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Impact of Cardiogenic Vomiting in Patients with STEMI: A Study From China

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Background: Different patients with ST-elevation myocardial infarction (STEMI) have different symptoms. A third of them may have medical emergencies caused by symptoms such as vomiting and syncope. These concomitant symptoms may influence subsequent therapy and final outcomes. The aim of this study was to determine whether cardiogenic vomiting is a predictor of clinical outcomes in patients with STEMI.





Material/Methods: We classified 152 STEMI patients from different areas into 2 groups on the basis of vomiting: group A and group B. Their demographics and conditions of hospitalization were recorded. After follow-up, major adverse cardiac events (MACE) were regarded as study endpoints for the effect of cardiogenic vomiting in STEMI patients.

Results: We found no significant difference in demographic and clinical characteristics of the 2 groups ($P > 0.05$). The hospitalized conditions of group A were more serious than in group B. During a follow-up of 6 months, MACE rate was higher in vomiting patients (42; 67.7%) compared with group B (25; 27.8%). Multivariate Cox regression analysis revealed that cardiogenic vomiting was an independent predictor of clinical outcomes.

Conclusions: Cardiogenic vomiting is a useful predictor of major adverse cardiac events in STEMI patients for the hospitalization and after discharge.

MeSH Keywords: **Myocardial Infarction • Prognosis • Vomiting**

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Background

ST-elevation myocardial infarction (STEMI) is a clinical syndrome defined by characteristic symptoms of myocardial ischemia in association with persistent electrocardiographic (ECG) ST elevation and subsequent release of biomarkers of myocardial necrosis. The pathogenesis of STEMI is thrombosis and occlusion of coronary arteries, which results from the formation and rupture of vulnerable coronary atherosclerotic plaques. It can lead to serious cardiovascular events such as malignant arrhythmia, cardiogenic shock, and sudden cardiac death. STEMI has become a major public health problem due to its high morbidity and mortality following the formation of the aging society [1].

The benefits of time-dependent therapeutic interventions for acute myocardial infarction (AMI) depend on prompt and accurate diagnosis of AMI by emergency department physicians. Most patients with STEMI have persistent and unbearable chest pain and one-third have medical emergencies due to symptoms such as vomiting and syncope [2,3], but in clinical work the importance of these simultaneous symptoms are often ignored. In addition, these concomitant symptoms and other diseases may have an influence on subsequent therapy and final outcomes. Recently, many studies have confirmed that hyperlipidemia, tobacco use, and some other factors are risk predictors of patients with STEMI. Hyperlipidemia is the condition of abnormally elevated levels of any or all lipids and/or lipoproteins in the blood. High concentrations of lipids damage the blood vessel wall, leading to atherosclerosis and formation of atherosclerotic plaque, which cause myocardial infarction. Smoking has been identified as a modifiable risk factor for acute myocardial infarction (AMI). The mechanism of the adverse effects of cigarette smoking on the coronary arterial circulation is complex and multifactorial. Smoking increases both heart rate and blood pressure and reduces the dimension of the coronary arteries and coronary blood flow. However, few researchers have focused on the significance of vomiting in STEMI patients, especially those patients without digestive diseases. Physicians usually think that vomiting is associated with a stress ulcer caused by STEMI, while ignoring cardiogenic vomiting. In fact, cardiogenic vomiting in STEMI usually prompts the massive infarction and multiple complications. It remains unknown whether vomiting affects the final outcome in STEMI patients. The purpose of this study was to investigate the relationship between vomiting and clinical outcomes in patients with STEMI.

Material and Methods

Data source and population of patients

From October 2011 to January 2014, a total of 152 patients diagnosed with STEMI were analyzed retrospectively. The

patients were divided into 2 groups on the basis of vomiting: 62 patients with vomiting were in group A and 90 patients without vomiting were in group B. Their demographics were documented, including age, gender, hypertension, tobacco use, diabetes mellitus, hyperlipidemia, and body mass index (BMI). We collected data on the Killip classification of cardiac function, left ventricular ejection fraction (LVEF), the culprit artery, and the peak level of troponin T (TnT), brain natriuretic peptide (BNP). We also compare various factors, such as acute heart failure, cardiogenic shock, malignant arrhythmia, and hospital mortality.

