospitalization, patients with liver diseases that impair liver function, and patients with pathological fractures.

Two types of surgery were performed on the patients. Patients with intracapsular proximal femur fractures (AO/ OTA classification 31B1.2, 31B1.3, 31B2.1, 31B2.2, 31B2.3) underwent bipolar hemiarthroplasty, while patients with extracapsular proximal femur fractures (AO/OTA classification 31A1.2, 31A1.3, 31A2.2, 31A2.3) were treated with a short proximal femoral nail (PFN) (Fig. 1).

### **Data Collection**

In the preoperative period, data were collected on patient age, gender, body mass index (BMI), the Mini Nutritional Assessment-Short Form (MNA-SF), and preoperative comorbidities such as diabetes, hypertension, coronary artery disease, asthma, heart failure, kidney failure, chronic obstructive pulmonary disease (COPD), dementia, and cerebrovascular disease. Additionally, the number of days from fracture to surgery was recorded. Operation-related data included the duration of surgery, type of surgical procedure, and the need for blood transfusion. In the postoperative period, data were collected on postoperative complications, length of stay in the intensive care unit, total hospital stay, and mortality during follow-up after surgery.

#### Mini Nutritional Assessment-Short Form (MNA-SF)

The short form of the MNA test, consisting of six screening questions that provide quick results, was used in this study. Scores of 0-7 indicated malnutrition, 8-11 indicated risk of malnutrition, and scores of 12 or higher indicated normal nutrition.<sup>[14,15]</sup>

#### Laboratory Tests

Fasting peripheral venous blood samples (5 mL) were obtained preoperatively. Complete blood counts including hemoglobin, white blood cells, and platelets, as well as biochemical tests such as urea, creatinine, aspartate aminotransferase (AST), and alanine aminotransferase (ALT), were performed preoperatively using an automatic blood analyzer in the hospital laboratory. Blood samples were centrifuged at 3000 rpm for 15 minutes to collect serum. CRP and albumin levels were measured using specific enzyme-linked immunosorbent assay (ELISA) kits. The CRP/albumin ratio (CAR) was calculated as the preoperative CRP (mg/L) divided by the preoperative albumin (g/dL).

#### **Statistical Analysis**

The distribution of normality was checked using the Shapiro-Wilk test. The Mann-Whitney U test was used to compare two independent groups of variables with a non-normal distribution, while the Chi-squared test was used to assess relationships between categorical variables. Potential confounders affecting mortality-such as age, gender, MNA score, comorbidities, time between fracture and surgery, duration of intensive care unit stay, duration of hospital stay, and the CRP/albumin ratio-were evaluated, and those with a p value <0.2 were included in the multivariate logistic regression analysis. Statistical analysis was performed using SPSS for Windows, version 22.0 (IBM Corp., Armonk, New York, USA). A p value of less than 0.05 was considered statistically significant.

# RESULTS

Of the 180 patients included in the study, 96 (53.7%) were female and 84 (46.7%) were male. The median (interquartile range) age was 78 (14) years, the mean body mass index (BMI) was 27.0 (4.9), the median time between fracture and surgery was 2 (2) days, the median duration of surgery was 90 (35) minutes, the median length of stay in the intensive care unit was 2 (4) days, and the median length of hospitalization was 7.5 (6) days.

