Turkish Journal of Geriatrics
DOI: 10.29400/tjgeri.2023.326
2023; 26(1):12–19

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RESEARCH

THE RELATIONSHIP OF THE C-REACTIVE PROTEIN /ALBUMIN RATIO TO IN-HOSPITAL MORTALITY IN ELDERLY PATIENTS WITH NON-ST-ELEVATION MYOCARDIAL INFARCTION WHO HAVE UNDERGONE PERCUTANEOUS CORONARY INTERVENTION

Abstract

Introduction: Acute myocardial infarction is the most common cardiovascular disease and the cause of significant mortality worldwide. The C-reactive protein/albumin ratio, which measures inflammatory conditions, can be used to predict mortality. In this study, we aimed to investigate the relationship between in-hospital mortality and the C-reactive protein/albumin ratio in patients diagnosed with non-ST-elevation myocardial infarction who underwent interventional treatment at our hospital.

Materials and Method: Two hundred and ninety-seven elderly patients were included in the study. The information of the patients was obtained from the hospital database. The C-reactive protein/albumin ratio was calculated for each patient. We used regression analysis to investigate the relationship between the C-reactive protein/albumin ratio and in-hospital mortality.

Results: A univariate analysis showed that gender, ejection fraction, white blood cell, glucose, creatinine, systolic and diastolic blood pressure, heart rate, GRACE risk score, and CAR ratio were significant predictors of mortality (Table 2). All parameters were added to a multivariable logistic regression, and multivariable logistic regression analysis showed that the GRACE risk score (OR: 0.956, 95% CI: 0.941–0.971; p<0.001) and the C-reactive protein/albumin ratio (OR: 0.812, 95% CI: 0.661–0.998; p=0.048) were the only significant predictors of mortality. Furthermore, bivariate correlation analysis showed a weak but statistically significant correlation between GRACE risk score and C-reactive protein/albumin ratio (r=0.180, p<0.001).

Conclusion: We found a significant relationship between C-reactive protein/albumin and in-hospital mortality. C-reactive protein/albumin ratio can be used in clinical practice because it is inexpensive and easy to apply and has a strong prognostic value for elderly non-ST-elevation myocardial infarction patients.

Keywords: Myocardial Infarction; Albumin; Inflammation; Mortality.

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Received : Jan 23, 2023
Accepted : Mar 22, 2023

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INTRODUCTION

Acute myocardial infarction (AMI) is the most common cardiovascular disease worldwide and is a significant cause of mortality (1). Today, with the increase in life expectancy, both the elderly population and the incidence of AMI are increasing. Non-ST-elevation myocardial infarctions (NSTEMI) are more common than ST-elevation myocardial infarctions (STEMI) and unstable angina pectoris (UAP) (1,2). With the increase in recent years of well-equipped health centers providing both emergency interventional treatment and complementary health services, these patients may receive early treatment, yet mortality and morbidity are still high, resulting in high health expenditures.

It is known that age, gender, obesity, smoking, preferred treatment method (interventional, surgical, medical), additional diseases (diabetes mellitus, hypertension, hyperlipidemia, etc.), physical activity, long-term follow-up management, and patient compliance with treatment contribute to a patient's prognosis (2). The current approach to the management of mortality and morbidity after AMI focuses on stratifying patients according to their risk and using an appropriate prognostic factor to determine treatment steps.

Malnutrition is a risk factor for coronary artery disease (CAD). Many studies investigating the relationship between CAD and malnutrition have focused on hypoalbuminemia which is also a risk factor for the development of AMI (3). To our knowledge, there is no evidence demonstrating the prognostic value of low albumin levels in elderly patients diagnosed with NSTEMI.

Inflammation plays an important role in both the initiation and progression of the atherosclerotic process (3,4). Many studies have shown that the serum level of C-reactive protein (CRP), which is an inflammation marker, is correlated with the severity of atherosclerosis and plaque burden (4). It has also been found that the severity of myocardial damage and serum CRP levels are correlated after acute coronary syndrome (4,5).

