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C-Reactive Protein to Albumin Ratio Predicts In-hospital Mortality in Patients with Acute Heart Failure

Akut Kalp Yetersizliği Olan Hastalarda C-reaktif Protein/Albümin Oranı Hastane İçi Mortaliteyi Öngörür

ORIGINAL ARTICLE
KLINIK ÇALIŞMA

ABSTRACT

Objective: Acute heart failure remains at high risk of mortality despite recent advances in the management and treatment of heart failure. Recently, C-reactive protein to albumin ratio has been shown to predict all-cause mortality in heart failure with reduced ejection fraction. The association between C-reactive protein to albumin ratio and in-hospital mortality in patients with acute heart failure regardless of the left ventricular ejection fraction remains unknown.

Methods: In this retrospective, single-center cohort study, we included 374 hospitalized patients with acute decompensated heart failure. We calculated C-reactive protein to albumin ratio and evaluated the relationship between the values and in-hospital mortality.

Results: During hospitalization duration of 10 [6-17] days, need for hemodialysis/ultrafiltration, acute ischemic hepatitis, coagulopathy, ventricular tachycardia, invasive mechanical ventilation, and shock were more prevalent in the high C-reactive protein to albumin ratio (≥0.78) group compared to low C-reactive protein to albumin ratio (<0.78) group. Mortality was higher in the high C-reactive protein to albumin ratio group in comparison to the low C-reactive protein to albumin ratio group (36.7% vs. 12%; $P < 0.001$). C-reactive protein to albumin ratio was independently and significantly associated with in-hospital mortality (hazard ratio=1.69, 95% CI: 1.02-2.82; $P=0.042$) by multivariate Cox proportional hazard analysis. In receiver operating characteristic analysis, C-reactive protein to albumin ratio was able to predict in-hospital mortality (area under the curve value for in-hospital mortality was 0.72; $P < 0.001$).

Conclusion: Admission C-reactive protein to albumin ratio was associated with increased all-cause mortality in hospitalized patients with acute decompensated heart failure.

Keywords: Acute heart failure, albumin, C-reactive protein, C-reactive protein to albumin ratio, mortality

ÖZET

Amaç: Akut kalp yetersizliği, kalp yetersizliğinin yönetimi ve tedavisindeki son gelişmelere rağmen yüksek mortalite ile ilişkilidir. Son zamanlarda, C-reaktif protein/albümin oranının (CAR), düşük ejeksiyon fraksiyonlu kalp yetersizliğinde tüm nedenlere bağlı mortaliteyi öngördüğü gösterilmiştir. Ancak akut kalp yetersizliği olan hastalarda sol ventrikül ejeksiyon fraksiyonuna bakılmaksızın CAR ve hastane içi mortalite arasındaki ilişki bilinmemektedir.

Yöntem: Bu retrospektif, tek merkezli kohort çalışmaya, akut dekompanse kalp yetersizliği ile hastaneye yatan 374 hasta dahil edildi. CAR hesaplandı ve değerler ile hastane içi mortalite arasındaki ilişki değerlendirildi.

Bulgular: Ortalama 10 günlük [6-17] hastane yatışı sırasında; hemodiyaliz/ultrafiltrasyon ihtiyacı, akut iskemik hepatit, koagülopati, ventriküler taşikardi, invaziv mekanik ventilasyon ve şok, düşük CAR (<0,78) grubuna kıyasla yüksek CAR (≥0,78) grubunda daha yaygındı. Yüksek CAR grubunda düşük CAR grubuna göre mortalite daha yüksekti (%36,7 vs %12; $P < 0.001$). Çok değişkenli Cox regresyon analizine göre CAR, hastane içi mortalite ile bağımsız ve anlamlı bir şekilde ilişkiliydi (hazard oranı=1.69; %95 GA: 1.02-2.82; $P=0.042$). "Receiver operating characteristic" eğrisi analizine göre CAR, hastane içi mortaliteyi tahmin edebilmiştir (hastane içi mortalite için eğri değerinin altındaki alan 0,72'dir; $P < 0.001$).

Sonuç: Hastaneye yatırılan akut dekompanse kalp yetersizliği tanılı hastaların yatış anındaki CAR değeri, hastane içi tüm nedenlere bağlı mortalite ile ilişkilendirilmiştir.

