Prognostic value of serum albumin-to-creatinine ratio in acute coronary syndrome

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Abstract

Aim: The association between serum albumin-to-creatinine ratio (sACR) and in-hospital mortality remains unclear in patients with acute coronary syndrome (ACS). In this study we aimed to investigate the prognostic value of sACR in predicting in-hospital mortality in ACS.

Materials and Methods: The study was conducted in a single tertiary center. Patients hospitalized with both ST Elevation Myocardial Infarction (STEMI) and Non-STEMI were retrospectively analyzed. The sACR and other clinically related parameters were recorded. The primary outcome was in-hospital mortality. Logistic regression (LR) models were used to investigate the association between sACR and in-hospital mortality. Receiver operating characteristic (ROC) curve was used to find out the cut-off level of sACR.

Results: A total of 686 patients with ACS were enrolled, of whom 59 (%8.6) died in-hospital follow-up. The sACR was significantly lower in patients who died in hospital (2.9 (2.3-3.7) vs 3.9 (3.3-4.6)). Multivariable LR analysis showed that sACR is an independent predictor of in-hospital mortality in patients with ACS. Area under the curve value generated by ROC curve analysis was 0.719 (95% CI: 0.656-0.783). The sensitivity of sACR predicting in-hospital mortality was 77.5% with the specificity of 59.3%.

Conclusion: In this study, lower sACR on admission was found significantly associated with in-hospital mortality in patients with ACS.

Introduction

Acute coronary syndrome (ACS) is associated with high mortality and morbidity despite advances in medical and interventional facilities. Risk assessment at the time of admission is recommended for prognosis estimation [1]. It helps to categorize patients according to the mortality risk and may improve the treatment effectiveness. GRACE (Global registry of Acute Coronary Events) and TIMI (Thrombolysis in Myocardial Infarction) risk scores have been widely used and established risk scores which consist of many parameters including clinical history, biochemical data and myocardial injury markers [2,3]. Despite the proven clinical validity of these risk scores, simpler biomarkers have been investigated to predict short and long-term mortality in ACS patients [4,5].

Reduced kidney function, whether acute or chronic, is one of the most well-known prognostic factors in patients with ACS and was incorporated into several risk prediction tools [6,7]. Besides, ACS is a pathophysiological clinical condition that includes inflammatory and thrombotic processes. Serum albumin (SA) is the major protein in the blood and is associated with the inflammatory process and platelet activation. It enhances the impairment of platelet aggregation with thromboxane synthase inhibition by increasing the formation of prostaglandin D2 (PGD2) [8]. It is an important biomarker for adverse outcomes in ACS [9]. Furthermore, it has been shown that as the albumin level decreases even within the normal range, cardiovascular disease incidence increases [10]. Based on the significant effects of albumin and creatinine levels on ACS prognosis, studies were conducted primarily on the urinary albumin, and urinary albumin/creatinine ratio (uACR) in stable coronary artery disease (CAD) and ACS and significant results were obtained in these studies [11,12]. However, studies investigating the effect of serum albumin/creatinine ratio (sACR) on the short-term out-

comes of ACS are very limited. Therefore, in this study, we wanted to investigate the effect of sACR on in-hospital mortality in ACS patients.

Materials and Methods

Study design and patient population

In this cross-sectional study, a total of 722 patients admitted to a tertiary center with the diagnosis of ACS were retrospectively analyzed. Patients older than 18 years of age with the diagnosis of ST Elevation Myocardial Infarction (STEMI) and non-STEMI were included in the study. A total of 36 patients were excluded from the study because of various reasons. The exclusion criteria were as follows: history of ischemic or hemorrhagic cerebrovascular event, presence of malignant tumor history, chronic hepatic disease and insufficient data (Figure 1). The diagnoses of STEMI and non-STEMI were based on the previously published guidelines released by the European Society of Cardiology and all patients were treated by the attending physician in accordance with the current guidelines [1,13]. The study was conducted in accordance with the Declaration of Helsinki and was approved by the local ethics committee (Non-Interventional Clinical Research Ethics Committee of the Kutahya Health Science University Evliya Celebi Research and Training Hospital, Date: 09.02.2022, Decision no: 2022/02-15).

Data collection and endpoints

Demographic characteristics and clinical and laboratory data of patients were recorded. Baseline vital signs, in-hospital treatments, echocardiographic and angiographic findings and in-hospital endpoints were collected from the medical records and patient files. The sACR was calculated by assessing the levels of serum albumin and creatinine on admission to the coronary care unit. The primary endpoint was in-hospital mortality and patients were divided into two groups according to their vital status at hospital discharge. The sACR was calculated for both groups.