The ratio of serum CRP level to albumin (CAR), which is considered a new indicator of inflammatory response, is thought to be a more accurate indicator than albumin and CRP levels alone in determining the prognosis of patients with many inflammatory diseases, such as sepsis, cancer, acute pancreatitis, and ulcerative colitis (5). In addition, the CAR ratio has been shown to predict stent restenosis in AMI patients during follow-up after interventional treatment (6). In this study, we aimed to investigate the relationship between in-hospital mortality and CAR in patients with a diagnosis of NSTEMI who underwent interventional treatment.

MATERIALS AND METHOD

Patient population

Our study is observational and retrospective. Two hundred and ninety-seven patients who applied to the emergency department of our clinic and who underwent interventional treatment in coronary angiography (CAG) with a diagnosis of NSTEMI were included by sequential screening. The study was approved by the local ethics committee and complies with the Declaration of Helsinki. Patient information was scanned retrospectively using the hospital registry system.

Patients who presented to the emergency department with chest pain and symptoms suggestive of ischemia (i.e., shortness of breath, palpitations, a squeezing sensation, fatigue, and dizziness), with cardiac enzymes exceeding the upper limit of normal, were included. Those with findings consistent with STEMI on electrocardiography, cardiac tamponade findings on echocardiography, acute valve pathology, aortic dissection and aneurysm, and systemic infection, and those who had taken medications (anti-inflammatory, antibiotic, statins, etc.) in the previous week were excluded.

The clinical features and laboratory data of the patients were recorded at the time of admission. Bedside echocardiography was performed on each patient. The left ventricular ejection fraction (LVEF) was calculated using the modified Simpson's method. The heart rhythm and heart rate of the patients were recorded. Demographics, fasting blood glucose levels, hemogram, kidney function parameters (urea, creatinine, glomerular filtration rate, and electrolyte levels), CRP, lipid profiles (low-density lipoprotein cholesterol [LDL-C]), high-density lipoprotein cholesterol [HDL-C]), triglyceride (TG) levels), albumin, and aspartate transaminase (AST) are among the clinical variables. Patients were considered hypertensive if their systolic blood pressure/diastolic blood pressure was greater than 140/90 mmHg on two or more measurements or if they were using any antihypertensive medication. Diabetes mellitus was defined as fasting blood sugar above 126 mg/dL, postprandial blood sugar above 200 mg/dL, glycosylated hemoglobin above 6.5%, or the use of any antidiabetic medication. Patients' CAR ratio was calculated and recorded upon admission.

Statistical analysis

All statistical analyses were performed using SPSS version 25.0 (IBM Corp., Armonk, NY, USA). Continuous variables were defined as mean ± standard deviation, and categorical variables were defined as numbers and percentages. The Kolmogorov–Smirnov, and Shapiro–Wilk tests were used to determine the normal distribution. The independent samples t-test was used when parametric test conditions were met for independent group comparisons, and the Mann–Whitney U test was used when parametric test conditions were not met. The difference between categorical variables was analyzed using the chi-square test. Logistic regression (LR) analysis was used to find predictors of in-hospital mortality in NSTEMI. Univariate analysis was performed in the first step. Independent variables were found to be statistically significant (p-value less than 0.05), and clinically important parameters were added to binary multivariable logistic regression.

RESULTS

Of the 297 patients with NSTEMI who underwent percutaneous coronary intervention at our institution, 270 were discharged, and 27 patients died while in the hospital. When the two groups were compared, no statistical difference was found in terms of age, gender, hypertension, diabetes mellitus, hyperlipidemia, smoking, or history of CAD (Table 1). The group who died in the hospital showed lower LVEF (50% [40–55] vs. 40% [30–45]; $p<0.001$) and systolic blood pressure (130 mmHg [110–142] vs. 95.5 mmHg [86.5–128], $p<0.001$). Additionally, the group who died in the hospital showed higher values for heart rate (80/min [70–90] vs. 90/min [79–10]), $p=0.008$), peak troponin (0.4 ng/mL [0.09–1.78] vs. 2.2 ng/mL [1.1–7.7], $p=0.001$), and creatinine (0.94 mg/dl [0.77–1.20] vs. 1.39 mg/dl [1.05–1.66], $p=0.047$), and their GRACE risk score (148 [121–167] vs. 203 (169–233), $p<0.001$) was higher (Table 1). CAR (0.20 mg/g (0.06-0.76) vs. 0.71 mg/g (0.35-1.80), $p=0.039$) was statistically significant. In univariate analysis, gender, ejection fraction, WBC, glucose, creatinine, systolic and diastolic BPs, heart rate, GRACE risk score, and CAR ratio were found to be significant predictors of mortality (Table 2). All parameters were added to multivariable LR, and multivariable LR analysis showed that the GRACE risk score (OR: 0.956, 95% CI: 0.941-0.971; $p<0.001$) and CAR ratio (OR: 0.812, 95% CI: 0.661-0,998; $p=0.048$) were the only significant predictors of mortality. Furthermore, bivariate correlation analysis showed that a weak but statistically significant correlation between GRACE risk score and CAR ratio ($r=0.180$, $p<0.001$) (Table 2).

