Clinical outcome of patients with diabetes mellitus and acute myocardial infarction treated with primary angioplasty

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Purpose
The purpose of the present study was to examine the influence of diabetes mellitus (DM) on the clinical outcome in patients with acute myocardial infarction (MI) treated with primary coronary stenting within 24 h of the onset of symptoms.
Methods
We enrolled 100 patients (50 diabetics and 50 nondiabetics) admitted to the coronary care units of Benha University hospitals and National Heart Institute from January 2015 to December 2015 with acute MI treated with primary coronary stenting within 24 h of the onset of symptoms. Clinical outcome was observed in every patient for major adverse cardiac events and hospital stay. Echocardiography was also performed before the patient's discharge from the hospital. Patients were followed up at 3 months for the occurrence of major adverse cardiac events.
Results
The diabetic patients showed higher incidence of hypertension (P=0.003), renal impairment (P=0.045) and dyslipidemia (P=0.05) and also higher incidence of heart failure (P=0.013) during admission and higher mean serum creatinine kinase MB mass assay levels (P=0.005). There were no statistically significant differences in other variables. Procedural success was similar in the two groups. With regard to in-hospital clinical course, diabetic patients were more likely to have early post-MI heart failure (P=0.013), target vessel revascularization (P=0.037) and longer hospital stay (P=0.019). At 3 months, diabetic patients were significantly more likely to experience revascularization (P=0.045) and were more likely to be rehospitalized for acute coronary syndrome and decompensated heart failure (P=0.037); however, there was no significant difference in mortality (P=0.307).
Conclusion
Compared with nondiabetics, diabetic patients are more likely to have early post-MI heart failure, target vessel revascularization, and longer hospital stay. Moreover, diabetic patients are significantly more likely to experience revascularization and are more likely to be rehospitalized for acute coronary syndrome or decompensated heart failure.

Keywords:
acute myocardial infarction, diabetes mellitus, primary coronary stenting

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Introduction

Diabetes is now considered to be a risk equivalent of coronary artery disease for future myocardial infarction (MI) and cardiovascular death [1]. The acute and long-term management of acute coronary syndromes (ACSs) does not differ for persons with diabetes; yet previous studies have suggested that patients with diabetes have not had a similar reduction in cardiovascular mortality as those of patients without diabetes despite receiving modern therapies [2,3]. In addition to being a risk factor for the development of coronary disease, diabetes influences outcomes following ACS. A subgroup analysis of patients with diabetes with ST-segment elevation MI (STEMI) in the Global Utilization of Streptokinase and Tissue Plasminogen Activator for Occluded Coronary Arteries (GUSTO-1) trial [4] demonstrated significantly higher all-cause mortality at 30 days compared with patients without diabetes (10.5 vs. 6.2%). Similarly, the Organization to Assess Strategies for Ischemic Syndromes (OASIS) registry [5] of patients with unstable angina/non-STEMI observed an increased rate of post-MI complications and mortality among patients with diabetes compared with patients without diabetes

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(odds ratio, 1.57) during 2 years of follow-up. The independent association of diabetes with mortality following ACS, especially STEMI, in the present era of coronary care remains uncertain. Primary percutaneous coronary intervention (PCI) is effective in securing and maintaining coronary artery patency and avoids some of the bleeding risks of fibrinolysis.

Patients and methods

Study patients

This is a prospective observational study that included 100 consecutive patients admitted to the coronary care unit of Cardiology Department, Benha Faculty of Medicine and National Heart Institute from January 2015 to December 2015. All patients selected had acute STEMI and underwent primary PCI within 24 h from the onset of chest pain. Fifty of them were diabetic and the other 50 were nondiabetic.

Exclusion criteria

Patients who refused to participate in the study; patients presented with cardiogenic shock or cardiac arrest that required cardiopulmonary resuscitation; patients who received thrombolytic therapy, PCI-related MI, coronary artery bypass grafting-related MI; patients with established MI with onset of symptoms of at least 24 h and patients with left main significant lesions.