Statistical analysis

The data analysis was performed by using the Statistical Package for Social Sciences Program for Windows version 23.0 (SPSS Inc., Chicago, IL, USA). Quantitative variables included in the analysis with a normal distribution were reported as mean ± standard deviation, and non-normally distributed variables were reported as median (interquartile range). Categorical variables were shown as number and percentage values. Differences between the groups were calculated with student's t test or Mann-Whitney U test for continuous data and chi-square test for categorical data as appropriate. Kolmogorov-Smirnov test was used to test the normality of distribution. All statistical tests were two-sided, and a p-value less than 0.05 was considered to be statistically significant for all analyses.

We analyzed 722 patients which is actually not very low. Because when the sample size was calculated after the data was collected, 80% power and 5% error rate, and when the odds ratio was calculated between 0.5 and 1.5, 288 for 0.5 and 684 for 1.5 were found, and a sufficient number of patients was reached.

A logistic regression model was used to identify the association between sACR and in-hospital mortality. In the first step, unadjusted model was used to test the hazard ratio (HR) and 95% confidence interval (CI) of sACR, with the values of survivors serving as a reference. Adjusted model was performed by adding age, heart failure (HF), hypertension (HT), diabetes mellitus (DM), CAD, peripheral artery disease (PAD), chronic renal disease (CRD) to the analysis. Receiver operating characteristic (ROC) curve was used to determine a cut-off value of sACR between the survivors and nonsurvivors. The area under the curve (AUC, C statistics) was used to present sensitivity and specificity.

Results

The median age of the study participants was 65 (57-737) and 72.9% were men. A total of 59 patients (8.6%) were died in-hospital follow-up. Conventional risk factors like HT, DM, smoking, CAD/PAD, and CRD were similar in survivors and nonsurvivors (all p values >0.05) while HF incidence was higher in nonsurvivors (p<0.001). There was a slight difference in mortality rates between STEMI and NSTEMI (p=0.047). Furthermore, sACR was similar between groups (3.9±1.2 vs 3.8±1.2, p=0.158). Baseline clinical, demographic and laboratory characteristics of the study population according to the survival status are shown in Table 1.

Unadjusted logistic regression analysis showed that patients with lower sACR had higher in-hospital mortality than those with higher sACR (OR: 0.532, 95% CI: 0.421-0.673, p<0.001). After adjusting the model with confounding factors (age, HF, HT, DM, CAD, PAD, CRD), multivariable logistic regression analysis showed that lower sACR was still an independent predictor of in-hospital mortality (OR: 0.461, 95% CI: 0.335-0.637, p<0.001, Table 2).

Discrimination ability of sACR was tested with ROC curve analysis. The sACR AUC value was 0.719 (95% CI: 0.656-0.783, p<0.001, Figure 2). The cut-off value for sACR was 3.182, with a sensitivity of 77.5% and a specificity of 59.3%.

The serum albumin/creatinine ratio was significantly lower in patients who developed acute renal failure (ARF) in
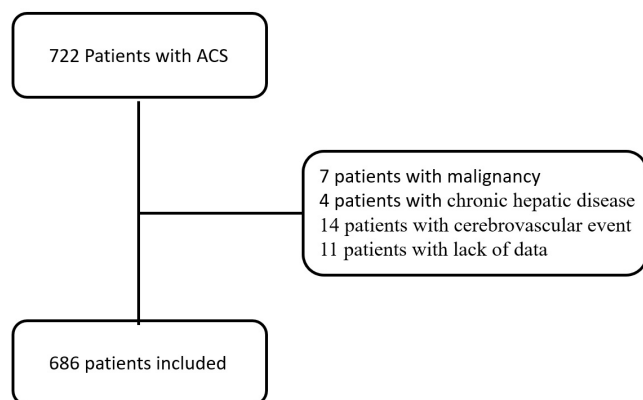

Figure 1. Inclusion and exclusion criteria.

722 Patients with ACS

7 patients with malignancy
4 patients with chronic hepatic disease
14 patients with cerebrovascular event
11 patients with lack of data

686 patients included

Table 1. Baseline clinical, demographic and laboratory characteristics of the study population according to the survival status.

