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The effect of serum potassium level on in-hospital and long-term mortality in ST elevation myocardial infarction

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ABSTRACT

Current studies evaluating the effect of serum potassium levels on mortality in patients with ST elevation myocardial infarction (STEMI) are lacking. We analyzed retrospectively 3760 patients diagnosed with STEMI. Mean serum potassium levels were categorized accordingly: <3.0, 3.0 to <3.5, 3.5 to <4.0, 4.0 to <4.5, 4.5 to <5.0, 5.0 to <5.5, and ≥5.5 mEq/L. The lowest mortality was determined in patients with serum potassium level of 4 to <4.5 mEq/L whereas mortality was higher in patients with serum potassium levels of ≥5.0 and <3.5 mEq/L. In a multivariable Cox-proportional regression analysis, the mortality risk was higher for patients with serum potassium levels of ≥5 mEq/L [hazard ratio (HR), 2.11; 95% confidence interval (CI) 1.23–4.74 and HR, 4.20; 95% CI 1.08–8.23, for patients with potassium levels of 5 to <5.5 mEq/L and ≥5.5 mEq/L, respectively]. In-hospital and long-term mortality risks were also higher for patients with serum potassium levels of ≤3.5 mEq/L. Conversely, ventricular arrhythmias were higher only for patients with serum potassium level of ≤3.5 mEq/L. Furthermore, a significant relationship was found between the patient with serum potassium levels of ≤3.5 mEq/L and ventricular arrhythmias.

1. Introduction

Serum potassium level has a substantial role in cardiovascular disorders. Total body potassium is 3500 mEq/L and most of the body potassium is located intracellularly [1]. The intracellular potassium concentration is approximately 140 mEq/L compared with 4 to 5 mEq/L in the extracellular fluid. This disributional diversity is maintained by the Na-K-ATPase pump in the cell membrane [2]. Hypokalemia is defined as serum potassium levels of <3.5 mEq/L and often been encountered in patients with acute myocardial infarction (AMI). As a consequence, ventricular arrhythmia after AMI has been observed based on ischemic state and hypokalemia. By virtue of previous studies, current guidelines for serum potassium in cardiovascular disorders recommend maintaining serum potassium level of 4 to 4.5 mEq/L in patients with AMI [3,4]. The recent studies examined the recommendations of guidelines and the lowest mortality was observed in serum potassium level of 3.5 to 4 mEq/L in patients with AMI [5–7]. Because of important improvements in revascularization and drug therapies, it is an obligation to re-evaluate the impact of serum potassium level with respect to mortality and ventricular arrhythmias in patients with AMI. Additionally, previous studies were performed without differentiating the patients with non-ST segment elevation myocardial infarction (NSTEMI) from ST-segment elevation myocardial infarction (STEMI). To address this critical diversity, further investigations were needed for confirmation. The aim of the current study is to assess the impact of serum potassium level on in-hospital mortality, ventricular arrhythmias and long-term mortality in patients with STEMI.

2. Methods

A total of 4470 consecutive patients who fulfilled the criteria of STEMI were admitted to the emergency department of a tertiary heart center from January 2010 to December 2012 were evaluated retrospectively. A total of 388 patients who had lower than two serum potassium measurements were excluded from the study and 286 patients were excluded from the study because of lost data after hospitalization. An additional 36 patients who died in first 24 h of hospitalization were excluded to reduce the possible survival bias. STEMI was diagnosed as the presence of new ST segment elevation of >0.1 mV (1 mm) in two contiguous leads or definite or probable a new left brunch bundle block. The patients were evaluated in a high volume tertiary heart center [>2500 percutaneous coronary intervention (PCI) per year] and this study was approved by the institutional review board.

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3. Data sources

Clinical, demographic, historical, angiographic, treatment and laboratory data were obtained from the hospital's medical database. Serum potassium levels for each patient during hospitalization were collected and reviewed by a trained coordinator. The mean serum potassium level is defined as the average of all measurements during hospitalization. Serum potassium level was measured by the ISE indirect method using Rosch, Cobas 6000 Biochemistry Auto-Analyzer, USA. Patients were classified into 7 groups to evaluate the association between the events (in-hospital mortality, in-hospital ventricular arrhythmia and long-term mortality) and mean serum potassium levels: ≤3.0, 3.0 to 3.5, 3.5 to <4.0, 4.0 to <4.5, 4.5 to <5.0, 5.0 to <5.5, and ≥5.5 mEq/L. The aim of this study was the prognostic impact of the mean serum potassium levels on in-hospital and long-term mortality in patients with STEMI. Because, recommendations of guidelines and previous studies were based on the potassium levels during the hospitalizaton in patients with AMI but not STEMI [3–7]. The primary end points were in-hospital and long-term (4-year) mortality. Evaluation of mortality was obtained from hospital's medical database or by follow-up interviews (directly or by telephone).

In-hospital procedures such as primary PCI, valve surgery or coronary artery by-pass graft surgery (CABG) were performed by expert interventional cardiologists and cardiovascular surgeons. Emergency PCIs were performed via percutaneous femoral approach and CABG's were performed by the median sternotomy. Echocardiogram was performed in 99% patients at the first 48 h in coronary care unit and left ventricular ejection fraction (LVEF) was calculated by using Simpson method [8]. Non-ionic low osmolality contrast media was used in all patients. The occurrences of ventricular arrhythmias were evaluated by a trained study coordinator. Following coronary angiography or PCI, the patients were allowed in the coronary care unit for observation. After cardiac surgery, the patient was allowed in the cardiovascular surgery care unit. The estimated glomerular filtration rate (eGFR) was calculated by using the Cockcroft–Gault equation [9]. The drugs were administered during the hospitalization according to the European Society of Cardiology Guidelines [10].

