Influence of Diabetes on the Outcome of Acute Coronary Syndrome in Kuwait

Hisham Saad^a Sana Sawan^a Wafa Rashed^a Mohammad Zubaid^b

Department of Medicine, ^aMubarak Al-Kabeer Hospital and ^bFaculty of Medicine, Kuwait University, Kuwait

Key Words

Acute myocardial infarction • Diabetes mellitus •
Coronary artery disease • Kuwait Acute Coronary
Syndrome Registry

Abstract

Objectives: To describe the baseline characteristics and management of patients with and without diabetes mellitus (DM) hospitalized with acute myocardial infarction (AMI) and to assess the influence of DM on hospital outcomes and hospital mortality. **Subjects and Methods:** We analyzed data from a 6-month observational study (Kuwait Acute Coronary Syndrome Registry) of unselected patients admitted with a diagnosis of AMI over a period of 6 months, from December 2003 through May 2004. **Results:** Of 1,295 patients enrolled, 609 (47%) were diabetics and 686 (53%) were non-diabetics. Diabetics were more likely to have a past history of coronary artery disease, hypertension and left ventricular systolic dysfunction than non-diabetics. There was less use of β -blockers and aspirin in diabetics as compared to non-diabetics (62 vs. 71% and 95.5 vs. 97.9%, $p < 0.03$, for β -blockers and aspirin, respectively). Left ventricular failure and cardiogenic shock occurred more often in diabetics compared to non-diabetics (16 vs. 7% and 5 vs. 3%, $p < 0.001$, for left ventricular failure and shock, respectively). The mortality rate was 6% for diabetics and 2% for non-diabetics ($p < 0.001$). **Conclusion:** DM is a major health problem among the adult population in Kuwait, and almost half the AMI population suffer from diabetes. Diabetic patients had higher rates of complications, especially left ventricular failure and cardiogenic

shock, as compared to non-diabetic patients. The in-hospital mortality among diabetics with AMI was almost triple that of non-diabetics. The results of this study highlight the need to improve adherence to evidence-based treatment in diabetic patients with AMI. Copyright © 2010 S. Karger AG, Basel

Introduction

Diabetes mellitus (DM) is a major risk factor for coronary artery disease (CAD). Due to its prognostic significance, the most recent National Cholesterol Education Program III guidelines classified it as a coronary disease equivalent [1]. A previous study has shown that diabetics have higher mortality and morbidity rates compared to non-diabetics after acute myocardial infarction (AMI) [2].

Prior to the advent of thrombolytic therapy, studies of patients with DM showed a greater than 2-fold increase in mortality in men [3], and an even higher rate in women compared with their non-diabetic counterparts [4]. In the thrombolytic era, epidemiological studies, including randomized trials, have demonstrated that hospital mortality remains 1.5–2 times higher among patients with DM [5]. Only a few studies have reported on the prognosis of diabetics with non-ST-segment elevation myocardial infarction, as exemplified by Malmberg et al. [6] who demonstrated that DM predicts a worse outcome.

Diabetes is a major health problem in Kuwait; its prevalence has increased dramatically and is now reported to

be present in about 15% of the adult population [7]. We aimed to describe the baseline characteristics and management of patients with and without DM hospitalized with AMI, and to assess the influence of DM on hospital outcomes and hospital mortality.

Subjects and Methods

We analyzed data from a nationwide prospective observational study (Kuwait Acute Coronary Syndrome Registry) [8] of unselected patients admitted over a period of 6 months, from December 2003 through May 2004. Consecutive patients were recruited from all 7 general hospitals in Kuwait. These hospitals are: Mubarak Al-Kabeer, Al-Amiri, Al-Adan, Al-Farwania, Al-Jahra, Al-Sabah, and Kuwait Oil Company. 97% of variables collected were available for analysis. Almost all consecutive patients were included, as every effort was made to enroll all consecutive patients admitted to hospital with a provisional diagnosis of acute coronary syndrome. Approval of the ethics board was obtained. Patients' identities were not revealed on the case report forms (CRFs), as they were identified on the CRFs by initials and file numbers only. We did not carry out any intervention (e.g. extra history taking or blood sampling) other than what is normally carried out for such patients. The management of each individual patient was left entirely up to the discretion of the treating physician. The registry was funded by the Merck Sharp and Dohme pharmaceutical company and the Kuwait Oil Company. The sponsors had no influence on the study design, data collection, entry and analysis or writing of this paper.

Data were collected using a structured CRF. This form included information on patients' demographics, past medical history, risk factors, physical examination, ECG at presentation, cardiac enzymes, blood glucose at admission, lipid profile, admission and discharge diagnosis, thrombolytic therapy administration, and hospital course and outcomes. The CRFs were checked for completeness and returned to the investigators for responses to data queries. However, we did not carry out site visits for data source verification.

