Coronary Heart Disease

Comparison of In-Hospital Outcome of Acute ST Elevation Myocardial Infarction in Patients with versus without Diabetes Mellitus

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Background: Diabetes mellitus (DM) is a stronger risk factor for coronary artery disease (CAD) and is associated with mortality and morbidity of cardiovascular disease. The in-hospital outcome in diabetic patients with acute ST elevation myocardial infarction (STEMI) is less known. The aim of this study is to evaluate in-hospital outcome of acute STEMI in patients with diabetes mellitus.

Methods: The patients with acute STEMI between November 2007 to June 2009 were enrolled, the traditional risk factors for CAD, the inflammatory marker and coronary angiographic results were recorded. The in-hospital outcome of patients with and without DM were compared.

Results: Total 239 patients with acute STEMI were enrolled. Of those, 94 (39%) were diabetic and 145 (61%) were non-diabetic patients. Older, multi-vessel diseases, poor renal function, higher killip class and the higher inflammatory marker level were associated with in-hospital mortality in patients with STEMI. In-hospital mortality was higher in diabetic than non-diabetic patients (23.4% vs. 7.6%, $p = 0.001$). Previous hypertension, cerebral vascular disease were more frequent in diabetic than in non-diabetic patients. Diabetic patients also demonstrated higher creatinine level than non-diabetic patients (creatinine: 2.14 ± 1.54 vs. 1.34 ± 0.99 mg/dl, $p < 0.001$).

Conclusion: This study suggests that in diabetic patients with acute STEMI, in-hospital mortality rate is higher than in non-diabetic patients. The aggressive treatment early in the course of diabetic patients with acute STEMI is important.

Key Words: Acute ST elevation myocardial infarction • Diabetes mellitus • Outcome

INTRODUCTION

Diabetes mellitus (DM), hypertension, hyperlipidemia, and other systemic diseases are all common risk factors of cardiovascular disease (CVD).[1-3] For risk stratification, DM is one of the strongest factor that is associated with a high rate of cardiovascular events.[4] Several studies also have demonstrated that elevated in-hospital glucose levels predict higher mortality in both diabetic and non-diabetic patients with acute myocardial infarction (AMI).[5,6] The inflammatory markers are also associated with an increased cardiovascular risk in type II diabetic patients.[7] In addition, some papers showed diabetic patients with acute coronary syndrome (ACS) had similar in-hospital mortality but higher 1-year mortality in comparison with non-diabetic patients.[8] However, there is little known about the role of DM in the in-hospital outcome in patients with acute STEMI in our population.

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The aim of present study was to evaluate the in-hospital outcome in diabetic and non-diabetic patients with acute STEMI and compare the results between two groups.

MATERIALS AND METHODS

Study population

The patients with diagnosis of acute ST-elevation myocardial infarction (STEMI) were enrolled between November 2007 and June 2009. Total 239 consecutive patients who were admitted to the Coronary Care Unit of Taipei Veterans General Hospital were included and acute STEMI was diagnosed by the following criteria as below: (1) chest pain ≥ 30 minutes in duration or more; (2) electrocardiographic (ECG) ST-segment elevation ≥ 0.1 mV in two or more leads; (3) elevated creatine kinase-MB (CK-MB) isoenzymes within 24 hours of chest pain. Most of these patients were treated according to the guideline published by American College of Cardiology/American Heart Association (ACC/AHA).[9] Information about demographic characteristics (age, gender) and traditional risk factors for ischemic heart disease [history of hypertension, coronary artery disease, cerebral vascular disease (CVD), smoking, hypercholesterolemia and diabetes mellitus] were acquired and blood samples were taken for biochemical analysis including blood glucose, lipid profile and inflammatory markers.