Patients who had a confirmed diagnosis of STEMI were eligible to participate in this study if: 1) the age was between 18 and 80 years old; 2) the patients were able to understand the study content and provide consent; and 3) the patients were willing to accept the necessary follow-up, therapy, and laboratory examination. The exclusion criteria were: 1) patients with other diseases which may lead to the vomiting, including acute gastritis, peptic ulcer, acute cholecystitis, and acute pancreatitis; 2) patients took medicines which may cause vomiting; 3) patients with a life expectancy of ≤ 12 months; 4) pregnant and lactating women; 5) the patients who were unable to understand the study content or provide consent; 6) the patients who participated in other study programs during the same period. The diagnosis of STEMI was according to the World Health Organization definition of myocardial infarction (2008-09 revision) [4]. The criteria include: persistent chest pain for more than 30 min and ST elevation on 2 or more adjacent leads on body surface ECG and elevation of cardiac troponin T (cTnT) and creatine kinase (CK)-MB.

Our study was approved by the Ethics Committee of the Department of Cardiology, Beijing Chaoyang Hospital Attached to Capital Medical University and all enrolled patients gave informed written consent.

Treatment and indexes

All the patients were asked to undergo the emergency percutaneous coronary intervention to open the culprit artery as soon as STEMI was diagnosed. The mainstay of drug therapy consists of dual-antiplatelet therapy (DAPT) and statins. Other medicines, like β -blockers, angiotensin-converting enzyme inhibitors (ACEI)/angiotensin II receptor antagonists (ARB), calcium channel blocker (CCB), diuretics, and nitrates were also used on occasion. Proton pump inhibitors (PPIs) were used to alleviate vomiting and prevent gastric mucosa damage from medicines (e.g., antiplatelet drugs) in patients with vomiting. After hospitalization, myocardial injury markers and BNP were tested every 8 hours in the first 24 hours and then on the following 2 days. According to the results, the highest level was defined as the peak level. Echocardiography was done on the

first day and before discharged to evaluate cardiac function. In addition, we recorded their culprit artery during coronary angiography. Patients who suffered from acute left heart failure, cardiogenic shock, malignant arrhythmia, and mortality in the hospital were recorded specially. Acute left heart failure was defined according to ESC guidelines for the diagnosis and treatment of acute and chronic heart failure [5]. Malignant arrhythmia consisted of ventricular tachycardia (sustained monomorphic, polymorphic), ventricular fibrillation, severe intraventricular block, complete atrioventricular block, and that Aase syndrome caused by these arrhythmia. Furthermore, only cardiac death was recorded to compare the mortality.

Follow-up and endpoints

All the patients were followed up for 6 months after discharge. The medical history was taken, and relevant examinations were performed if necessary. Patients were also asked carefully at each follow-up regarding the presence or absence of relevant symptoms. Rehospitalization at 1 month and 6 months were important indexes to evaluate cardiac conditions. Clinical follow-up data were gathered by reviewing outpatient records. The study endpoint was 6-month major adverse cardiac events (MACE). The MACE contains a composite of: 1) cardiac death; 2) cardiogenic shock; 3) severe acute ventricular failure; and 4) malignant arrhythmia. Cardiac mortality was also analyzed separately in the study.

Statistical analysis

Results are expressed as mean \pm standard deviation (SD) for continuous variables and as frequencies for categorical variables. Differences between groups were examined by nonparametric test and chi-square test for continuous and categorical variables, respectively. The effect of vomiting on clinical outcomes was assessed with the use of a multivariate Cox proportional hazards model. Other variables that were significantly associated with outcome were entered into the model in a stepwise procedure. An alpha value of 0.05, corresponding to a p value < 0.05 , served as criterion for establishing statistical significance. The 95% confidence intervals of the hazard ratio were reported for all of the significant risk factors. Analysis was performed using SPSS (Version 19.0) and STATA (Version 16.0).