Anahtar kelimeler: Akut kalp yetersizliği, C-reaktif protein albümin oranı, mortalite

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Acute heart failure (AHF) is a common cardiovascular syndrome with the potential to deteriorate rapidly and was associated with mortality and rehospitalization.[1] Despite recent advancements in the management and treatment of patients with chronic heart failure, both in-hospital mortality (10.7% in the Acute Heart Failure Global Survey of Standard Treatment) and 1-year mortality (17.4% in the European Society of Cardiology Heart Failure Pilot Study) were reported to be high.[2,3] In-hospital mortality was 3.4% in a Turkish registry—a lower rate in comparison to the aforementioned registries.[4] The authors stated that the lower mean age of the cohort may have indicated a lower-risk cohort. Nevertheless, the need to initially stratify AHF patients to their risk remains, which eventually affects the pace of the interventions to improve patient outcomes. Risk stratification models in AHF were developed,[5,6] but the large number, around 7-10, of average clinical parameters included in the models limit the usefulness in daily practice. Simpler risk scores consisting of a few parameters may aid in the prediction of clinical course in these patients.

Recently, C-reactive protein to albumin ratio (CAR) has been evaluated in several clinical scenarios for predicting prognosis: osteosarcoma,[7] colorectal surgery,[8] and acute coronary syndrome.[9] Its association with proinflammatory state and nutritional condition is hypothesized. C-reactive protein to albumin ratio may have a role in prognostication in AHF because the inflammation was established as the cornerstone for the pathophysiology of heart failure.[10] Moreover, malnutrition was associated with worse outcomes in AHF.[11] Indeed, Çinier et al[12] found out that elevated CAR increased the risk of long-term all-cause mortality among heart failure patients with reduced ejection fraction (HFrEF) who underwent implantation of implantable cardioverter defibrillator. We aimed to determine if baseline CAR predicts in-hospital mortality in patients with AHF.

Material and Methods

Study Design

The retrospective cohort study was approved by the local ethic committee (number: 2022.06.214, day: 30.06.2022) and the Istanbul Provincial Health Directorate. Adult inpatients (≥ 18 years old) who were hospitalized between June 2020 and April 2022 in the coronary care unit in our hospital for acute heart failure (AHF), which was diagnosed in accordance with the 2021 European Society of Cardiology Guidelines, were included.[13] We excluded the patients with (a) active Covid-19, (b) acute coronary syndrome, (c) known malignancy, (d) missing value of C-reactive protein (CRP) or serum albumin concentration, (e) history of transfer to another department or hospital. The primary endpoint for the study was all-cause in-hospital mortality.

Demographic information, comorbidities, vital signs, physical examination findings, electrocardiographic and echocardiographic parameters, laboratory results, medical therapy, interventions, complications, and outcomes of the patients were obtained from the hospital electronic records.

Laboratory results obtained 24 hours after admission to the emergency department and/or coronary care unit were analyzed. Serum CRP level was analyzed with nephelometric method (UniCel DxC 800 System; Beckman Coulter Inc), and serum albumin concentration was analyzed by using the automatic photometry commercial kits (Abbott C8000i). C-reactive protein to albumin ratio (mg/g) was calculated as the ratio of CRP (mg/dL) to the serum albumin (g/dL) concentration.

Statistical Analysis

We divided the study population into 2 groups: low CAR (< 0.78) and high CAR (≥ 0.78) group. We established this cut-off point via receiver operating characteristic (ROC) curves shown later. Continuous data are expressed as the mean (SD) or median (interquartile range) values, whereas categorical data are described as proportions and are evaluated via the chi-square test. Independent predictors of in-hospital mortality were determined by the Cox proportional hazard analysis. The predictive accuracy and performance of the CAR, CRP, and serum albumin were calculated with ROC curves for mortality. Kaplan–Meier method was used for comparing the survival times of patients during hospitalization. Long-rank test was performed for the comparison of groups.

Univariate analysis was calculated using single-factor regression analysis to detect the potential risk factor for in-hospital mortality in AHF. The significant factors ($P < 0.1$) in the univariate analysis were brought into Cox proportional hazard analysis to explore the predictors for mortality in acute heart failure. Data were analyzed using Statistical Package for Social Sciences version 28.0 (IBM). For all the statistical analyses, $P < 0.05$ was considered significant.