Hypertension (HTN) was defined as a history of HTN or antihypertensive drug therapy and diabetes mellitus was defined as a history of DM and/or usage of anti-diabetic drugs before admission. The past history of coronary artery disease was defined according to the result of previous coronary angiography (CAG) or patients who had received percutaneous coronary intervention (PCI) in the past. The past history of cerebral vascular disease was defined as a history of stroke by imaging study. Current smokers were defined as patients reported to have smoked cigarettes in previous years. Hypercholesterolemia was defined as total cholesterol level ≧ 220 mg/dl. Blood pressure and fasting glucose levels were also recorded during the in-hospital period and patients with high blood pressure (systolic blood pressure ≧ 140 mmHg or diastolic blood pressure ≧ 90 mmHg) were recorded. Admission blood samples were taken within 24 hours of onset of symptoms. Total cholesterol (TC), low-density lipoprotein cholesterol (LDL-C), high-density lipoprotein cholesterol (HDL-C), triglyceride (TG), HbA1C, and creatinine levels were measured. The admission glucose and C-reactive protein (CRP) levels were also checked immediately when the patient arrived at our emergency room (ER).

Coronary angiography and study outcome

Coronary angiography was performed on all patients during the hospitalization period. Angiographic images were assessed by at least one independent cardiologist. The infarct-related artery was identified by coronary angiography, regional wall motion abnormality and ejection fraction were recorded by the left ventriculography. Coronary artery stenosis > 50% in diameter was regarded as significant. Multi-vessel diseases was defined as more than two diseased arteries. In-hospital death was defined as any cause of death during the hospital course after onset of acute STEMI by chart record.

Statistic analysis

Data were presented as mean ± standard deviation for continuous variables. Differences in baseline characteristics between groups were determined by the unpaired *t* test for continuous variables and the $\chi 2$ test for categorical variables. Using multiple logistic regression with stepwise selection, the all variables were examined to determine the predictors of in-hospital outcome. Adjusted odds ratios with 95% confidences were calculated for in-hosital mortality. The Killip class on admission was regarded as potential confounders for the effect of DM on in-hospital mortality. All statistical analyses were performed with SPSS, version 17.0 (SPSS Inc, Chicago, Ill). Two-sided values of $p < 0.05$ were considered statistically significant.

RESULTS

The clinical baseline characteristics of the patients are presented in Table 1. Of the 239 patients with acute STEMI, 94 (39%) had type II DM. In-hospital death was observed in 33 patients including decompensated heart failure (n = 19), recurrent infarction (n = 2), ventricular arrhythmia (n = 9) and non-cardiac death (n = 3). Most of the patients were male, 125 (86.2%) in non diabetic patients and 71 (75.5%) in diabetic patients. The mean age was 66.7 ± 14.9 years in non-diabetic patients and 71.2 ± 11.9 years in diabetic patients (p = 0.011). Previous HTN and CVD were more frequently observed in diabetic patients. In diabetic patients, plasma creatinine, HbA1C and CRP level were higher than in non-diabetic patients. Admission glucose was also higher in diabetic patients compared to non-diabetic patients (212.38 ± 107.9 mg/dl vs. 128.89 ± 52.76 mg/dl, p < 0.001). Al-

Table 1. Baseline and angiographic characteristics of diabetic and non-diabetic patients