	Survival Group (n=145)	Deceased Group (n=35)	р	Total (n=180)
Gender				
Female	75 (51.7%)	21 (60.0%)	0.378	96 (53.3%)
Male	70 (48.3%)	14 (40.0%)		84 (46.7%)
Age (years)#	77 (16)	81 (14)	0.030*	78 (14)
3MI (kg/m²)#				
	27.1 (4.6)	26.1 (5.2)	0.711	27.0 (4.9)
Number of comorbidities#	I (2)	2 (2)	0.124	1(1)
Comorbidities				
Hypertension	75 (51.7%)	20 (57.1%)	0.564	95 (52.8%)
Diabetes mellitus	55 (37.9%)	14 (40.0%)	0.821	69 (38.3%)
Asthma/COPD	22 (15.2%)	10 (28.6%)	0.063	32 (17.8%)
Congestive heart failure	20 (13.8%)	7 (20.0%)	0.356	27 (15.0%)
Dementia	18 (12.4%)	8 (22.9%)	0.115	26 (14.4%)
Coronary artery disease	17 (11.7%)	3 (8.6%)	0.594	20 (11.1%)
Cerebrovascular disease	7 (4.8%)	2 (5.7%)	0.829	9 (5.0%)
Smoker	(7.6%)	4 (11.4%)	0.460	15 (8.3%)
Time between fracture and surgery (days)#	2 (2)	3 (1)	0.003*	2 (2)
Duration of surgery (minutes)#	90 (35)	90 (58)	0.463	90 (35)
Duration of intensive care unit stay (days)#	2 (3)	4 (4)	0.000*	2 (4)
Duration of hospital stay (days)#	7 (5)	10 (6)	0.001*	7.5 (6)
Surgical method				
PFN	102 (70.3%)	27 (77.1%)	0.423	129 (71.7%)
Hemiarthroplasty	43 (29.7%)	8 (22.9%)		51 (28.3%)
MNA score <sup>#</sup>	(4)	10 (4)	0.432	(4)
CRP (mg/L)#	4.1 (11.4)	18.8 (50.2)	0.002*	6.2 (17.6)
Albumin (g/dL)#	34.0 (7.0)	31.0 (6.9)	0.003*	34.0 (7.3)
CAR <sup>#</sup>	0.12 (0.4)	0.52 (1.6)	0.001*	0.18 (0.6)
WBC <sup>#</sup>	10,000 (5,475)	I I,400 (6,440)	0.016*	10,145 (5,740)
Hemoglobin (g/dL)#	12.0 (2.9)	12.0 (2.1)	0.813	12.0 (2.4)
Platelet#	255,000 (103,500)	245,000 (161,000)	0.132	255,000 (125,500
Creatinine (mg/dL)#	0.90 (0.30)	0.90 (0.43)	0.685	0.90 (0.30)

\*p≤0.05. #Data are presented as median (interquartile range); COPD: Chronic Obstructive Pulmonary Disease; BMI: Body Mass Index; PFN: Proximal Femoral Nail; MNA: Mini Nutritional Assessment-Short Form; CRP: C-Reactive Protein; CAR: CRP/Albumin Ratio; WBC: White Blood Cells.

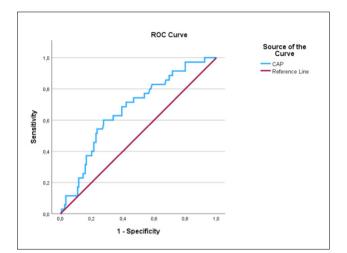


Figure 2. Receiver operating characteristic (ROC) curve of mortality

Table 2. Multivariate logistic regression analysis results of independent variables for mortality					
Mortality Risk					
Variable	OR [95% CI]	p value			
Age	1.04 [0.99-1.10]	0.103			
Time between fracture and surge	ry 1.33 [1.01-1.75]	0.044*			
Duration of intensive care unit sta	ay 1.07 [0.95-1.20]	0.236			
Duration of hospital stay	1.02 [0.96-1.09]	0.521			
CRP/Albumin Ratio	1.37 [1.03-1.84]	0.003*			

\*p<0.05 according to multivariate binary logistic regression analysis. Cl: Confidence Interval; OR: Odds Ratio.

Gender, number of comorbidities, and type of operation showed statistically similar distributions between the survival and deceased groups (p>0.05). Considering the type of surgery, 70.3% of patients in the survival group were treated with a PFN, while 29.7% underwent cementless bipolar hemiarthroplasty. This ratio was the same among patients who died. Additionally, BMI, duration of surgery, and length of hospitalization did not differ statistically between the groups (p>0.05).

On the other hand, a statistically significant difference was found between the two groups in terms of the timing of surgery and the length of stay in the intensive care unit (p<0.05). Patients who died had a longer wait before undergoing surgery and stayed in the intensive care unit longer. The patients in the deceased group were operated on an average of three days after the fracture, while those in the survival group were operated on after an average of two days. The patients in the deceased group spent an average of four days in the intensive care unit, whereas the survival group spent an average of two days in the intensive care unit.

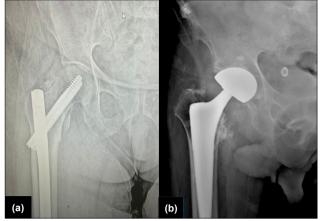


Figure 1. (a) Extracapsular proximal femur fracture treated with PFN, (b) Intracapsuler femur fracture treated with bipolar prothesis.

MNA-SF scores, white blood cell counts, hemoglobin, platelet counts, and creatinine values did not show statistically significant differences according to survival status (p>0.05). However, CRP, albumin, and the CAR showed statistically significant differences according to survival status (p<0.05). CRP and CAR values were higher in deceased patients, while albumin levels were lower. The mean preoperative CRP levels in the survival group were 4.1 mg/L, compared to 18.8 mg/L in the deceased group. The mean CAR was 0.12 in the survival group and 0.52 in the deceased group in the preoperative period (Table 1).