Table 1. Demographic and Clinical Characteristics of Patient Population

	Survivors (n=270)	Non-survivors (n=27)	p value
Age (years)	76 (70-82)	77 (73-86)	0.648
Gender male (n, %)	184 (%68.1)	21 (%77.8)	0.385
HT (n, %)	162 (60)	19 (70.4)	0.408
DM (n, %)	107 (39.6)	15 (55.6)	0.150
HL (n, %)	45 (16.7)	2 (7.4)	0.276
CRD (n, %)	55 (20.5)	6 (23.1)	0.800
Smoking (n, %)	58 (21.5)	4 (14.8)	0.665
CAD history (n, %)	142 (52.6)	19 (70.4)	0.104
LVEF (%)	50 (40-55)	40 (30-45)	**<0.001**
Systolic blood pressure	130 (110-142)	95.5 (86.5-128)	**<0.001**
Diastolic blood pressure	72.5 (68-72.5)	62.5 (59-70)	**0.002**
Heart rate (bpm)	80 (70-90)	90 (79-101)	**0.008**
Hemoglobin (mg/dl)	12.6±1.85	11.7±1.88	0.067
White blood cell 10^9/l	9 (7.2-11.1)	12.6 (9.4-15.9)	0.121
Glucose (g/dl)	121 (102-166)	170 (130-262)	**0.006**
Peak Troponin (ng/mL)	0.4 (0.09-1.78)	2.2 (1.1-7.7)	**0.001**
Peak CK-MB (U/L)	13.1 (4.3-43)	91.4 (14.2-196.3)	**0.002**
Creatinine (mg/dl)	0.94 (0.77-1.20)	1.39 (1.05-1.66)	**0.047**
Albumin (g/dl)	3.6 (3.2-3.9)	3.4 (3.1-3.7)	0.445
Total cholesterol (mg/dl)	173±46	162±44	0.202
LDL (mg/dl)	105±39	93±27	**0.021**
HDL (mg/dl)	41 (34-51)	36.5 (26-46)	0.869
Triglycerides (mg/dl)	109 (80-158)	113 (98-176)	0.242
CRP (mg/dl)	0.7 (0.2-2.8)	2.5 (1.1-6.3)	0.078
CRP to albumin ratio	0.20 (0.06-0.76)	0.71 (0.35-1.80)	**0.039**
GRACE risk score	148 (121-167)	203 (169-233)	**<0.001**

Continuous variables were summarized as mean ± SD, categorical variables were summarized as counts and percentages.
Abbreviations: HT: Hypertension, DM: Diabetes Mellitus, HL: Hyperlipidemia, CRD: Chronic Renal Disease, CAD: Coronary artery disease, LVEF: Left ventricular ejection fraction, LDL: Low density lipoprotein cholesterol, HDL: High density lipoprotein cholesterol, CRP: C-reactive protein.

Table 2. Independent Predictors of in-hospital mortality

Variables	Univariate analysis		Multivariable analysis	
	OR (95% CI)	p	OR (95% CI)	p
Gender (female)	0,611 (0,238-1.569)	0.306		
LVEF	1.087 (1.046-1.131)	**<0.001**		
WBC	0.836 (0.760-0.919)	**<0.001**		
GLUCOSE	0.994 (0.991-0.997)	**<0.001**		
CREATININE	0.690 (0.519-0.917)	**0.011**		
SBP	1.046 (1.024-1.068)	**<0.001**		
DBP	1.054 (1.019-1.091)	**0.002**		
HEART RATE	0.977 (0.959-0.994)	**0.010**		
GRACE RİSK SCORE	0.956 (0.941-0.970)	**<0.001**	0.956 (0.941-0.970)	**<0.001**
CAR	0.796 (0.670-0.947)	**0.010**	0.812 (0.661-0.998)	**0.048**