	Non-diabetic (n = 145)	Diabetic (n = 94)	p value
Clinical characteristics and risk factors			
Age (years)	66.74 ± 14.95	71.20 ± 11.94	0.011
Male gender	125 (86.2%)	71 (75.5%)	0.054
Hypertension	90 (62.1%)	72 (76.6%)	0.027
Hypercholesterolemia	48 (33.1%)	26 (27.7%)	0.456
Current smoker	39 (42.9%)	13 (26.0%)	0.07
Hx of CAD	23 (15.9%)	21 (23.3%)	0.275
Hx of CVD	12 (8.3%)	21 (22.3%)	0.004
Height (cm)	164.84 ± 7.31	164.28 ± 5.77	0.751
Weight (kg)	67.75 ± 10.97	67.10 ± 10.58	0.817
Body mass index (BMI)	24.96 ± 3.66	24.70 ± 3.54	0.781
Heart rate (bpm)	81.82 ± 24.17	86.43 ± 24.17	0.351
Systolic pressure (mmHg)	128.14 ± 30.88	129.40 ± 39.12	0.800
Diastolic pressure (mmHg)	75.87 ± 18.47	71.99 ± 19.33	0.155
Plasma creatinine (mg/dl)	1.34 ± 0.99	2.14 ± 1.54	< 0.001
HbA1c (%)	5.91 ± 1.16	7.52 ± 1.37	< 0.001
Triglyceride (mg/dl)	104.99 ± 89.03	100.57 ± 59.41	0.679
Total cholesterol (mg/dl)	172.93 ± 42.15	145.58 ± 38.99	< 0.001
HDL-cholesterol (mg/dl)	43.75 ± 12.63	36.81 ± 11.73	< 0.001
LDL-cholesterol (mg/dl)	111.62 ± 37.30	92.33 ± 33.73	< 0.001
Total cholesterol/HDL-C	4.19 ± 1.33	4.18 ± 1.16	0.935
Triglyceride > 150 mg/dl	23 (16.8%)	13 (14.3%)	0.747
C-reactive protein (mg/dl)	1.81 ± 0.36	3.08 ± 0.55	0.057
Angiographic characteristics			
Primary PCI	116 (80.0%)	80 (85.1%)	0.406
LV ejection fraction (%)	45.01 ± 12.31%	42.61 ± 13.46%	0.352
Multi-vessel disease	88 (64.7%)	76 (80.9%)	0.01
Infarct related artery			0.140
LAD	68 (50.4%)	47 (51.1%)	
LCX	12 (8.9%)	12 (13.0%)	
RCA	46 (34.1%)	28 (30.4%)	
LM	3 (2.2%)	5 (5.4%)	
Killip class on admission			0.004
I	61 (42.1%)	29 (30.9%)	
II	39 (26.9%)	16 (17.0%)	
III	19 (13.1%)	13 (13.8%)	
IV	26 (17.9%)	36 (38.3%)	
In-hospital death	11 (7.6%)	22 (23.4%)	0.001

CAD, coronary artery disease; CVD, cerebral vascular disease; HDL, high density lipoprotein; LDL, low density lipoprotein; HbA1c, hemoglobin A1c; PCI, primary coronary intervention; LAD, left anterior descending artery; LCX, left circumflex artery; RCA, right coronary artery; LM: left main trunk.

though the total cholesterol and HDL-C levels were higher in non-diabetic patients, there was no statistically significant difference in TC/HDL ratio in both groups.

According to the coronary angiographic results, there was no significant difference between diabetic and non-diabetic patients regarding the infarct-related artery and percentage of primary percutaneous coronary intervention (PCI) procedure. Diabetic patients were older than non-diabetic patients. Multi-vessel diseases was known frequently in diabetic group than non-diabetic group. The overall in-hospital mortality rate in our study was 13.8% and there was a significant difference between diabetic and non-diabetic patients (23.4% vs. 7.6%, p = 0.001). Older, multi-vessel diseases, poor renal function, higher killip class and the higher inflammatory marker level were associated with in-hospital mortality in patients with STEMI in Table 2.

Diabetic patients, who died in the hospital, had higher plasma creatinine level and higher CRP levels (6.24 ± 1.33 mg/dl vs. 2.01 ± 0.51 mg/dl, p = 0.01) in Table 3. Most of these patients received insulin treatment to control their blood sugar. However, only serum CRP level might be a predictor of in-hospital death in diabetic patients with acute STEMI in Table 4.

DISCUSSION

The present study demonstrates that diabetic patients has poor in-hospital outcomes after acute STEMI. Because killip class on admission was strong confounding factor for the effect of DM on in-hospital mortality and we did not put this into our analysis.

