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Impact of serum albumin levels on long-term all-cause, cardiovascular, and cardiac mortality in patients with first-onset acute myocardial infarction

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ABSTRACT

Background: To evaluate the association of serum albumin (SA) with long-term all-cause, cardiovascular, and cardiac mortality in patients with first-onset acute myocardial infarction (AMI).

Methods: The cohort study enrolled 2305 patients with first-onset AMI. The median follow-up was of 1088 days (3 years). Impacts of SA on long-time mortality after AMI were determined using multivariate Cox proportional hazard regression analysis with backward selection.

Results: The patients were divided into three categories by SA tertiles (≤ 3.62, 3.63–4.08, > 4.08 g/dl). High tertile group was used as reference, the adjusted HRs for all-cause death were 1.21 (P = 0.338) and 1.74 (P = 0.003) for intermediate and low tertile, respectively (p-for-trend = 0.001); The equivalent values for cardiovascular death were 1.13 (P = 0.588) and 1.64 (P = 0.022), respectively (p-for-trend = 0.009); The corresponding values for cardiac death were 1.07 (P = 0.806) and 1.59 (P = 0.048), respectively (p-for-trend = 0.022). Moreover, adjusted HRs per 1-g/dl decrease in SA concentrations were 1.66 (P = 0.001) for all-cause death, 1.47 (P = 0.024) for cardiovascular death, and 1.61 (P = 0.012) for cardiac death.

Conclusions: Low SA level (≤ 3.62 g/dl) on admission was an independent predictor of long-term all-cause, cardiovascular, and cardiac mortality in patients with first-onset AMI. There was a dose–response relationship between decreased SA concentrations and increased long-term all-cause, cardiovascular, and cardiac mortality.

1. Introduction

Albumin, a major protein in plasma, is routinely detected on admission. Its main clear functions include maintaining vascular osmotic pressure, binding and transporting varieties of endogenous or exogenous substances, and influencing the pharmacokinetics of many drugs [1,2]. Moreover, serum albumin (SA) was found to be an important extracellular antioxidant [1,3]. SA within normal concentrations may play an important role in inhibiting platelet activation and aggregation [4,5] and vascular endothelial apoptosis [6]. A number of studies have revealed that SA levels are negatively related to incidence of acute myocardial infarction (AMI) [7,8] and stroke [9]. Low SA levels in patients with ACS was found to be an independent predictor of in-hospital all-cause mortality [10] and new-onset heart failure [11]. Low SA level (< 3.8 g/dl) before percutaneous coronary intervention (PCI) is independently associated with worse long-term outcomes [12].

The wide use of primary PCI and the improvement of pharmacotherapy have led to dramatic reduction of short-term mortality after AMI in the past 3 decades [13–15]. Therefore, long-term outcome prediction for AMI has become a concern now. Previous studies showed low SA levels are an independent predictor for long-term all-cause mortality in patients with AMI [16,17]. However, little is known about the relationship between SA and long-term cardiovascular and cardiac mortality. The aim of this study was to evaluate the association of SA with long-term all-cause, cardiovascular, and cardiac mortality in patients with first-onset AMI.

2. Materials and methods

2.1. The database and patients

The cohort study enrolled consecutive AMI patients that were admitted to the Department of Cardiology at the First Affiliated Hospital of Soochow University from January 1, 2011, to June 30, 2016. Only

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native Suzhou residents were included. Demographic data were collected from the hospital medical records, including clinical characteristics, risk factors, laboratory blood analysis, echocardiography, comorbidities, and interventions. Mortality data were obtained from the mortality database set up by the Suzhou Center for Disease Control and Prevention. The time and cause of death were described in detail in the database. Exclusion criteria included (1) those with chronic inflammatory diseases; (2) those with malignant tumors; (3) those with uremia or on dialysis; (4) those without SA laboratory results; (5) those with a confirmatory history of myocardial infarction; and (6) those died during hospitalization. The study was approved by the ethics committee of Soochow University and complied with the principles outlined in the Declaration of Helsinki.

2.2. Definitions and diagnoses

The first-onset AMI was defined as acute myocardial infarction diagnosed for the first time in our department without a history of myocardial infarction [18]. Cardiac death was defined as death from coronary artery disease (CAD), cardiogenic shock, or sudden death. Cardiovascular death was defined as death from cardiac disease, ischemic stroke (Is-stroke), or hemorrhagic stroke (He-stroke). Heart failure was defined as Killip class ≥ 2. Kidney dysfunction was defined as eGFR < 60 ml/min/1.73 m^2, calculated with the MDRD equation [19].

2.3. Lab measurements

Fasting blood (8 h) on the second-day morning after admission was drawn to detect SA and lipid profiles. In addition, all the blood biomarkers were detected within 24 h after admission. SA concentrations were quantified by Bromcresol Green from Sekisui Co. Ltd.