Results

Baseline characteristics

We collected 152 patients with STEMI. The mean age of the 152 patients was 66.63 ± 9.62 . We enrolled 98 male patients and 54 female patients. According to the occurrence of vomiting, 62 patients were divided into Group A, while the other

90 patients without vomiting were in Group B. The comparison between the baseline information and previous medical history of 2 groups are shown in Table 1. There were no significant differences in the ratios of sex, hypertension, hyperlipidemia, diabetes mellitus, and tobacco use in the 2 groups, which may have an effect on the outcomes. In addition, no significant differences were found in their BMI, age, and other baseline characteristics. STEMI with vomiting is usually associated with the inferior myocardial infarction or the lesion in right coronary artery. To our surprise, the comparison showed no significant difference in the distribution of culprit artery in our study. Echocardiography was used to evaluate their condition of cardiac function. The result showed that the differences of cardiac function were not significant. Taken together, the 2 groups were comparable with regard to their demographic and clinical characteristics ($P > 0.05$).

Hospitalization characteristics and follow-ups

All the 152 patients underwent emergency PCI and standard medical therapy, including aspirin, clopidogrel, statins, and other necessary medicines. During their hospitalization, their serum peak levels of TNT and BNP were recorded, as well as the occurrence of acute heart failure, cardiogenic shock, malignant arrhythmia, and hospital mortality. Furthermore, the days of hospitalization were also recorded to study the effect of vomiting. Results showed that something different about hospitalized conditions happened in the 2 groups (Table 2). Firstly, the peak levels of TNT and BNP in group A were higher than in group B, although the differences were not significant (both $p > 0.05$). The comparable peak levels of myocardial injury markers had similar size of infarction and severity. Then, several cardiac events were also recorded to evaluate the short-term prognosis and hospitalized conditions. In total, 33 patients suffered from acute heart failure in group A, but only 25 patients in group B, and the difference was significant ($p < 0.05$). Furthermore, the incidences of cardiogenic shock and malignant arrhythmia were also significantly different in the 2 groups ($p < 0.01$; $p < 0.05$). In addition, 2 patients died during hospitalization in group A and 1 in group B ($p > 0.05$). Because the number of deaths was not enough, the significance of the comparison is limited. We also focused on their days of hospitalization. Taken together, we mixed all these events above as MACE to study the effect on STEMI. Results showed that MACE appeared in 45 patients in group A and 30 in group B. Statistical testing demonstrated that the difference was significant ($p < 0.01$). The average days of hospitalization in group A was 10.6 ± 1.2 , while the result was 9.1 ± 0.8 in group B. The result was significantly different between the 2 groups ($p < 0.01$) and it showed the potential significance of vomiting in STEMI patient short-term outcomes. After discharge, all the patients received a 6-month follow-up. As major endpoints, MACE and cardiac death received special attention to evaluate whether vomiting was a useful prognosis factor of

Table 1. Baseline characteristics.

Characteristic	Group A (n=62)	Group B (n=90)	P-value
Age (years)	65.38±12.43	68.18±9.48	0.240
Gender (M/F)	40/22	58/22	–
Hypertension (% , n)	58.1 (36)	48.9 (44)	0.316
Hyperlipidemia(% , n)	48.4 (30)	45.6 (41)	0.884
Diabetes mellitus (% , n)	61.3 (38)	55.6 (50)	0.786
Tobacco use (% , n)	56.5 (35)	61.1 (55)	0.788
BMI (kg/m ²)	24.1±2.2	24.6±2.1	0.428
LVEF	48.2±16.0	51.6±13.5	0.357
Culprit artery			
LAD	37.1 (23)	33.3 (30)	0.749
LCX	19.4 (12)	24.4 (22)	0.699
RCA	43.5 (27)	42.3 (38)	0.518

BMI – body mass index; LVEF – left ventricular ejection fraction; LAD – left anterior descending; LCX – left circumflex artery; RCA – right coronary artery.

Table 2. Hospitalization and follow-up characteristics.

