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

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\textbf{Abstract}

\textbf{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.

\textbf{Materials and Methods:} The study was conducted in a single tertiary center. Patients hospitalized with both STElevation 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.

\textbf{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%.

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

\textbf{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 (57-73) 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...
Table 1. Baseline clinical, demographic and laboratory characteristics of the study population according to the survival status.

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

Continuous variables are presented as mean ± SD or median (IQR), categorical variables are presented as frequency (%).

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...
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 NSTE MI 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.

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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 Kocatepe Training Hospital, prior to the initiation of the research work (Date: 09.02.2022, Decision No. 2022/02-15).

References