2.4. Statistical analysis

Continuous variables were expressed as mean ± standard deviation (SD) or median (interquartile range, IQR) as appropriate. Categorical variables were expressed as frequencies and percentages. SA was grouped into tertiles for analysis. One-way analysis of variance or the Kruskal-Wallis test was used to compare continuous variables between the SA groups. Chi-squared test was performed to compare categorical variables. Unadjusted cumulative mortality rates were estimated using Kaplan-Meier curves and compared across SA tertiles. Effects of SA levels on mortality rates after AMI were determined using multivariate Cox proportional hazard regression analysis with backward selection. The candidate covariates included in the multivariate analysis were those associated with corresponding mortality rates in the respective univariate analyses. The data were analyzed using Stata 13.0. $P < 0.05$ represented statistically significant differences.

3. Results

The study enrolled 2949 consecutive patients with AMI for potential analysis, among whom, 287 based on a confirmatory history of myocardial infarction, 56 patients with no SA exams, 219 with confounding comorbidity (malignant tumors, chronic inflammatory diseases, decreased liver function, and uremia or on dialysis), 82 died during hospitalization. Finally, 2305 patients with first-onset AMI were included in the analysis.

3.1. Demographic and baseline data of study subjects

The characteristics grouped by SA levels are summarized in Table 1. Among 2305 patients, 1836 (79.7%) were males. The median age was 65 years, and the median SA concentration was 3.92 mg/l. SA levels ≤ 3.62, 3.63–4.08, > 4.08 g/dl were defined as low, intermediate, and high tertile, respectively. Patients in low tertile were older and more likely to experience heart failure, kidney dysfunction, ischemic or hemorrhagic stroke, atrial fibrillation/flutter, anemia, and triple-vessel disease. Patients in high tertile were more likely to receive PCI during hospitalization and had higher levels of hyperlipidemia and a current smoking habit.

The median follow-up was 3 years. During this period, a total of 262 (11.4%) patients died, among whom, 198 (75.6%) died of cardiovascular diseases and 159 (60.7%) died of cardiac diseases.

3.2. Association of albumin levels with long-term all-cause, cardiovascular, and cardiac mortality in patients with first-onset AMI

Fig. 1 shows the unadjusted cumulative all-cause, cardiovascular, and cardiac mortality after AMI by SA tertiles. The results of log-rank test showed that cumulative incidences of all-cause, cardiovascular, and cardiac death were significantly different among SA tertiles (three $P < 0.001$).

Table 2 shows Cox proportional hazard analysis for all-cause, cardiovascular and cardiac death. The high-tertile group was used as reference. In univariate Cox modeling, hazard ratios (HRs) for all-cause death were 1.81 (95% CI, 1.22–2.67; $P = 0.003$) and 4.34 (95% CI, 3.07–6.15; $P < 0.0001$) for intermediate and low tertile, respectively (p-for-trend < 0.0001). Similarly, cardiovascular and cardiac mortality also increased clearly as SA levels declined (both p for trend < 0.0001). In multivariate-adjusted Cox modeling, the adjusted HRs for all-cause death were 1.21 (95% CI, 0.82–1.8; $P = 0.338$) and 1.74 (95% CI, 1.21–2.52; $P = 0.003$) for intermediate and low tertile, respectively (p-for-trend = 0.001); The equivalent values for cardiovascular death were 1.13 (95% CI, 0.72–1.79; $P = 0.588$) and 1.64 (95% CI, 1.07–2.49; $P = 0.022$) for intermediate and low tertile, respectively (p-for-trend = 0.009); The corresponding values for cardiac death were 1.07 (95% CI, 0.64–1.77; $P = 0.806$) and 1.59 (95% CI, 1.004–2.53; $P = 0.048$) for intermediate and low tertile, respectively (p-for-trend = 0.022). The multivariate-adjusted HRs showed that Low SA level was an independent predictor of long-term all-cause, cardiovascular, and cardiac mortality in patients with first-onset AMI. There was a dose–response relationship between decreased SA levels and increased long-term all-cause, cardiovascular, and cardiac mortality.

Univariate Cox modeling of each candidate variable and multivariate-adjusted Cox modeling with backward selection for all-cause, cardiovascular and cardiac death were described in detail in Table 3. After adjustment for confounding variables, adjusted HRs per 1-g/dl decrease in SA concentrations were 1.66, 95% CI (1.24–2.22), $P = 0.001$ for all-cause death, 1.47 (1.05–2.05), 0.024 for cardiovascular death, and 1.61 (1.11–2.34), 0.012 for cardiac death.

4. Discussion

The report was based on a cohort study of 2305 patients with first-onset AMI. The major finding was that low SA level on admission was an independent predictor for long-term all-cause, cardiovascular, and cardiac mortality among patients with first-onset AMI. Moreover, there was a dose–response relationship between decreased SA concentrations and increased long-term all-cause, cardiovascular, and cardiac mortality.

Previous studies have shown that low SA levels are associated with the development of coronary heart disease and all-cause mortality risk [7,20]. Low SA levels predict higher incidence of AMI [7,8]. A previous study by Plakht et al. at 2016 demonstrated that the reduction of SA levels is a strong marker of all-cause mortality in 8750 patients admitted AMI in Israel [16]. Our report was consistent with this conclusion. In addition, our work focused on the association between SA and long-term cardiovascular and cardiac mortality, which was still significant after adjustment for many important covariates. Consistent with previous studies [12,16,21], our data indicated that the patients