4. Statistical analysis

Baseline characteristics were compared among the patients by mean serum potassium level and categorized accordingly; ≤3.0, 3.0 to <3.5, 3.5 to 4.0, 4.0 to <4.5, 4.5 to <5.0, 5.0 to <5.5, and ≥5.5 mEq/L. Kolmogorov–Smirnov test was used for testing of normality. Continuous variables with normal distributions were expressed as mean ± SD and compared using one-way analysis of variance. Continuous variables with skewed distributions were expressed as median (25th and 75th percentiles) and compared using the Kruskal–Wallis test. Categorical variables were expressed as number and percentages and Pearson's chi-square or Fisher's exact tests were used to evaluate the differences. Hierarchical logistic regression was used to assess the independent relationship between mean serum potassium levels and in-hospital mortality, after adjustment for confounders. The odds ratios indicate the relative risk of in-hospital mortality or in-hospital ventricular arrhythmias in each potassium level compared with those in the lowest-risk subgroup (4.0 to <4.5 mEq/L). After follow-up periods of 23.7 ± 12.3 months, the median survival time (MST) of seven groups was compared using the Kaplan–Meier survival method. Overall survival was calculated from the day of diagnosis to the day of death or last follow-up. Patients lost to follow-up were censored at the time of last follow-up. Differences between the groups were analyzed by the log-rank test. A forward Cox proportional regression model was used for multivariable analysis. The hazard ratios indicate the relative risk of death in each potassium level subgroup compared with those in the lowest-risk subgroup (4.0 to <4.5 mEq/L). In multivariable models, confounders in bivariate analysis as predictors of in-hospital and long-term mortality were considered. Four models were generated to obtain the impact of potential confounders on the association between mean serum potassium level and mortality. These 4 models include: (1) unadjusted; (2) adjusted for age, sex, Killip class, and LVEF; (3) adjusted for comorbidities and eGFR; (4) adjusted for all confounders including demographics (age, sex); first measurement during hospitalization of the following laboratory values (eGFR, CRP, potassium, glucose, white blood cell count, hematocrit); peak troponin level; presence of cardiogenic shock and acute respiratory failure on admission; procedures during hospitalization; acute kidney injury during hospitalization; comorbidities (diabetes, heart failure, hypertension, cerebrovascular disease, peripheral vascular disease, chronic obstructive pulmonary disease, dialysis); and medications during hospitalization. Acute kidney injury is defined as an increase in serum creatinine level of ≥0.3 mg/dL or a relative increase in serum creatinine level of ≥50% [11,12]. A two-tailed p value of <0.05 was considered as statistically significant, and 95% CIs were presented for all odds ratios and hazard ratios. Analyses were performed using Statistical Package for Social Sciences software, version 20.0 (SPSS; IBM, Armonk, New York, USA).

5. Results

A total of 3760 patients (mean age 58.0 ± 11.6 years; men 81%) with STEMI had at least 2 serum potassium measurements during hospitalization were included. Potassium level at admission was measured within the first 6 h of hospitalization. Second potassium level was measured 18–24 h after the first measurement. There was significant difference in terms of gender ($p < 0.001$) among the subgroups of serum potassium level. The groups were similar with respect to age ($p = 0.412$). The mean number of serum potassium measurements per patient was 4.2 ± 3.3 The patients' baseline characteristics, categorized by mean serum potassium level, are listed in Table 1. Complex differences were observed between baseline variables and among the groups, especially at the extremes of serum potassium level (>5 or <3.5 mEq/L). The history of patients showed significant difference in terms of CABG ($p = 0.022$) and chronic kidney disease ($p = 0.002$. The other history of patients were similar in terms of hypertension ($p = 0.077$), diabetes mellitus ($p = 0.143$), hyperlipidemia ($p = 0.860$), current smoking status ($p = 0.705$), myocardial infarction ($p = 0.165$), percutaneous coronary intervention ($p = 0.996$), and dialysis ($p = 0.361$). There was no significant difference in terms of, systolic blood pressure ($p = 0.073$), diastolic blood pressure ($p = 0.141$), heart rate ($p = 0.453$), Killip Class ($p = 0.362$), LVEF ($p = 0.214$), chest pain period ($p = 0.278$) and door-to-balloon time ($p = 0.090$). In laboratory parameters, the groups were similar with respect to admission creatine kinase-MB ($p = 0.226$), peak creatine kinase-MB ($p = 0.141$), creatinine ($p = 0.068$), white blood cell count ($p = 0.185$), glucose ($p = 0.136$), hematocrit ($p = 0.366$) and platelet count ($p = 0.617$). The lowest in-hospital and long-term mortality and in-hospital arrhythmia occurred in patients with serum potassium levels of 4 to <4.5 mEq/L. The highest in-hospital and long-term mortality and in-hospital ventricular arrhythmia occurred in patients with extreme serum potassium levels of <3 and >5.5 mEq/L ($p < 0.001$). In-hospital ventricular arrhythmia and mortality were different in that its frequency increased by not only increasing serum potassium level but also decreasing serum potassium level ($p < 0.001$) (Fig. 1). But significant differences were only observed in decreasing serum potassium level.

The patients were followed up for a mean period of 23.7 ± 12.3 months. The 4-year Kaplan–Meier overall survival (OS) were 44%, 86%, 94%, 96%, 93%, 87% and 77% respectively. The Kaplan–Meier cumulative survival curve was shown in Fig. 2. Table 2 lists unadjusted and adjusted hierarchical logistic regression for in-hospital events (mortality and ventricular arrhythmia) and Cox proportional regression analysis for long-mortality categorized by serum potassium levels. Unadjusted analysis showed a U-shaped relation between serum potassium levels