According to the receiver operating characteristic (ROC) analysis, when the cutoff value for CAR was set at >0.15, CAR could predict mortality after geriatric hip fracture surgery with a sensitivity of 74% and specificity of 53%. The area under the ROC curve (AUC) for CAR was 0.67 (95% confidence interval [CI]: 0.57-0.76, p<0.001) (Fig. 2).

CAR and the time between fracture and surgery were found to be independent predictors of mortality according to multivariate logistic regression analysis (p=0.003, odds ratio [OR]=1.37 and p=0.044, OR=1.33, respectively) (Table 2).

# DISCUSSION

This study demonstrated that the preoperative CAR and the time from fracture to surgery are significant prognostic factors for survival in older adults undergoing hip fracture surgery. Linear regression analysis identified CAR as a potential risk factor for mortality in this population. Given the poor prognosis of geriatric hip fracture, biomarkers play an important role in the clinical management of these patients.

The current study reported a mortality rate of 19% following surgical treatment for geriatric hip fractures, which is at the lower end of the values found in the literature.<sup>[16,17]</sup> Some studies have raised skepticism regarding the association between early hip fracture surgery and postoperative mortality. <sup>[18,19]</sup> However, our findings indicate a significant association between the time from fracture to surgery and mortality. Patients who died had longer surgery wait times and were more frequently admitted to the postoperative intensive care unit. Similar to our findings, a study by Anthony et al. showed higher mortality in 4,215 hip fracture patients who experienced a surgical delay of more than two days.<sup>[20]</sup> Additionally, a study of older adults in Türkiye found that a delay of more than two day between fracture and surgery was associated with higher mortality rates.<sup>[13]</sup> A meta-analysis also suggested that orthopedic surgery should be performed within two days of the fracture and reported more complications in cases of delay.<sup>[21]</sup>

In our study, the deceased group had significantly higher preoperative serum CRP levels, lower albumin levels, and a higher CAR compared to the survival group. We also found a statistically significant positive correlation between CAR and the length of stay in the intensive care unit. Kim et al. identified elevated preoperative CRP levels as a primary risk factor for mortality following total hip arthroplasty in older patients.<sup>[12]</sup> Several studies have utilized serum albumin as a prognostic indicator in older adults with hip fractures.<sup>[11,22]</sup>

A meta-analysis of 19 studies involving 34,363 older adults confirmed the prognostic value of malnutrition, with albumin and total lymphocyte count serving as proxies for mortality in hip fracture patients. This meta-analysis and systematic review also demonstrated that malnutrition, as classified by the MNA, predicts increased mortality after hip fracture surgery in older adults.<sup>[23]</sup> Additionally, a recent study found that malnutrition is a risk factor for mortality following hip fracture in older adults.<sup>[24]</sup> In our study, malnutrition status was assessed using the MNA-SF, and no statistically significant difference was found between the two groups. This may be due to the small number of patients who died.

The CAR is considered a more accurate indicator of both inflammatory and nutritional status compared to either index alone. Recently, CAR has been investigated as an independent prognostic marker in patients with conditions such as infection and malignancy.<sup>[25,26]</sup> However, few studies have focused on its use in older adults undergoing orthopedic surgery.<sup>[5,27]</sup>

A recent prospective study found that low albumin and high CRP levels in older adults had a direct and significant effect on I-year mortality after hip fracture surgery. However, the study did not determine independent variables affecting mortality risk and preoperative CAR values and nutritional status were not evaluated.<sup>[28]</sup>

A meta-analysis of 33 cohort studies involving 462,699 patients showed that low hemoglobin and chronic renal failure are moderate-quality preoperative predictors of 30-day mortality after hip fracture.<sup>[29]</sup> A recent retrospective study suggested that preoperative CAR can serve as a predictor of I-year mortality in elderly patients with hip fractures. However, the study did not assess patients' nutritional status, which may influence albumin levels.<sup>[10]</sup> Moreover, a recent study demonstrated that CAR was a strong indicator of mortality in older patients who had undergone surgery for hip fracture. However, the evaluation of other factors contributing to postoperative mortality risk, such as malnutrition<sup>[23]</sup> and anemia,<sup>[30]</sup> as well as laboratory parameters like baseline hemoglobin levels<sup>[31]</sup> and creatinine,<sup>[32]</sup> were not mentioned in the study.<sup>[13]</sup>

Our study has some potential limitations. First, it includes a limited number of patients. Second, it was conducted at a single center. Despite these limitations, the study also has notable strengths. First, unlike most studies, only older participants were included. Second, the similarity in age, gender, BMI, MNA results, comorbidities, operation type, and other laboratory measurements (white blood cell [WBC] count, hemoglobin [Hb], serum creatinine) between the survival and deceased groups allowed for a more transparent comparison of CAR values. Third, the preoperative nutritional status of the patients was assessed using the MNA-SF, which is not frequently employed in clinical orthopedic practice. Further studies with larger sample sizes and prospective designs are needed to confirm these preliminary results.