In addition to diabetes, hypertension, hyperlipidemia are all well-known risk factors for coronary artery disease. On the other hand, about 25% to 47% of hypertensive patients also have insulin resistance or impaired glucose tolerance, which further increase risk of cardiovascular disease development.[10] Combined presence of these diseases in the same patient is devastating to cardiovascular system, and is more easily to develop acute myocardial infarction. This complex pathophysiology may include tissue inflammation, more reactive oxygen species production, endothelial dysfunction, and increased activity of tissue renin-angiotensin-aldosterone system, which are all well-defined factors for atherogenesis.[11]

Several studies discussed about whether the role of admission glucose levels was more important than diabetes history in patients with AMI. Goyal A, et al. found patients with AMI with in-hospital glucose ≧ 144 mg/dL had a high risk of death regardless of diabetes mellitus.[12] Admission glucose levels in non-diabetic patients with AMI could also offer a good screening tool to evaluate the high risk for future type II DM patients.[13] Hsu CW, et al. also found a high initial glucose level in the emergent department was an indepdendent predictor of short- and long-term adverse prognosis in patients with first acute myocardial infarction.[14] However, admission glucose levels were not associated with in-hospital outcome in our diabetic or non-diabetic patients with acute STEMI. There were some patients died of ventricular ar-

Table 2. Predictors of in-hospital outcome in patients with STEMI

Predictors	Odds ratio	95% Confidence Interval		p value
		Lower	Upper	
Age*	1.028	0.978	1.080	0.279
Hypertension	0.875	0.181	4.235	0.868
CVD	0.602	0.157	2.305	0.458
Multi-vessel disease	1.011	0.185	5.532	0.990
Killip class on admission		0.026	0.766	0.003
I	1 (reference)			
II	2.3			
III	3.2			
IV	14			
Creatinine*	1.231	0.815	1.857	0.324
CRP*	1.018	0.922	1.124	0.724

*Continuous variable.

Table 3. Clinical and angiographic characteristics of survival and in-hospital death in diabetic patients

	Survival (n = 72)	In-hospital Death (n = 22)	p value
Clinical characteristics and risk factors			
Age (years)	70.5 ± 12.4	73.5 ± 10.2	0.32
Male gender	55 (76.4%)	16 (72.7%)	0.95
Hypertension	53 (73.6%)	19 (86.4%)	0.34
Hypercholesterolemia	23 (31.9%)	3 (13.6%)	0.16
Current smoker	12 (30.8%)	1 (9.1%)	0.25
Hx of CAD	15 (20.8%)	6 (27.3%)	0.56
Hx of CVD	16 (22.2%)	5 (22.7%)	1.00
Systolic pressure (mmHg)	117 ± 46	134 ± 36	0.09
Diastolic pressure (mmHg)	74 ± 19	66 ± 18	0.15
Plasma creatinine (mg/dl)	1.96 ± 1.53	2.73 ± 1.43	0.04
HbA1c (%)	7.63 ± 1.44	7.18 ± 1.15	0.40
Admission glucose (mg/dl)	216.8 ± 114.0	199.0 ± 89.0	0.57
Triglyceride (mg/dl)	99.9 ± 62.2	102.8 ± 49.4	0.85
Total cholesterol (mg/dl)	145.9 ± 38.9	144.4 ± 40.5	0.88
HDL-cholesterol (mg/dl)	37.5 ± 11.2	34.1 ± 13.8	0.31
LDL-cholesterol (mg/dl)	91.8 ± 33.6	94.4 ± 35.2	0.79
Total cholesterol/HDL-C	4.08 ± 1.13	4.58 ± 1.25	0.13
Triglyceride > 150 mg/dl	9 (12.7%)	4 (20.0%)	0.47
C-reactive protein (mg/dl)	2.01 ± 0.51	6.24 ± 1.33	0.01
Angiographic characteristics			
Primary PCI	63 (87.5%)	17 (77.3%)	0.30
LV ejection fraction (%)	44.0 ± 12.8	33.6 ± 15.6	0.11
Multi-vessel disease	56 (77.8%)	20 (90.9)	0.23
Infarct related artery			0.15
LAD	35 (49.3%)	12 (57.1%)	
LCX	10 (14.1%)	2 (9.5%)	
RCA	24 (33.8%)	4 (19.0%)	
LM	2 (2.8%)	3 (14.3%)	
DM medication			
Sulfonylurea	24 (37.5%)	3 (12.0%)	0.04
Metformin	26 (40.6%)	2 (8.0%)	0.01
TZD	5 (7.8%)	1 (4.0%)	1.00
Acarbose	7 (10.9%)	2 (8.0%)	1.00
Insulin	29 (45.3%)	22 (88.0%)	0.001

CAD, coronary artery disease; CVD, cerebral vascular disease; HDL, high density lipoprotein; LDL, low density lipoprotein; HbA1c, hemoglobin A1c; PCI, primary coronary intervention; LAD, left anterior descending artery; LCX, left circumflex artery; RCA, right coronary artery; LM, left main trunk; DM, diabetes mellitus.

