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Original article

Impact of symptom presentation on in-hospital outcomes in patients with acute myocardial infarction

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ABSTRACT

Background: Limited data exist regarding the association between symptom presentation of acute myocardial infarction (AMI) and in-hospital outcomes.
Methods: We analyzed data of the Japanese registry of acute Myocardial INfarction diagnosed by Universal dEfiniTion (J-MINUET). This was a prospective and multicenter registry consisting of 3085 AMI patients with available data of symptoms, who were hospitalized within 48 h from onset during July 2012 to March 2014. We defined typical symptoms as any of chest pain or pressure due to myocardial ischemia.
Results: Of this study population, 642 patients (20.8%) had atypical symptoms (atypical group) and the remaining 2443 patients (79.2%) showed typical symptoms (typical group). Compared to the typical group, the atypical group was associated with higher age, more females, hypertension, diabetes, chronic kidney disease, history of cardiovascular disease, non-ST elevation MI, and Killip class $\geq$2. In the atypical group, urgent percutaneous coronary intervention was less frequently performed than in the typical group, and in STEMI patients door-to-balloon time was longer in the atypical than typical group.

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Atypical group had larger infarct size than typical group. Furthermore, in-hospital mortality was significantly higher in atypical than in typical group (19.5% vs. 3.3%, $p < 0.001$). In multivariable analysis, presence of atypical symptoms was an independent predictor of in-hospital mortality (odds ratio 3.12, 95% confidence interval 2.19 to 4.47, $p < 0.001$). Moreover, the association between atypical symptoms and mortality was consistent across each subgroup.
Conclusions: Atypical symptoms of AMI were associated with less invasive therapy and poor outcome. Attention should be directed to these high-risk patients.

Introduction

Acute myocardial infarction (AMI) is a leading cause of death in developed countries. Timely reperfusion is essential to afford benefits of reperfusion therapy for ST-elevation MI (STEMI). For patients undergoing primary percutaneous coronary intervention (PCI), it is recommended to achieve door-to-balloon or emergency medical contact-to-balloon time less than 90 min [1]. In patients with non ST-elevation MI (NSTEMI) who had elevated troponin, urgent angiography with intent to perform revascularization if appropriate (early invasive strategy) is indicated. Although recognition of AMI symptoms is essential, it is sometimes difficult to make a prompt diagnosis of AMI for patients complaining of atypical symptoms [2–6]. It is worthwhile to recognize clinical presentation, background, management, and outcomes of patients with atypical symptoms in the contemporary era. The Japanese registry of acute myocardial infarction diagnosed by universal definition (J-MINUET) is the latest multicenter registry that enrolled 3283 Japanese patients with AMI [7]. In this post hoc analysis of the J-MINUET study, we investigated clinical presentation, background, management, and outcomes of AMI patients presenting with atypical symptoms in comparison to those with typical symptoms.

Materials and methods

The J-MINUET is a large-scale, prospective, multicenter registry of Japanese patients hospitalized for AMI diagnosed by the universal definition (UMIN000010037) [7]. We have already described this registry in detail. Briefly, it enrolled 3283 consecutive patients who were admitted within 48 h from onset of AMI at 28 Japanese medical institutions between July 2012 and March 2014. Diagnosis of AMI was based on the ESC/ACCF/AHA/World Heart Federation Task Force for the Universal Definition of Myocardial Infarction [8] and depended on the rise and/or fall of cardiac biomarkers (preferred: troponin) with at least 1 value above the 99th percentile of the upper reference limit observed together with evidence of myocardial ischemia with at least one of the following: symptoms of ischemia, electrocardiographic changes indicative of new ischemia, development of pathological Q waves in the electrocardiograph and imaging evidence of new loss of viable myocardium or new regional wall motion abnormalities. The J-MINUET study included only type 1 (spontaneous MI related to ischemia from primary coronary event) and type 2 (MI secondary to ischemia because of either increased oxygen demand or decreased supply). This study was conducted in accordance with the Declaration of Helsinki. The protocol was approved by the ethics committees of every participating institution.

In the present study, typical symptoms were defined as any symptom of chest pain or pressure due to myocardial ischemia, indifferent to the pain radiating to arm, neck, or jaw, and we instructed researchers, experienced physicians, to tick a 'yes' or 'no' box about typical symptoms using their own clinical judgment and taking into account all factors from history and examination [9]. We considered the specific symptoms of shortness of breath, chest discomfort, nausea, vomiting, syncope, or none of those symptoms as atypical symptoms. In case patients had several symptoms, we divided patients with typical chest pain or compression into typical group, even if they had other specific symptoms such as nausea or syncope, and patients with only atypical symptoms were divided into the atypical group.

The primary endpoint was in-hospital mortality. The secondary endpoint was major adverse cardiac events (MACE), defined as a composite of all-cause death, cardiac failure, ventricular tachycardia and/or ventricular fibrillation, and bleeding during hospitalization. Cardiac failure was defined as congestive heart failure and/or cardiogenic shock that required treatment.

All values are expressed as medians (interquartile range) for continuous variables, or counts and percentages for categorical variables. Univariate and multivariate logistic regression models are used to calculate odds ratios (ORs) for all cardiac events and 95% confidence intervals (CIs). Variables with $p < 0.05$ in a univariate analysis were included in a multivariate model to find the independent predictors for mortality. The consistency of the primary endpoint in eleven clinically relevant subgroups was examined with formal interaction testing. Missing values were imputed by using the multivariate normal model, using the chained equations approach [10]. Multiple imputation method was previously described [11]. Cardiovascular disease was defined as any of previous myocardial infarction, stroke, or peripheral artery disease. Chronic kidney disease was defined as estimated glomerular filtration rate $\leq$60 ml/min/1.73 m^2 in this study. Urgent PCI consisted of primary PCI for STEMI and urgent angiography followed by PCI for NSTEMI. Urgent revascularization was either urgent PCI or urgent coronary artery bypass graft. All statistical tests were 2-sided and $p < 0.05$ was regarded as significant. All statistical analyses were carried out using JMP, version 11.0.0 (SAS Institute Inc, Cary, NC, USA) and STATA, version 12 (StataCorp LP, College Station, TX, USA).

Results

Among 3283 enrolled in the J-MINUET study, we excluded 198 patients without available data of symptoms. This study was conducted in the remaining 3085 patients with AMI. There were 642 patients (20.8%) who presented with atypical symptoms (atypical group) and 2443 patients (79.2%) with typical symptoms (typical group). In the atypical group, 197 patients (30.7%) presented with chest discomfort, 166 (25.9%) with dyspnea, 124 (19.3%) with syncope, 100 (15.6%) with nausea or vomiting, 10 without symptoms (1.6%), and 51 (7.9%) with other miscellaneous symptoms (Fig. 1).

Baseline characteristics are shown in Table 1. Atypical symptoms were associated with a higher frequency of advanced age, females, hypertension, diabetes, chronic kidney disease, previous myocardial infarction, previous myocardial revascularization, stroke, peripheral artery disease, non-ST elevation MI, and Killip

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