Results

Patient Characteristics

Between June 2020 and April 2022, a total of 702 patients were admitted to the coronary care unit in our institution with the diagnosis of AHF. Among them, 137 patients had acute coronary syndrome, 34 patients were found to have Covid-19 infection, 33 had known malignancy, and 124 had a missing value of CRP or serum albumin concentration. These patients were excluded from the study. The remaining 374 patients were included in the study and were divided into 2 groups: high CAR group (n=216) and low CAR group (n=158) (Figure 1).

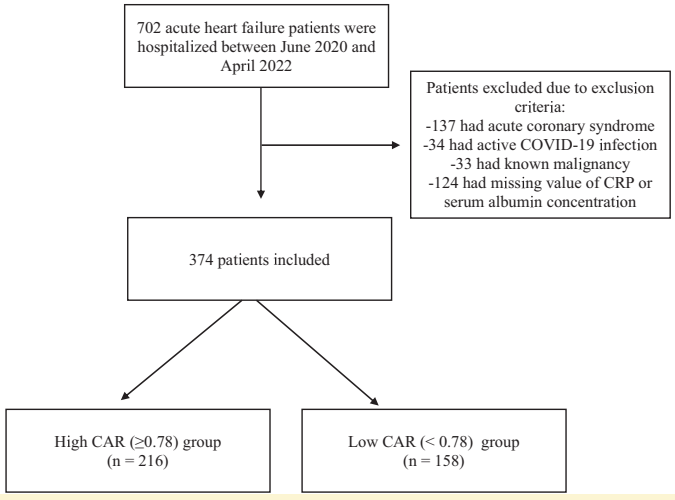

Figure 1. Flowchart demonstrating the design of the study. CAR, C-reactive protein to albumin ratio; CRP, C-reactive protein.

Table 1. Comparison of Demographics, Comorbidities, and Functional Class of the Patients Stratified by C-reactive Protein to albumin Ratio (CAR) at Admission

	All Patients (n=374)	CAR < 0.78 (n=216)	CAR ≥ 0.78 (n=158)	*P*
Age, years	69 (13)	68 (13)	70 (14)	0.302
Male gender	198 (52.9)	102 (47.2)	96 (60.8)	0.010
Hypertension	183 (48.9)	114 (52.9)	77 (49)	0.468
Diabetes mellitus	134 (35.8)	78 (36.2)	56 (35.3)	0.854
Coronary artery disease	212 (56.7)	126 (58.3)	86 (54.4)	0.452
History of valvular intervention	26 (7)	17 (7.9)	9 (5.7)	0.410
Chronic kidney disease	183 (49.6)	100 (46.5)	83 (53.9)	0.162
Cerebrovascular disease	32 (8.6)	13 (6)	19 (12.1)	0.038
History of hospitalization due to heart failure in previous 12 months, n (%)	157 (42.5)	82 (38.3)	75 (48.4)	0.053
NYHA class at the time of admission				0.001
II	31 (8.4)	20 (9.3)	11 (7)	
III	273 (73.6)	172 (80.4)	101 (64.3)	
IV	67 (18.1)	22 (10.3)	45 (28.7)	

NYHA, New York Heart Association.

The mean age of the study population was 69 (13) and it was similar in both high and low CAR groups. However, the male sex was more prevalent in the high CAR group compared to the low CAR group (60.8% vs. 47.2%, *P*=0.010). The prevalence of hypertension, diabetes mellitus, coronary artery disease, chronic kidney disease, and history of hospitalization due to heart failure within 12 months did not differ between groups. Cerebrovascular disease was more frequent in the high CAR group in comparison to the low CAR group (12.1% vs. 6%; *P*=0.038). Baseline functional class III was more prevalent in the low CAR group, whereas

Table 2. Comparison of Vital Signs, Physical Examination Findings, Electrocardiography, and Echocardiography Parameters of the Patients Stratified by CAR at Admission