Table 4. Predictors of in-hospital outcome in diabetic patients with STEMI

Predictors	Odds ratio	95% Confidence Interval		p value
		Lower	Upper	
Age*	1.020	0.958	1.085	0.540
Hypercholesterolemia	3.064	0.590	15.907	0.183
Creatinine*	1.075	0.749	1.543	0.695
CRP*	1.163	1.019	1.328	0.025

* Continuous varible.

rhythmia in our study. Chen JH found that initial serum glucose level and white blood cell might be used as predictors for ventricular arrhythmia attack in young patients with first acute myocardial infarction.[15]

There were some evidences that have shown that the in-hospital mortality rate of diabetic patients who have suffered from myocardial infarction are 1.5 to 2 times higher than those of non-diabetic patients.[16] Diabetic women particularly have a poor prognosis, with mortality rates nearly twofold higher than those of diabetic men. Oswald GA, et al. showed no relation between the duration of known diabetes and in-hospital mortality after myocardial infarction.[17] Our study was focused on acute STEMI and showed same finding in our people.

Recently, it has been reported that serum CRP correlates with histological staining of CRP in fatal coronary artery lesions.[18] Biaseucci et al. found hsCRP was the only predictor of events in non-diabetic patients but not in diabetic patients in 1-year follow-up. Our study suggested that there was a trend in CRP levels of acute STEMI between patients with and without diabetes (3.08 ± 0.55 mg/dl vs. 1.81 ± 0.36 mg/dl, $p = 0.057$). Although CRP was not the independent predictor of events in our non-diabetic or diabetic patients. Higher CRP was associated with death in diabetic patients but not in non-diabetic patients. That means different pathophysiological mechanisms for cardiac events in unstable angina or acute myocardial infarction patients with or without diabetes.[19]

It has been demonstrated that impaired renal function is associated with poorer clinical outcome after percutaneous coronary intervention.[20] Pitsavos et al. found creatinine clearance rate was an independent predictor of in-hospital mortality in patients with ACS.[21] In the present study, diabetic patients with higher plasma creatinine levels got adverse in-hospital outcomes after acute STEMI attack.

The excess short-term mortality of diabetic patients is primarily caused by an increased incidence of congestive heart failure.[22,23] Other possible mechanisms include increasing reinfarction rate, extension of infarction area, and recurrent ischemia. Although survival after AMI is related to residual left ventricular function and the amount of damaged myocardium,[21] several previous studies found no evidence that diabetic patients have more extensive infarctions than do non-diabetic patients, whether assessed by total CK activity,[13,24] radionuclide ventriculography,[14] or echocardiography.[25] But congestive heart failure and cardiogenic shock in patients with diabetes after acute MI are more common and more severe than that would be predicted from infarction size.[26]

Thus diabetes mellitus exerts a deleterious effect on the short- and long-term course after AMI through various mechanisms, so application of intensive and effective preventive and therapeutic measures may result in a particularly large survival benefit. Primary angioplasty and thrombolysis have been shown to reduce mortality rate during hospitalization in 3 years follow-up.[27] In another study, anterior infarction or early renal dysfunction remained critical to the one-third mortality of successful intervention for patients with STEMI and cardiogenic shock.[28]

Study limitation

There are several limitations in this study including small population and incomplete pre-hospital medication recording.

CONCLUSION

This study suggests that in diabetic patients with acute STEMI, in-hospital mortality rate is higher than in non-diabetic patients. The aggressive treatment early in the hospital course of diabetic patients with acute STEMI may be helpful.

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