# **CONCLUSION**

In conclusion, our study showed that elevated preoperative CAR is an important risk factor for mortality after geriatric hip fracture surgery. Mortality was found to be higher in elderly patients with hip fractures whose post-traumatic preoperative CAR value was above 0.15. Additionally, the time between fracture and surgery was associated with mortality in these patients. These preoperative predictors can be used to better inform patients about their prognosis, contributing to improved shared decision-making in the preoperative phase.

**Ethics Committee Approval:** This study was approved by the Gaziantep University Hospital Ethics Committee (Date: 17.08.2022, Decision No: 2022/223).

Peer-review: Externally peer-reviewed.

Authorship Contributions: Concept: E.M.E., O.K.; Design: O.K.; Supervision: E.M.E., O.K.; Resource: E.M.E., O.K.; Materials: E.M.E., O.K.; Data collection and/or processing: E.M.E., O.K.; Analysis and/or interpretation: E.M.E., O.K.; Literature search: E.M.E., O.K.; Writing: E.M.E., O.K.; Critical reviews: E.M.E., O.K.

Conflict of Interest: None declared.

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# ORİJİNAL ÇALIŞMA - ÖZ

# Geriatrik kalça kırıklarında preoperatif C-reaktif protein-albümin oranının mortaliteyle ilişkisi: Kesitsel çalışma

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AMAÇ: Geriatrik dönem kalça kırıklarının hem hasta açısından hem de maliyet üzerine etkisi büyüktür. Geriatrik kalça kırığı cerrahisi sonrası mortaliteyi öngörebilecek preoperatif belirteçler hakkında az bilgi mevcuttur. Bu çalışma, kalça kırığı için cerrahi geçiren yaşlı hastalarda mortalite için C-reaktif protein/albümin oranı (CAR) dahil olmak üzere potansiyel risk faktörlerini araştırmayı amaçlamıştır.

GEREÇ VE YÖNTEM: Bu kesitsel çalışmaya 180 yaşlı kalça kırığı hastası dahil edildi. Hastalar, hayatta kalanlar ve ölenler olmak üzere iki gruba ayrıldı. Serum CRP ve albümin düzeyleri, CAR ile birlikte, bu iki grup arasında CAR'ın yaşlı yetişkinlerde kalça kırığı ameliyatı geçiren hastalarda mortaliteyi öngörüp öngöremeyeceğini belirlemek için karşılaştırıldı. Hastaların beslenme durumunu değerlendirmek için Mini Beslenme Değerlendirme-Kısa Formu kullanıldı.

BULGULAR: 180 katılımcının ortalama yaşı 78 idi ve %53.3'ü kadındı. Hastane ve yoğun bakım ünitesinde kalış süresi açısından bu iki grup arasında istatistiksel olarak anlamlı fark bulundu (p<0.05). Alıcı işletim karakteristiği (ROC) analizine göre, CAR (C-reaktif protein/albumin oranı) için kestirim değeri >0.15 olarak belirlendiğinde, CAR, geriatrik kalça kırığı ameliyatı sonrası mortaliteyi %74 duyarlılık ve %53 özgüllük ile öngördüğü görüldü. CAR'ın ROC eğrisi altında kalan alan (AUC) değeri 0.67 idi (95% CI: 0.57-0.76, p<0.001). CAR ve kırık ile cerrahi arasındaki zamanın mortalite için bağımsız bir değişken olduğu bulundu (sırasıyla, p=0.003, OR=1.37 ve p=0.044, OR=1.33).

SONUÇ: Ameliyat öncesi dönemde bakılan CAR düzeyi yüksek olan ve kalça kırığı nedeniyle operasyon geçiren yaşlı hastalarda ölüm riskinde anlamlı bir artış olduğu görüldü. Ayrıca, kırıktan cerrahiye kadar geçen sürenin kısa olması bu hastalarda daha düşük mortalite ile ilişkili olarak bulundu.

Anahtar sözcükler: CRP/albümin oranı; kalça kırığı; mini beslenme değerlendirme-kısa form; mortalite; yaşlı yetişkinler.

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