	All Patients (n=374)	CAR < 0.78 (n=216)	CAR ≥0.78 (n=158)	*P*
Vital signs				
Systolic arterial pressure, mmHg	123 [109-141]	127 [111-146]	119 [100-135]	<0.001
Heart rate, bpm	92 (24)	93 (26)	92 (21)	0.552
Fingertip oxygen saturation, %	96 (4)	96 (4)	95 (5)	0.032
Physical examination				
Pretibial edema	299 (79.9)	175 (81)	124 (78.5)	0.545
Rales	307 (82.5)	172 (80.4)	135 (85.4)	0.203
S3	95 (25.6)	48 (22.4)	47 (29.9)	0.102
Electrocardiographic findings				
Atrial fibrillation	162 (43.3)	98 (45.6)	64 (40.4)	0.341
Left bundle branch block	24 (6.4)	16 (7.4)	8 (5.1)	0.361
Echocardiographic findings				
Groups according to LVEF				0.481
LVEF ≤ 40 %	233 (62.8)	135 (63.1)	98 (62.4)	
LVEF=41–49%	25 (6.7)	17 (7.9)	8 (5.1)	
LVEF ≥ 50%	113 (30.5)	62 (29)	51 (32.5)	
Estimated pulmonary artery systolic pressure, mmHg	47 (13)	47 (13)	49 (14)	0.505
Severe valvular disease	81 (22.6)	52 (24.8)	29 (19.6)	0.250

CAR, c-reactive protein to albumin ratio; LVEF, left ventricular ejection fraction.

Table 3. Comparison of Laboratory Findings at Admission of the Patients Stratified by C-reactive Protein to Albumin Ratio (CAR) at Admission

Laboratory Findings at Admission	All Patients (n=374)	CAR < 0.78 (n=216)	CAR ≥0.78 (n=158)	*P*
Leucocytes/μL	9485 [7390-12 235]	8790 [6875-11 725]	10420 [8095-12 570]	0.001
Lymphocytes/μL	1210 [768-1885]	1315 [830-2048]	1090 [690-1590]	0.002
Neutrophils/μL	6880 [5083-9370]	6300 [4542-8557]	7910 [5695-10 220]	<0.001
Neutrophil-lymphocyte ratio	5.41 [3.26-9.33]	4.50 [2.73-7.65]	6.76 [4.29-14.3]	<0.001
Haemoglobin, g/dL	11.6 (2.5)	11.6 (2.6)	11.3 (2.4)	0.234
C-reactive protein, mg/dL	23 [10-50]	12 [5-20]	58 [36-107]	<0.001
High-sensitivity troponin T, pg/mL	53 [30-103]	47 [27-83]	62 [36-145]	<0.001
N-terminal pro-B-type natriuretic peptide, pg/mL	7541 [3249-17 991]	6037 [2985-14 857]	10 136 [3904-23 084]	0.002
Creatinine, mg/dL	1.3 [1-1.7]	1.3 [1.0-1.8]	1.5 [1.1-2.3]	<0.001
Sodium, mEq/L	137 [134-140]	136 [132-139]	132 [128-136]	<0.001
Potassium, mEq/L	4.6 (0.7)	4.7 (0.7)	4.6 (0.7)	0.323
Alanine aminotransferase, U/L	22 [14-43]	20 [13-37]	24 [15-64]	0.011
Aspartate aminotransferase, U/L	29 [21-49]	27 [19-42]	35 [23-60]	<0.001
Lactate dehydrogenase, U/L	294 [229-357]	289 [215-335]	312 [248-439]	0.010
Albumin, g/dL	3.7 [3.3-4.0]	3.9 [3.5-4.2]	3.3 [2.8-3.7]	<0.001

CAR, C-reactive protein to albumin ratio.

functional class IV was more frequent in the high CAR group (80.4% vs. 64.3%; 10.3% vs. 28.7%, *P*=0.001). Table 1 summarizes the demographics, comorbidities, and functional class of the patients.

Systolic arterial pressure and fingertip oxygen saturation were lower in the high CAR group compared to the low CAR group (119[100-135] vs. 127[111-146]; *P* < 0.001; 95% (5) vs. 96% (4); *P*=0.032). Physical examination findings, electrocardiographic, and echocardiographic parameters did not differ between groups. Heart failure patients with reduced ejection fraction was present in 62.8% of study population, whereas 6.7% had heart failure with mildly reduced ejection fraction and 30.5% had heart failure with preserved ejection fraction. Table 2 demonstrates the comparison of vital signs, physical examination findings, electrocardiography, and echocardiography parameters of the patients.

Comparison of Laboratory Findings at Admission

Table 3 summarized baseline laboratory parameters. Leucocyte count, neutrophil count, neutrophil-lymphocyte ratio, Leucocyte count, neutrophil count, neutrophil - lymphocyte ratio, CRP, high sensitive troponin T, N- terminal pro-B-type natriuretic peptide, creatinine, sodium, alanine transferase, aspartate transferase levels, and lactate dehydrogenase levels were higher in the high CAR group compared with the low CAR group, whereas lym- phocytes and albumin were lower.