The diagnosis of AMI was based on the definitions made by the American College of Cardiology in their clinical data standards document [9]. Briefly, a diagnosis of AMI was made when there was elevation of troponin I or creatinine kinase (2 or more times the normal value with at least 3% MB fraction) with at least one of the following two criteria: ischemic type chest pain or diagnostic serial ECG changes (e.g. development of pathological Q waves or ECG changes indicative of ischemia, like ST-segment elevation or depression). Patients were considered to be diabetic if they had been told by a physician to have the disease or if they were on any treatment including a diabetic diet, antidiabetic agents or insulin therapy.

Statistical Analysis

Baseline clinical characteristics of patients were presented as frequencies and means. Continuous variables were compared using the Mann-Whitney U test and categorical variables were compared using the Z-test of proportion; a value of $p < 0.05$ was considered statistically significant. All data analyses were carried out using SPSS version 10.0.

Results

Patient Characteristics

Of 1,295 patients enrolled, 609 (47%) were diabetics, whereas 686 (53%) were non-diabetics. The baseline characteristics and risk factors are listed in table 1. Diabetic patients were older, with a mean age of 60 ± 11.1 years compared to a mean age of 52.1 ± 12.2 years for non-diabetics ($p < 0.001$). There was higher proportion of females in the diabetic group. Diabetics were more likely to have a past history of CAD, hypertension and left ventricular systolic dysfunction than non-diabetics. ST-segment elevation was found in only 42% of diabetic patients, in contrast to 60% of non-diabetic patients. The mean blood sugar at presentation (random) for diabetics was higher than for non-diabetics (14 vs. 7 mmol/l).

Management Practice

The hospital and discharge medications are given in table 2. Irrespective of their diabetic status, almost all patients were prescribed heparin (the majority of patients received unfractionated heparin, 84.4% for diabetics vs. 87.4% for non-diabetics, whereas the minority received low-molecular-weight heparin, 9.5% for diabetics vs. 8.5% for non-diabetics), while very few were prescribed clopidogrel and glycoprotein IIb/IIIa inhibitors. Thrombolytic therapy was used less in diabetics compared to non-diabetics (66.5 vs. 80.4%, $p < 0.001$). The thrombolytic agents that were administered were reteplase, streptokinase and tenecteplase (tissue plasminogen activator). The rate of cardiac catheterization during hospitalization was 18% for both diabetics and non-diabetics. β -Blockers and aspirin were used less in diabetics compared to non-diabetics (62 vs. 71% and 95.5 vs. 97.9%, $p < 0.001$ and $p = 0.03$, for β -blockers and aspirin, respectively).

At discharge, angiotensin-converting enzyme inhibitors (ACEIs)/angiotensin receptor blockers (ARBs) and statins were prescribed more often to diabetics as compared to non-diabetics (70 vs. 56% and 70 vs. 55%, for ACEIs/ARBs and statins, respectively, $p < 0.001$ for both). At discharge from hospital, calcium channel blockers were prescribed more often to diabetics as compared to non-diabetics (20.2 vs. 12.6%, $p < 0.001$).

Hospital Outcome

Hospital outcomes are listed in table 3. Left ventricular failure and cardiogenic shock occurred more often in diabetics compared to non-diabetics (16 vs. 7% and 5 vs.

Table 1. Baseline patient characteristics

	Diabetics (n = 609)	Non-diabetics (n = 686)	p value
Age			
Mean $\pm$ SD, years	60.1 $\pm$ 11.9	52.1 $\pm$ 12.2	<0.001
Median, years	60	50	
$\leq$ 75 years	536 (88.0)	642 (93.6)	<0.001
>75 years	73 (12.0)	43 (6.3)	<0.001
Male gender	434 (71.3)	620 (90.4)	<0.001
Kuwaiti citizens	305 (50.1)	174 (25.4)	<0.001
History of CAD			
Angina	266 (43.7)	165 (24.0)	<0.001
Myocardial infarction	189 (31.0)	143 (20.8)	<0.001
Percutaneous coronary intervention	59 (9.7)	34 (4.9)	<0.001
Coronary artery bypass grafting	60 (9.8)	10 (1.4)	<0.001
Hypertension	373 (61.2)	185 (27.0)	<0.001
Left ventricular failure at presentation	182 (29.9)	79 (11.5)	<0.001
ST-segment elevation at presentation	256 (42.0)	415 (60.5)	<0.001
Blood sugar level at presentation, mmol/l	14.8 $\pm$ 6.4	8.2 $\pm$ 3.8	<0.001

Figures in parentheses are percentages.

3% for left ventricular failure and shock, respectively, $p < 0.001$ for both). Stroke was a rare event in all patients. The rate of coronary angiography and the median length of hospital stay was almost the same for both groups. The mortality rate was 6% for diabetic patients and 2% for non-diabetic patients ($p < 0.001$).

Discussion

Our study showed that differences exist between myocardial infarction patients with and without diabetes in regards to characteristics, management and outcomes. The findings of our study are consistent with those of prior studies showing that diabetic patients with AMI are older [2, 10], more often women [2], more likely to be hypertensive [10], and more likely to have a history of angina [2, 10] and congestive heart failure [2].