Characteristic	Group A (n=62)	Group B (n=90)	P-value
Hospitalization	4.8±3.6	4.6±3.8	0.890
TNT (ng/ml)	6560±602	5988±625	0.465
BNP (pg/ml)	53.2 (33)	27.8 (25)	0.044*
Acute heart failure (% , n)	37.1 (23)	13.3 (12)	0.009**
Cardiogenic shock (% , n)	16.1 (10)	4.4 (4)	0.045*
Malignant arrhythmia (% , n)	3.2 (2)	1.1 (1)	0.569
Hospital mortality (% , n)	72.6 (45)	33.3 (30)	0.007**
MACE (% , n)	10.6±1.2	9.1±0.8	0.009**
Hospitalized days			
Follow-up	67.7 (42)	27.8 (25)	0.003**
MACE (% , n)	9.7 (6)	3.3 (3)	0.169
Cardiac death (% , n)			

TNT – troponin T; BNP – brain natriuretic peptide; MACE – major adverse cardiac events; * p<0.05; ** p<0.01.

MACE in STEMI patients. Firstly, cardiac mortality was higher in group A than in group B but the difference was not significant ($p>0.05$). At the same time, the incidence of MACE in group A was significantly higher than in group B after the follow-up ($p=0.003$) (Figure 1). The multivariate Cox regression analysis showed a significant association between vomiting and MACE after adjusting for other relevant factors, regardless of whether MACE occurred during hospitalization or follow-up (Table 3).

Discussion

STEMI is a serious cardiovascular disorder with high morbidity and mortality. Therefore, all influencing factors should be taken into consideration so physicians can more accurately judge prognosis. In the past, many researches have elaborated the prognostic predictive value of STEMI patient outcomes, including demographics, symptoms, and treatment.

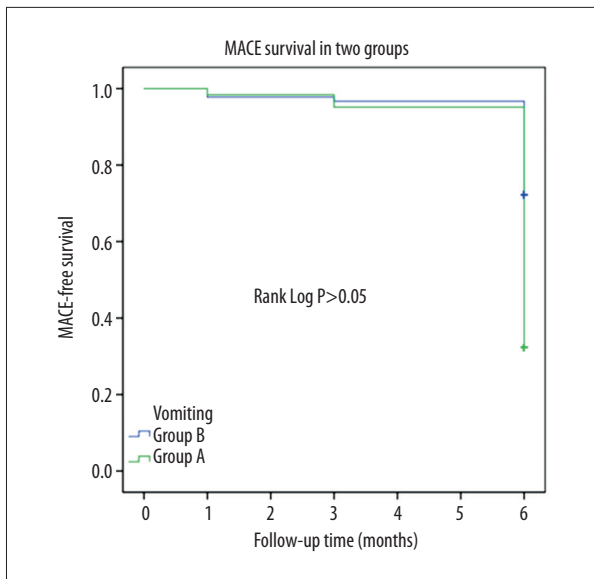


Figure 1. The Kaplan-Meier survival analysis for MACE.

Levy suggested that with limited cardiac reserve, anemia may compromise aerobic splanchnic circulation and effect the prognosis [6]. Smoking affects prognosis by prompting thrombosis and myocardial remodeling [7]. High concentrations of uric acid can lead to oxidative stress and increase the risk of cardiovascular events [8]. Other diseases also play a role, including hyperlipidemia, diabetes mellitus, and old age [9–11].

However, few studies have attached significance to vomiting in the prognosis of STEMI. It is not rare that vomiting happens to STEMI patients in the clinic. Furthermore, vomiting usually leads to aspiration or insufficient oral medication and make the condition worse. Here, we divided vomiting into 2 parts: cardiogenic vomiting and non-cardiogenic vomiting.