Medical Treatment, Interventions, Complications, and Clinical Course

Table 4 shows the medical treatment, intervention, complications, and clinical outcome of the study group. The use of intravenous diuretics, anticoagulants, angiotensin inhibitors, angiotensin receptor blockers, beta-blockers, mineralocorticoid receptor antagonists, ivabradine, digoxin, and intravenous vasodilator agents did not differ between groups. Antiarrhythmics and inotropic agents were more frequently used in the high CAR group in comparison to the low CAR group (25.9% vs. 12.1%; *P*< 0.001; 53.8% vs. 27.1%, *P*< 0.001, respectively).

The median length of stay was longer in the high CAR group than in the low CAR group (11[7-20] vs. 9[6-15]; *P*=0.043). Acute kidney injury/worsening renal functions did not differ between groups. On the other hand, non-invasive mechanical ventilation, need for ultrafiltration/hemodialysis, infection, acute ischemic hepatitis, coagulopathy, ventricular tachycardia, and invasive mechanical ventilation were more prevalent in the high CAR group compared with the low CAR group. In-hospital mortality was higher in the high CAR group in comparison to the low CAR group (Figure 2).

Risk Factors for In-Hospital Mortality

To determine the risk factors for in-hospital mortality in patients with AHF, a univariate analysis with demographic, clinical data, and laboratory findings was performed, showing that age, functional class at admission ≥2, presence of S3, fingertip oxygen saturation, left ventricular ejection fraction, neutrophil-lymphocyte ratio, creatinine ≥ 1.5 mg/dL, lactate dehydrogenase ≥ 280 U/L, and CAR ≥0.78 may be significant factors of mortality (all *P* < 0.1). Multivariate Cox proportional hazard analysis (Table 5) demonstrated that high CAR (≥ 0.78) (hazard ratio, 1.69; 95% CI, 1.2-2.82; *P*=.042) may be associated with increased in-hospital mortality in AHF. We found out that functional class at admission ≥ 2 (hazard ratio, 2.47; 95% CI, 1.59-3.90; *P* < .001) and baseline creatinine level ≥1.5 mg/dL (hazard ratio, 2.13; 95% CI, 1.24-3.67; *P*=.007) may be the most critical risk factors

Table 4. Medical Therapy, Interventions, Complications, and Clinical Outcomes of the Patients Stratified by C-reactive Protein to albumin Ratio (CAR) at Admission

	All Patients (n=374)	CAR <0.78 (n=216)	CAR ≥0.78 (n=158)	*P*
Medical therapy				
Anticoagulants	280 (75.1)	162 (75.3)	118 (74.7)	0.883
Intravenous diuretics	344 (92.2)	200 (93)	144 (91.1)	0.502
ACE-i/ARB	183 (48.9)	119 (55.1)	64 (40.5)	0.684
Beta-blockers	287 (77.2)	168 (78.5)	119 (75.3)	0.469
Mineralocorticoid receptor antagonists	161 (43.2)	101 (47)	60 (38)	0.083
Ivabradine	20 (5.4)	14 (6.5)	6 (3.8)	0.250
Digoxin	86 (23.1)	43 (20)	43 (27.2)	0.102
Antiarrhythmics	67 (18)	26 (12.1)	41 (25.9)	<0.001
Inotropic agents	143 (38.4)	58 (27.1)	85 (53.8)	<0.001
Intravenous vasodilator agents	64 (17.2)	36 (16.7)	28 (17.7)	0.805
Interventions, complications, and clinical outcomes				
Non-invasive mechanical ventilation	66 (17.7)	30 (14)	36 (22.8)	0.027
Acute kidney injury/worsening renal function	279 (75)	160 (74.4)	119 (75.8)	0.762
Ultrafiltration/hemodialysis	32 (8.6)	12 (5.6)	20 (12.7)	0.015
Infection	191 (51.1)	83 (38.4)	108 (68.4)	<0.001
Acute ischemic hepatitis	42 (11.2)	14 (6.5)	28 (17.7)	<0.001
Coagulopathy	47 (12.7)	8 (3.7)	39 (24.8)	<0.001
Ventricular tachycardia	23 (6.1)	8 (3.7)	15 (9.5)	0.021
Invasive mechanical ventilation	75 (20.1)	20 (9.3)	55 (34.8)	<0.001
Shock	93 (25.1)	31 (14.4)	63 (39.9)	<0.001
In-hospital mortality	84 (22.5)	26 (12)	58 (36.7)	<0.001
Median length of stay, days [IQR]	10 [6-17]	9 [6-15]	11 [7-20]	0.043

ACE-i, angiotensin-converting enzyme inhibitor; ARB, angiotensin receptor blocker; IQR, interquartile range.

for mortality in AHF. These effects consisted of the unadjusted and adjusted multivariable models (Table 6).