We found less use of thrombolytic therapy among diabetic patients with ST-segment elevation myocardial infarction compared to non-diabetic patients. This is in agreement with Hansen et al. [11]. Possible explanations for less thrombolysis in diabetics are late presentation, atypical symptoms due to neuropathy [12] and a higher proportion of females, especially as we know that women seek medical attention later than men when suffering from cardiovascular symptoms [13].

Table 2. Use of medications in the first 24 h of admission and at discharge

Characteristics	Diabetics	Non-diabetics	p value
<i>First 24 h after admission</i>	n = 609	n = 686	
Aspirin	583 (95.7)	267 (97.9)	0.035
Clopidogrel	34 (5.6)	20 (2.9)	0.222
β -Blockers	376 (61.7)	487 (71.0)	<0.001
Calcium blockers	74 (12.2)	55 (8)	<0.015
Lysis in eligible patients ¹	218 (66.5)	265 (80.4)	<0.001
Intravenous heparin	520 (84.4)	603 (87.4)	0.081
LMWH	58 (9.5)	58 (8.5)	0.595
GPI	13 (2.1)	16 (2.3)	0.956
<i>At hospital discharge (alive)</i>	n = 573	n = 668	
Aspirin	549 (95.8)	647 (96.8)	0.433
Clopidogrel	72 (12.6)	50 (7.5)	0.003
β -Blockers	430 (75.0)	554 (82.9)	<0.001
Calcium blockers	116 (20.2)	84 (12.6)	<0.001
ACEIs/ARBs	398 (69.4)	375 (56.1)	<0.001
Statins	398 (69.4)	366 (54.8)	<0.001

Figures in parentheses are percentages. GPI = Glycoprotein IIb/IIIa inhibitors; ACEIs/ARBs = angiotensin-converting enzyme inhibitors/angiotensin receptor blockers.

¹ Patients with ST-segment elevation and left bundle branch block, with symptom onset $\leq$ 12 h without contraindication.

Table 3. Hospital outcomes of patient populations

Characteristics	Diabetics (n = 609; 47%)	Non-diabetics (n = 686; 53%)	p value
Recurrent ischemia	126 (20.7)	135 (19.7)	0.705
Re-infarction	18 (2.9)	21 (3.1)	0.962
Left ventricular failure	97 (15.9)	49 (7.1)	<0.001
Cardiogenic shock	32 (5.2)	20 (2.9)	0.049
Stroke	3 (0.5)	1 (0.1)	0.415
Hospital cardiac catheterization	113 (18.5)	126 (18.4)	0.979
Duration of hospital stay (median), days	6	6	NS
Hospital mortality	36 (5.9)	14 (2.0)	<0.001

Figures in parentheses are percentages.

The underuse of β -blockers in our diabetic patients was in concordance with a prior study [2]. The reason for that may be the misconception held by many physicians that β -blockers are considered harmful in diabetics as they mask hypoglycemic symptoms and exacerbate impaired glucose tolerance. We found more use of ACEIs/ARBs in diabetic patients as compared to non-diabetic counterparts; this was also observed by Galcera-Tomas et al. [2]. This reflects physicians' awareness of the benefits of ACEIs after AMI, especially in diabetics. ACEIs have proven beneficial in patients with diabetes as they reduce subsequent major cardiovascular events and slow myocardial remodeling. ACEIs are also prescribed for diabetics to slow the progression of diabetic nephropathy.

We also showed that diabetic patients had higher rates of complications, especially left ventricular failure and cardiogenic shock, which is in agreement with other studies [11, 14]. This could be explained by a previously depressed systolic function due to a greater prevalence of hypertension in diabetics. In addition, diabetes is associated with severer CAD [14], with impairment of regional left ventricular function in non-infarct-related areas [14], left ventricular diastolic dysfunction [15], impaired reflex adaptation to hemodynamic stress and occult cardiomyopathy [15].

The hospital mortality among diabetic patients with AMI was found to be almost triple that of non-diabetic patients in our study. This is higher than reported by Granger et al. [14]. There are several explanations for this finding. First, diabetic patients had a worse risk profile as they were older, more often females, more often hypertensive and more often had previous CAD. Second, diabetic patients received less thrombolysis. Last, diabetics had higher levels of blood glucose at admission, and hy-

perglycemia is known to be an independent predictor of cardiovascular death [16].

A limitation of our study is the fact that the classification of patients as diabetics or non-diabetics was based on information reported by the patients or their relatives. Therefore, patients with undiagnosed diabetes may have been misclassified. However, this would underestimate the effect of diabetes rather than overestimate it. No data were available regarding diabetes duration, antidiabetic agents use, or intensity of glycemic control.

Conclusion

DM is a major health problem among the adult population in Kuwait, and almost half the AMI population suffer from diabetes. Diabetic patients had higher rates of complications, especially left ventricular failure and cardiogenic shock, as compared to non-diabetic patients. The in-hospital mortality among diabetics with AMI was almost triple that of non-diabetics. The results of this study highlight the need to improve adherence to evidence-based treatment in diabetic patients with AMI.

Acknowledgement

The authors would like to thank Miss Rihab Moneer, MSC, for her valuable contributions to data analysis.

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