Study method

All the patients were assessed by clinical history, Full clinical data were obtained from every patient; clinical evaluation and electrocardiographic analysis of standard 12-lead ECG were recorded at admission, then every 6 h in the first day, then every 12 h in the following days and whenever the patient had chest pain. Significant ST-elevation was measured at 60 msec from the J point. Then laboratory data: creatine kinase (CK) MB was measured at baseline and serially, plasma glucose, serum creatinine, hemoglobin levels, and complete blood count were measured. Following that primary PCI coronary angiography and subsequently angioplasty was performed in the conventional manner (GE Health care New York, 2009 or Siemens, German, Berlin 2013). Target lesion revascularization was performed in all patients. Before hospital discharge, every patient was assessed by clinical history, clinical examination, and transthoracic echocardiogram.

In-hospital outcome

Successful angioplasty which was defined as post-treatment residual stenosis less than 30% with thrombolysis in myocardial infarction flow grade.

Major adverse cardiac events

(1) Recurrent ischemia.
(2) Target vessel revascularization (TVR) procedures.
(3) Major bleeding complications.
(4) Ischemic and hemorrhagic stroke.
(5) Heart failure.
(6) Incidence of death.

Duration of hospitalization

Three months follow-up

Patients were followed up for the occurrence of major adverse cardiac events (MACE) during 3 months after discharge from hospital (by telephone or during readmission).

Study end points

Primary end points

Assessing the potential role of diabetes on:

(1) The occurrence of in-hospital MACE as early post-MI angina, development of heart failure, significant arrhythmias, major bleeding, stroke or mortality.
(2) Development of MACE, cardiac mortality, revascularization (PCI or coronary artery bypass grafting), hospitalization for ACSs or heart failure and functional class after 3 months.

Secondary end points

Comparing the two groups regarding the occurrence of successful angioplasty and predischarge left ventricular global and regional function.

Statistical analysis

The statistical analysis was done using SPSS, version 17 (SPSS IBM 2016). Descriptive statistics were done to obtain frequencies, mean±SD of the required variables. The tests that were used to test the differences among different variables: *t*-test for the numerical variables and χ^2-test for the categorical variables. Correlation analysis was done using Spearman's correlation coefficient. Univariate analysis was used to determine the variables that predicted major cardiac adverse effects at follow-up. A two-sided *P* value up to 0.05 was considered to indicate statistical significance.

Results

This study was a prospective observational study that included 100 consecutive patients with STEMI who were admitted to Benha University Hospital and National Heart Institute Coronary Care Units from January 2015 to December 2015 where they underwent primary angioplasty.

Patient characteristics

Baseline characteristics and risk factors for coronary artery disease are shown in Table 1.

Clinical and ECG parameters at presentation

There was only a significant difference regarding time from onset of chest pain and location of MI as described in Table 2.

In-hospital parameters

Laboratory parameters

Diabetic patients had a significantly higher mean blood myocardial specific creatine kinase (CK-MB) level, Random Blood Sugar (RBS), and lower mean hemoglobin level as described in Table 3.

Diagnostic catherization laboratory data

There was no difference between both groups as regards target vessels and the number of vessels affected (Table 4).

Coronary revascularization

There was significant difference regarding adjuvant therapy and suction device during and after PCI (Table 5).

Echocardiographic parameters

There was a trend toward increase in left ventricular end diastolic dimension and left ventricular end systolic dimension and higher diastolic dysfunction in diabetics (Table 6).

In-hospital clinical course

There was significant difference between diabetic and nondiabetic patients as regards TVR and duration (days) of hospital stay. There was no report of stroke or mortality among both groups (Table 7).

Follow-up data

At 3 months, diabetic patients were significantly more likely to undergo revascularization, rehospitalized for ACS, and decompensated heart failure; however, they had a nonsignificant increase in mortality (Table 8).