Receiver operator characteristic analysis comparing the predictive accuracy of CAR, C-reactive protein, and albumin for in-hospital mortality is shown in Figure 3. Based on a 95% CI, the areas under the curve (AUC) for CAR, C-reactive protein, and albumin were 0.72, 0.70, and 0.30, respectively ($P < 0.001$, for all). C-reactive protein to albumin ratio of ≥0.78 was able to predict mortality with a sensitivity of 69% and a specificity of 66%.

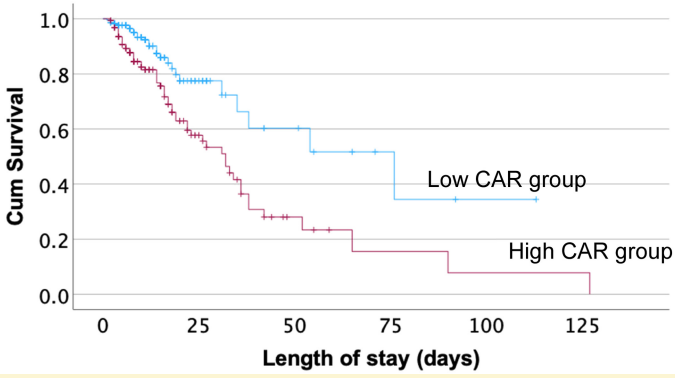

Figure 2. Kaplan–Meier analysis for mortality showing an early divergence in the patients during follow-up. CAR, C-reactive protein to albumin ratio.

Discussion

In this retrospective cohort study of AHF patients, the main findings were as follows: (1) baseline levels of high-sensitivity troponin T and N-terminal pro-B-type natriuretic peptide were higher in the high-CAR (≥ 0.78) group than in the low-CAR (< 0.78) group; (2) need for haemodialysis/ultrafiltration, acute ischaemic hepatitis, coagulopathy, ventricular tachycardia, invasive mechanical ventilation and shock were more frequent in the high CAR group compared to the low CAR group; (3) in-hospital mortality was higher in the high CAR group compared to the low CAR group; (4) high CAR (≥ 0.78), functional class at admission ≥ 2 and baseline creatinine ≥ 1.5 mg/dL were independent predictors of all-cause in-hospital mortality in AHF.

Systemic inflammation has been considered one of the main features of the pathophysiology in both acute and chronic heart failure.[14] C-reactive protein reflects the presence of inflammation

Table 5. Univariate and Multivariate Cox Regression Analysis on the Risk Factors Associated with the In-hospital Mortality in the Patients with Acute Heart Failure

	Hazard Ratio (95% CI)	*P*	Hazard Ratio (95% CI)	*P*
Age	1.016 (0.997-1.034)	0.094	0.998 (0.978-1.018)	0.819
Male gender	1.214 (0.784-1.882)	0.385		
Functional class ≥ 2	3.299 (2.145-5.074)	<0.001	2.465 (1.558-3.903)	<0.001
S3	1.522 (0.971-2.384)	0.067	1.041 (0.645-1.681)	0.868
Fingertip oxygen saturation	0.952 (0.928-0.997)	0.033	0.976 (0.939-1.015)	0.225
Left ventricular ejection fraction	0.984 (0.967-1.000)	0.052	0.985 (0.968-1.003)	0.110
Neutrophil-lymphocyte ratio	1.023 (1.007-1.039)	0.004	1.013 (0.992-1.035)	0.231
Creatinine ≥ 1.5 mg/dL	2.829 (1.717-4.660)	<0.001	2.129 (1.235-3.670)	0.007
Lactate dehydrogenase ≥ 280 U/L	2.154 (1.228-3.779)	0.007	1.604 (0.896-2.870)	0.112
C-reactive protein to albumin ratio ≥ 0.78	2.321 (1.455-3.703)	<0.001	1.694 (1.019-2.818)	0.042
Infection	1.182 (0.712-1.962)	0.517		

and has a prognostic role in HF patients.[15] On the other hand, hypoalbuminemia is common in AHF patients, and it was associated with the burden of comorbidities, inflammatory state, and cachexia in HF.[16] Ancion et al[17] found out that baseline serum albumin level could serve as a simple prognostic factor in AHF for predicting long-term outcome. In our study, both variables were important indicators of in-hospital mortality in AHF.