Usually, non-cardiogenic vomiting is caused by drug stimulation, stress ulcer, vagal reflex, myocardial inflammatory exudation and stimulation of the diaphragm and nervus phrenicus. Non-cardiogenic vomiting is an accompany symptom of STEMI and the predictive value of severity and prognosis is limited and inexact. Intensive nursing, acid inhibition, and gastric mucosa protection are alternative therapy. The most important contribution of this study was the demonstration of a direct relationship between cardiogenic vomiting and clinical outcomes in STEMI patients. In our study, the severity of STEMI in group A was higher than in group B, which is expressed in the peak level of TNT and BNP. In addition, the number of cardiac events and hospitalized days were also significantly higher in group A. After hospitalization, the conditions did not improve. The incidence of MACE was higher in group A and the multivariate Cox regression analysis showed a significant association between vomiting and MACE. All the results showed the important influence of cardiogenic vomiting on the prognosis of STEMI.

In the past, several primary mechanisms were used to explain the vomiting in STEMI. Firstly, the necrotic, ischemic, and injured cardiomyocytes from infarcted regions release lactic acid, pyruvic acid, and other metabolites. These metabolites stimulate the autonomic nerve peripheral receptors of the infarcted regions. Then, the stimulation leads to cardiogenic nausea and vomiting. Secondly, total and subtotal coronary occlusion and myocardial necrosis cause the decrease of cardiac function and ventricular dilatation, which will trigger the Bezold-Jarisch reflex and result in nausea and vomiting [12]. The impulse of unmyelinated C fibers is usually irregular and sparse. When STEMI occurs, the impulse become regular and intensive. The intensive impulse will induce vomiting [13]. In conclusion, cardiogenic vomiting is the specific performance of

Table 3. Results of multivariate Cox regression analysis with all-cause cardiac mortality and major cardiac events.

Characteristics	Hospitalization		Follow-up	
	Hazard ratio (95% CI)	p value	Hazard ratio (95% CI)	p value
Gender	0.912 (0.338–2.463)	0.856	0.996 (0.166–5.986)	0.997
BMI	1.097 (0.916–1.313)	0.315	1.173 (0.795–1.731)	0.422
TNT	0.974 (0.885–1.073)	0.597	0.994 (0.792–1.248)	0.961
LVEF	0.985 (0.957–1.013)	0.290	0.956 (0.905–1.009)	0.105
Hypertension	1.134 (0.541–2.376)	0.739	1.432 (0.251–8.182)	0.686
Diabetes	1.912 (0.880–4.156)	0.019	1.868 (0.467–7.478)	0.037
Hyperlipidemia	2.876 (1.243–6.658)	0.014	2.804 (1.206–8.826)	0.035
Tobacco use	1.762 (0.793–3.913)	0.047	1.302 (0.284–5.968)	0.734
vomiting	0.478 (0.290–0.787)	0.004	0.843 (0.679–0.980)	0.030

MACE – major adverse cardiac events; BMI – body mass index; TNT – troponin T; LVEF – left ventricular ejection fraction.

neuroregulation on STEMI. The distribution of culprit arteries in our study also confirmed that cardiogenic vomiting has nothing to do with the location of infarction, which has been reported by Fuller [14].

Several limitations to this study cannot be ignored. Firstly, the sample size of our study was small, especially the number of vomiting patients, and the follow-up time was relatively short, which may have an influence on the evaluation of the relationship between vomiting and prognosis of STEMI. Additionally, several other indexes we did not include in our study may have affected the results, including the effect of heart rate on vomiting and the reviewed coronary angiogram. Proton pump inhibitors are supposed to influence the antiplatelet effect of clopidogrel [15]. In our study, patients with vomiting were given PPIs to protect the gastric mucosa. Although the treatment is short, we could not evaluate the effect. Thrombelastogram is currently used to judge the antiplatelet effect of clopidogrel and aspirin [16]. These limitations are the key points which we

should focus on in the future. However, the achievements of our study provide certain experiences in the therapy of STEMI patients with vomiting. These patients usually have worse conditions and outcomes and therefore need to receive timely, careful, and effective treatment.

Conclusions

The current data showed that STEMI patients with vomiting usually have worse cardiac function and cardiovascular events. Cardiogenic vomiting is a useful prognostic factor of major adverse cardiac events in STEMI patients both during hospitalization and after discharge.

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