	Survivors (n=627)	Nonsurvivors (59)	P value
Age, years (median, IQR)	64 (55-72)	78 (68-83)	<0.001
Gender, male (%)	459 (73.2)	41 (69.5)	0.542
Hypertension (n,%)	287 (45.8)	32 (54.2)	0.222
Diabetes Mellitus (n,%)	222 (35.4)	27 (45.8)	0.121
CAD/PAD (n,%)	352 (56.1)	26 (44.1)	0.077
Smoking (n,%)	266 (42.4)	17 (34.7)	0.477
Heart Failure (n,%)	18 (2.9)	11 (18.6)	<0.001
Chronic Kidney Disease (n,%)	140 (22.3)	16 (27.1)	0.417
BUN	17 (14-22)	24 (18-33)	<0.001
Creatinine (mg/dL)	1 (0.88-1.2)	1.2 (1-1.4)	<0.001
GFR (ml/min)	72.9 (60.1-85.8)	55 (42-72)	<0.001
CRP (mg/L)	6 (2.7-15.6)	18 (4.6-92)	<0.001
Glucose (mg/dL)	146 (116-214)	224 (184-320)	<0.001
Sodium (mEq/L)	138 (136-140)	137 (135-140)	0.766
Potassium (mEq/L)	4.2 (3.9-4.5)	4.6 (4.1-5.1)	<0.001
Albumin (g/dL)	3.9 (3.6-4.1)	3.6 (3.3-3.7)	<0.001
Hematocrit (g/dL)	42.7 (38.9-45.8)	41.3 (35.8-46.4)	0.101
WBC (g/dL)	10.2 (8.3-12.8)	13.5 (10.2-17.3)	<0.001
Platelet (10^3/μL)	237 (197-280)	225 (189-299)	0.891
Neutrophil (10^3/μL)	6.9 (5.1-9.3)	9.4 (7.3-14.6)	<0.001
Lymphocyte (10^3/μL)	2 (1.4-2.9)	1.88 (1.0-3.2)	0.666
Ejection fraction, mean±SD	52±8.6	36.5±11.1	<0.001
Acute Renal Failure (n,%)	24 (3.8)	47 (79.7)	<0.001
sACR (g/mg)	3.9 (3.3-4.6)	2.9 (2.3-3.7)	<0.001

Continuous variables are presented as mean ± SD or median (IQR), categorical variables are presented as frequency (%).
BUN: blood urea nitrogen; CAD/PAD: Coronary Artery Disease/Peripheral Artery Disease; CRP: C-reactive protein; GFR: glomerular filtration rate; IQR: interquartile range; SD: standard deviation; sACR: serum albumin creatinine ratio, WBC: white blood cell.

Table 2. Logistic regression analysis regarding correlations between sACR and in-hospital mortality.

Variables	Odds ratio (95% CI)	P value
sACR		
Unadjusted	1.120 (1.056 – 1.188)	<0.001
Adjusted	1.190 (1.079 – 1.313)	<0.001

Risk factors adjusted by age, HF, HT, DM, CAD/PAD, CRD CAD: coronary artery disease, CI: confidence interval, CRD: chronic renal disease, DM: diabetes mellitus, HF: heart failure, HT: hypertension, PAD: peripheral artery disease, sACR: serum albumin creatinine ratio.

Figure 2. Receiver operating characteristics curve of serum Albumin Creatinine Ratio for predicting in-hospital mortality.

hospital (2.9±0.9 vs 3.9±1.2). Besides, mortality rate was significantly higher in patients with ARF (%3.8 vs %79.7, p<0.001, Table 1).
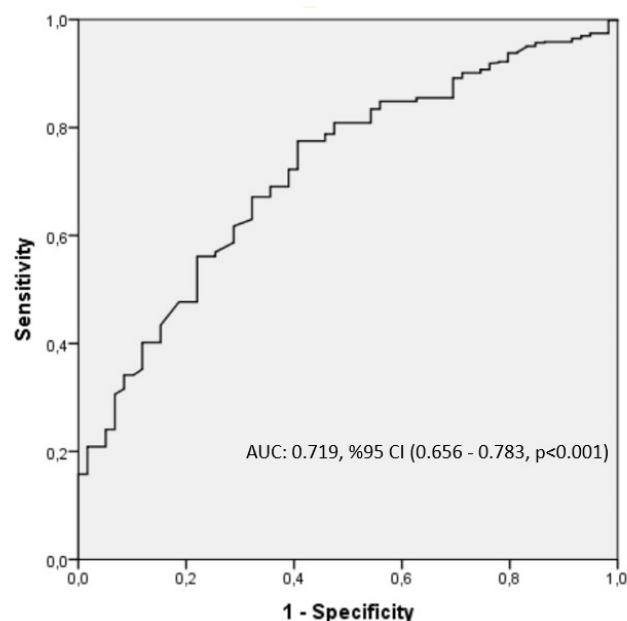
Discussion

In this study, we investigated the prognostic value of sACR and found that a low level of sACR is significantly associated with in-hospital mortality in ACS patients.

Optimal management of ACS is crucial due to affecting short and long-term results. To deal with this, a multitude of risk scores have been developed. GRACE, TIMI and PURSUIT risk scores are some of these of which derived from different patient populations. Yan et al. compared the discriminative performances of these scores, which found that all three risk scores conferred additional prognostic value beyond global risk assessment in non-STEMI patients [14]. Due to their critical prognostic features, risk scores (especially GRACE) have been recommended for risk assessment and adjustment in ACS guidelines. However, despite these risk scores yielding significant results in predicting mortality, simpler risk markers have always been the subject of research.