Discussion

In this study, there was no significant difference in the diagnostic angiographic criteria while in Fujiwara *et al.* [6] there was a higher prevalence of multivessel disease in diabetics. In Syed *et al.* [7] there was also a

Table 1 Baseline characteristics and risk factors for CAD in both groups

Variables	All population (*n*=100) [*n* (%)]	Nondiabetics (*n*=50) [*n* (%)]	Diabetics (*n*=50) [*n* (%)]	*P* value
Men	79 (79)	40 (80)	39 (78)	0.806
Current smokers	71 (71)	30 (60)	41 (82)	**0.015**
Hypertension	31 (31)	9 (18)	22 (45.8)	**0.003**
Dyslipidemia	87 (87)	37 (74)	50 (100)	**0.000**
Positive FH For CAD	91 (91)	44 (88)	47 (94)	0.295
Renal impairment	10 (10)	2 (4)	8 (16)	**0.045**
Past history of CAD	11 (11)	6 (12)	5 (10)	0.749

CAD, coronary artery disease; FH, family history. Bold is for significant values.

Table 2 ECG and clinical parameters at presentation across groups

Variables	Nondiabetics (*n*=50)	Diabetics (*n*=50)	*P* value
Anterior MI	35 (70)	29 (58)	0.211
Inferior MI	11 (22)	9 (18)	0.617
Posterior MI	0 (0)	0 (0)	NA
Extensive anterior MI	4 (8)	12 (24)	**0.029**
Onset of chest pain (h)	3.62±2.10	5.2±4.22	**0.020**
Admission HR	83.22±8.11	83.68±10.15	0.803
HF on admission	10 (20)	14 (28)	0.349
Elevated JVP	5 (10)	8 (16)	**0.04**
Galloping	8 (16)	14 (28)	0.218
Both S3 and elevated JVP	3 (6)	8 (16)	0.110
ECG			
No of leads with ST elevation	4.28±1.18	4.98±1.87	0.180
Magnitude ST elevation	3.44±0.79	3.52±0.65	0.580

Values are presented as mean±SD or *n* (%). HF, heart failure; HR, heart rate; JVP, jugular venous pressure; MI, myocardial infarction. Bold is for significant values.

Table 3 Laboratory parameters across diabetic and nondiabetic groups

Variables (mean±SD)	Nondiabetics (*n*=50)	Diabetics (*n*=50)	*P* value
CK-MB (ng/dl)	66.6±66.2	103±62.38	**0.005**
HB (g/dl)	13.88±1.14	13.34±1.36	**0.034**
Serum creatinine (mg/dl)	1.06±0.39	1.06± 0.59	0.968
RBG (mg/dl)	124.68±69.95	381.56±91.28	**0.000**

CK, creatine kinase; HB, hemoglobin; RBG, random blood glucose. Bold is for significant values.

Table 4 Diagnostic catherization laboratory data across diabetic and nondiabetic groups

Variables	Nondiabetics (*n*=50)	Diabetics (*n*=50)	*P* value
LAD	48 (96)	44 (88)	0.140
LCX	9 (18)	13 (26)	0.334
RCA	18 (36)	19 (38)	0.836
Single vessel	30 (60)	26 (52)	0.420
Two vessel	15 (30)	23 (46)	0.099
Multivessel	5 (10)	2 (4)	0.240

LCX, left circumflex; LAD, left anterior descending; RCA, right coronary artery.

Table 5 Coronary revascularization across diabetic and nondiabetic groups

Variables	Nondiabetics (*n*=50)	Diabetics (*n*=50)	*P* value
Procedure failure	0 (0)	1 (2)	0.315
PCI with BMS	48 (96)	44 (88)	0.258
PCI with DES	2 (4)	7 (14)	0.616
No adjuvant therapy	25 (50)	36 (72)	**0.024**
Add glycoprotein IIb/IIIa	21 (42)	14 (28)	0.142
Usage of suction device	11 (22)	0 (0)	**0.001**
Both	7 (14)	0 (0)	**0.006**

BMS, bare metal stent; DES, drug eluting stent; PCI, percutaneous coronary intervention. Bold is for significant values.

higher prevalence of multivessel disease and Saphenous Venous Graft (SVG) occlusion or left circumflex as the target vessel in diabetics. In the GUSTO IIb substudy [8], the multivessel disease was more prevalent in diabetic patients than it was in nondiabetics and the minimum luminal diameter was smaller in diabetics resulting in a greater percent diameter stenosis among diabetics. These differences may be attributed to the lower mean age of diabetics in the present study (53.16±6.94 years) than in Fujiwara and colleagues study (64.2±11.2 years), while in Syed and colleagues (63.85±12.95 years), even though the GUSTO IIb substudy has shown that the diabetic patients were older (64.8±6.1 years).