The superior role of the CAR for predicting prognosis in comparison to either CRP or albumin alone was established in several acute medical conditions.[18] But the data on the association between CAR and prognosis in AHF are scarce. Çinier et al[12] performed a 1011-patient study on the usefulness of CAR in predicting long-term mortality in patients with HFrEF who underwent an implantable cardioverter defibrillator.[12] They divided patients into 3 tertiles according to their basal CAR value and found out that patients in higher tertile had higher mortality over the long term compared with those in other tertiles (4.2% vs. 11.0% vs. 28.5%). But they included only stable, chronic patients with HFrEF who were planned to undergo the device implantation. In our study, we included decompensated AHF patients in the entire ejection fraction spectrum and analyzed only all-cause in-hospital mortality. The higher the CAR, the more prevalent the mortality, consistent with the findings of Çinier et al.

Another study addressing the prediction of the prognosis in AHF was conducted by Namiuchi et al.[19] and they offered the Glasgow Prognostic Score in AHF patients. This score was calculated as follows: 1 point for each abnormal biomarker (albumin <3.5 g/dL, CRP >1.0 mg/dL) for a possible score ranging from 0 to 2. They hypothesized that each variable was individually evaluated in predicting prognosis in AHF patients[20,21] and tried to determine if the score 1 or 2 would be a prognostic indicator. In the cohort study of 336 patients, authors stated that the score was useful for predicting all-cause mortality. However, the study was limited by the fact that the baseline use of guideline-directed medical therapy was quite low, with only 25% use of beta-blockers and 44% use of angiotensin-converting enzyme inhibitors/angiotensin receptor blockers; therefore, the results should be analyzed cautiously in current clinical practice. Besides, there were large numbers of patients lost to follow-up who could not provide endpoint data.[22] In our study, beta-blockers and angiotensin-converting enzyme inhibitors/angiotensin receptor blockers were more frequently used in all study population (77.2% and 48.9%, respectively). Moreover, we had no data loss on patients' endpoints.

Table 6. Cox Regression Analysis and Regression Models for In-hospital Mortality by C-Reactive Protein to Albumin Ratio

	Mortality, HR (95% CI)
Model 1: unadjusted	2.321 (1.455-3.703)
Model 2: adjusted for age, LVEF	2.337 (1.458-3.746)
Model 3: adjusted for covariates[a]	1.694 (1.019-2.818)

HR, hazard ratio; LVEF, left ventricular ejection fraction.
[a]Includes age, gender, functional class ≥ 2, presence of S3, fingertip oxygen saturation, left ventricular ejection fraction, neutrophil to lymphocyte ratio, creatinine ≥ 1.5 mg/dL, lactate dehydrogenase ≥ 280 U/L, C-reactive protein to albumin ≥ 0.78, infection.

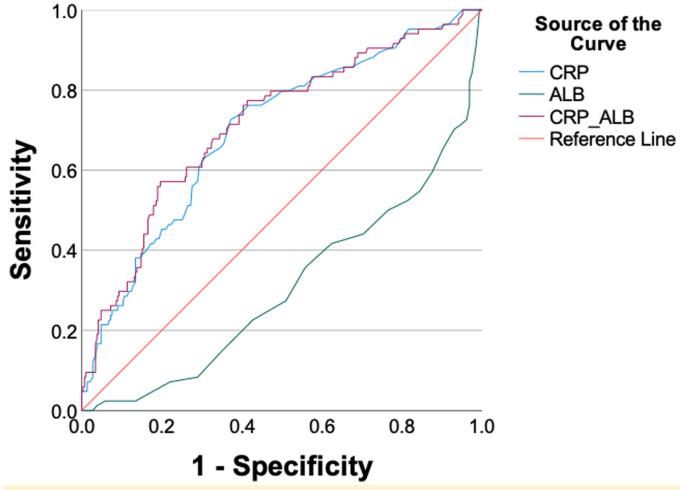

Figure 3. Receiver operating characteristic curves for C-reactive protein to albumin ratio (CAR), C-reactive protein, and albumin to predict in-hospital mortality in acute heart failure.