Abbreviations: LVEF: Left ventricular ejection fraction, WBC: White blood cell, SBP: Systolic blood pressure, DBP: Diastolic blood pressure, CAR: C-reactive protein to albumin ratio

DISCUSSION

Our study is the first to investigate the relationship between in-hospital mortality and CAR ratio in elderly patients with NSTEMI who have undergone interventional treatment. Today, the prevalence of CAD is increasing with the prolongation of life expectancy and the increase in the elderly population (7). Despite the increase in both early interventional treatment and complementary health services in addition to medical treatment, mortality and morbidity are still high in these patients (8).

CRP, which is an acute-phase reactant, is used as a marker showing the presence of inflammation and tissue damage. The most common cause of CAD is atherosclerosis. The most important reason for the onset and progression of atherosclerosis is inflammation (9). Pro-inflammatory cytokines, which are released by immunological reactions in the initial stages of atherosclerotic plaque formation, increase the release of CRP from the liver (10). The predictive value of increased CRP levels for CAD has been emphasized in many studies. A study on healthy people showed that those with a plasma CRP level above 2 mg/L had a greater five-year risk of atherosclerotic cardiovascular disease than those with a CRP level of 0.5 mg/L or less (11). In another study, the long-term follow-up of approximately 700 patients hospitalized for AMI showed a significant correlation between CRP levels and mortality (12). In our study, the mean CRP value was higher in the group of patients who died in the hospital.

Hypoalbuminemia is a strong prognostic marker of inflammation and malnutrition. Recent studies have shown that a low albumin level is an independent risk factor for ischemic heart disease, heart failure, atrial fibrillation, stroke, and venous

thromboembolism (13). In the ARIC study, which included 14,506 patients, low albumin plasma levels were found to be associated with ischemic heart disease in the smoking group, independent of traditional risk factors and inflammation (14). In the Framingham Offspring Study, which included 4,506 people, a low plasma albumin level was an independent predictor of the first AMI during the 22-year follow-up period (15). In a recent study involving 7,647 individuals, low plasma albumin levels were strongly associated with the occurrence of a first or recurrent AMI, independent of traditional risk factors (16). Low albumin levels have also been associated with poor in-hospital outcomes in STEMI patients (17).

CAR is a new prognostic measure of inflammation associated with inflammation severity and mortality (17). Several studies have shown that increased CAR values have prognostic value for STEMI (18). Increased CAR values were also found to be associated with increased in-hospital mortality in STEMI patients (19). An increased CAR ratio was also associated with thrombus burden and a greater extent of coronary artery disease in AMI patients (20,21). Increased CAR levels were found to be associated with increased intent restenosis in STEMI patients (22,23). Increased CAR levels were also associated with increased contrast-induced nephropathy levels in NSTEMI patients (24). A study conducted in 2020 found that the CAR ratio predicted coronary microvascular dysfunction better than CRP and albumin levels alone in patients with celiac disease (25). Our study found that high CAR levels were associated with in-hospital mortality in elderly patients diagnosed with NSTEMI. In addition, CAR levels were also associated with a high GRACE risk score. The CAR ratio can reduce potential bias and can be used as a more reliable prognostic parameter than either CRP or albumin levels alone.

Limitations

The limitations of our study are, first, that it does not provide prognostic data due to its cross-sectional design. In addition, it is a single-center study that included a relatively small number of patients. In addition, some patients were excluded due to missing clinical data and/or laboratory variables. Finally, the presence of multiple comorbidities and vulnerabilities may have affected in-hospital mortality.

CONCLUSION

Our study investigates the association between CAR and in-hospital mortality in elderly patients following in-hospital treatment for NSTEMI. Multivariate regression analysis revealed a significant relationship between CAR and in-hospital mortality. The CAR ratio may have a stronger prognostic value than either CRP or albumin levels alone. It can be used in clinical practice because it is inexpensive and easy to apply and has a strong prognostic value in NSTEMI patients.

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