Since ACS is known to be a thrombotic and inflammatory process, studies have mostly focused on parameters related to these pathological pathways. Many different inflammation markers like C-reactive protein (CRP), neutrophil-lymphocyte ratio and white blood cells have been tested in clinical trials and found that they significantly correlate with short and long-term outcomes in CAD and ACS patients [15,16]. Serum albumin is the major blood protein that can cause inflammatory regulatory changes with its antioxidant functions [17]. It has an anti-inflammatory and antiatherogenic effect through many pathways, such as

selectively inhibiting tumor necrosis factor alpha-induced VCAM-1 expression, monocyte adhesion and endothelial apoptosis [18,19]. In an experimental study, exogenously added albumin increased the production of antiaggregatory PGD2 from cyclic endoperoxides and impaired platelet aggregation [8]. Due to these properties, albumin has been the subject of research, like other inflammatory markers in different patient populations, including stable CAD and ACS, both of which are thromboinflammatory processes. Low SA level has been associated with both in-hospital and long-term outcomes in patients with acute ischemic stroke and acute MI [20,21], although it is known that it is an acute phase reactant, and its level shows a 20% reduction during the inflammatory setting [22]. Besides, Hartopo et al. showed that SA level is associated with in-hospital outcomes in ACS, and Oduncu et al. found that hypoalbuminemia on admission is a strong independent predictor of long-term mortality and HF development in patients with STEMI [23,24]. In our study, the SA level was also lower in non-survivors; however, we investigated more sensitive markers for predicting in-hospital mortality. Due to its unique properties, SA has been used in different combinations in predicting the severity of CAD and in the prognosis of acute MI. Cınar et al. found CRP albumin ratio (CAR) to be a potentially useful prognostic tool for predicting a poor prognosis in STEMI patients [25]. Cagdas et al. reported that CAR was superior to CRP and albumin in prediction of intermediate–high syntax score in patients with ACS [26].

Despite many laboratory parameters being tested in different patient populations to predict outcomes, sACR has not been tested in almost any patient group. In one study investigating sACR in the literature, Liu et al. aimed to determine the prognostic value of sACR in predicting long-term survival in patients with acute MI 27. They found that sACR at admission was independently associated with all-cause mortality within the median follow-up period of 10.7 months. We also found that sACR is a good short-term prognostic factor in patients with ACS. Nevertheless, the study by Liu et al. has some differences from ours. First, they did not carry out the study in an independent population but selected the study population from a previously conducted multicenter retrospective evaluation of acute chest pain (REACP) study. Second, they categorized the patients into tertiles (T1, T2, T3) based on the admission sACR level. Categorizing numeric values for which not been investigated previously may be a limiting factor in evaluating results independently. So we made our analyses without categorizing sACR level in order to determine an independent cut-off point with high sensitivity and specificity. We found that sACR has 77.5% sensitivity and 59.3% specificity with a cut-off value of 3.182. Third, they used sACR in combination with the GRACE score, which improved the prognostic value of the GRACE risk score. Our study tested the prognostic value of sACR independent of GRACE.

Our study showed that sACR is a good prognostic factor in in-hospital mortality even if adjusting confounding factors. Furthermore, these findings were also shown valid in the subgroup analysis of patients with CKD and who developed AKD. Our study may be very useful in terms of making a new contribution to a point that is seriously lacking in the literature. Based on these findings, it would be favorable to use sACR in the management of patients with ACS. Moreover, it may be tested in several groups of patients with NSTEMI to predict totally occluded arteries and high risk patients or may be added to scoring systems to increase their prediction capacity. However, larger and prospective studies are needed to substantiate these predictions.

Limitations

With its significant results, our study has also some limitations. First, it is a retrospective study and it is needed to conduct prospective and multicenter studies to confirm these findings. Second, we did not compare the prognostic value of sACR with evidence-based risk scores like GRACE and TIMI. However, we believe that its very well predictive ability and the fact that it is a parameter that can be calculated very easily may be sufficient to eliminate this deficiency. Third, uACR which was found as a significant predictor in previous studies, we could not compare sACR with uACR due to the retrospective nature of the study.

Conclusion

Our study showed that sACR on admission is an independent prognostic factor to predict in-hospital mortality in patients with ACS regardless of the presence of CKD.

Declaration of conflict of interest

The authors declare that there are no conflicts of interest regarding the publication of this article.

Ethics approval

Ethical approval was obtained from Non-Interventional Clinical Research Ethics Committee of the Kutahya Health Science University Evliya Celebi Research and Training Hospital, prior to the initiation of the research work (Date: 09.02.2022, Decision No. 2022/02-15).

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