End-organ damage from AHF can occur due to elevated venous and/or ventricular filling pressures; hence, lungs, kidneys, liver, and gut were affected by congestion.[23] Exacerbation of these hemodynamical effects can occur through increased inflammation and oxidative stress. The CAR is known to be associated with inflammatory status and malnutrition,[9] and synergistic adverse effects may occur in short term when high CAR is present. Our study is the first study to address the role of CAR in AHF to the best of our knowledge. We demonstrated that the need for hemodialysis/ultrafiltration, acute ischemic hepatitis, coagulopathy, invasive mechanical ventilation, and shock during hospital stay were more prevalent in high CAR group. These adverse effects are clinical signs of severity of the AHF and could be related to profound inflammation. It was previously established that cascades of cytokines (i.e., tumor necrosis factor], transforming growth factor-β, and interleukins-6 and -1) independently can lead to endothelial dysfunction, pulmonary edema, and left ventricular dysfunction, which may contribute to the adverse prognosis in AHF. Furthermore, markers of inflammation predicted persistent congestion and renal dysfunction in AHF.[24] Therefore, high CAR as an inflammatory marker may have a role of a predictor of severity and ominous prognosis in AHF. Further studies including larger study groups are needed to evaluate the relationship between CAR and long-term prognosis in AHF.

There were several limitations to our study. First, it was a modest-size case series of hospitalized AHF patients. Second, due to the retrospective nature of this study, some parameters (i.e., comorbidities, in-hospital medications, etc) were not available for all patients or might not have been precisely recorded. Moreover, longer follow-up data from the survivors would add invaluable data to the study. Besides, we did not precisely evaluate the relationship between serum albumin levels and nutritional status of the patients because the international Societies of Clinical Nutrition and Metabolism recommend focusing on parameters like "insufficient energy intake," weight loss, and other functional measures to document and identify malnutrition.[25] Nevertheless, our findings emphasize the predictor role of the CAR for the severity and worse prognosis in hospitalized AHF patients.

Our data demonstrated that baseline high CAR (≥0.78) was an independent predictor of in-hospital mortality in AHF. Using this simple predictor may allow the physicians to monitor closely patients admitted to the hospital with the diagnosis of AHF.

Ethics Committee Approval: The retrospective cohort study was approved by the Başakşehir Çam & Sakura City Hospital ethic committee (Approval no:2022.06.214, date:30.06.2022) and the Istanbul Provincial Health Directorate.

Peer-review: Externally peer-reviewed.

Author Contributions: Concept – M.R.S., Z.E., K.K.Ş., Y.S.Ö., A.G., A.İ.T.; Design – M.R.S.; Supervision – N.K., Ç.Y., Z.E., K.K.Ş., Y.S.Ö., A.G., A.İ.T.; Materials – M.R.S., N.K., Ç.Y., Z.E., K.K.Ş., Y.S.Ö.; Data Collection and/or Processing – M.R.S., N.K., Ç.Y., Z.E., K.K.Ş., Y.S.Ö.; Analysis and/or Interpretation – M.R.S., A.G., A.I.T.; Literature Review – M.R.S.; Writing – M.R.S.; Critical Review – Y.S.Ö., A.G., A.İ.T.

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Declaration of Interests: The authors declare that they have no competing interests.

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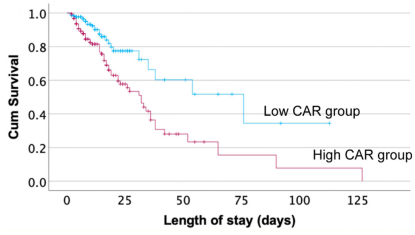
C-Reactive Protein to Albumin Ratio Predicts In-hospital Mortality in Patients with Acute Heart Failure

374 hospitalized pts
w/ Acute Decompensated Heart Failure



Kaplan-Meier analysis for mortality

	High CRP/Albumin Ratio ≥ 0.78		Low CRP/Albumin Ratio < 0.78	
Mortality	36.7%	Vs	12%	P < 0.001

Admission C-reactive protein to albumin ratio was associated with increased all- cause mortality in hospitalized patients with acute decompensated heart failure.

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