Table 6 Echocardiographic parameters across diabetic and nondiabetic groups

Variables	Nondiabetics (*n*=50)	Diabetics (*n*=50)	*P* value
LVEDD (cm)	4.83±0.77	5.20±0.77	**0.016**
LVESD (cm)	3.45±0.67	3.85±0.68	**0.003**
EF	53.26±8.88	50.74±8.06	0.141
Normal diastolic function	4 (8)	0 (0)	**0.041**
Grade I diastolic dysfunction	37 (74)	37 (74)	1.00
Grade II diastolic dysfunction	9 (18)	10 (20)	0.799
Grade III diastolic dysfunction	0 (0)	3 (6)	0.079

Values are presented as mean±SD or *n* (%). LVEDD, left ventricular end diastolic dimension; LVESD, left ventricular end systolic dimension; EF, ejection fraction. Bold is for significant values.

Table 7 In-hospital clinical course across diabetic and nondiabetic groups

Variables	Nondiabetics (*n*=50)	Diabetics (*n*=50)	*P* value
TVR	5 (10)	13 (26)	**0.037**
Major bleeding	0 (0)	2 (4)	0.153
HF	8 (16)	19 (38)	**0.013**
MI	0 (0)	2 (4)	0.153
Stroke	0 (0)	0 (0)	NA
Mortality	0 (0)	0 (0)	NA
Hospital stay days	3.82±1.16	4.36±1.12	**0.019**

Values are presented as mean±SD or *n* (%). HF, heart failure; MACE, major adverse cardiac events; MI, myocardial infarction; TVR, target vessel revascularization. Bold is for significant values.

Table 8 MACE at 3 months follow-up across diabetic and nondiabetic groups

Variables	Nondiabetics (*n*=50) [*n* (%)]	Diabetics (*n*=50) [*n* (%)]	*P* value
Recurrent MI	2 (4)	5 (10)	0.240
Hospitalization	5 (10)	13 (26)	**0.037**
Revascularization	18 (36)	28 (56)	**0.045**
Cardiac mortality	1 (2)	3 (6)	0.307

MACE, major adverse cardiac event; MI, myocardial infarction. Bold is for significant values.

In this study, while diabetics and nondiabetics had no significant differences as regards target vessel and type of stent implanted, diabetics had higher incidence of procedure failure, higher percentage of those who need adjuvant therapy, and higher percentage of those who need suction devices than in nondiabetics; use of GP IIb/IIIa inhibitors in diabetic patients was significantly higher than in diabetics, also the use of drug eluting stent (DES) was higher in diabetics (though in small numbers). Both had a significant effect on the outcome but both were not reported in Fujiwara and colleagues, and

there was no clinical difference in the use of DES, GP IIb/IIIa, or suction devices in Syed and colleagues, while in Shaikh *et al.* [9] all cases used DES with no differences between both groups. On the other hand, in the GUSTO IIb substudy balloon angioplasty alone was the major modality used in both groups.

According to the procedure success defined (as thrombolysis in myocardial infarction flow grade 3 flow and ≤50% residual stenosis), the present study showed that there was one case of procedure failure in the diabetic group while no patient in the nondiabetic group showed such complication. In the GUSTO IIb substudy that examined angiographic success there were no significant differences between diabetic and nondiabetic groups who underwent balloon angioplasty without stenting, while in Syed and colleagues there was significant difference toward a higher percentage of success in nondiabetics than in diabetic patients although that significant difference was in the use of intravascular ultrasound in diabetic patients than in nondiabetics.

In-hospital clinical outcome

As regards in-hospital clinical outcomes in the present study, there was significant difference between diabetic and nondiabetic patients as regards target vessel revascularization (TVR), heart failure, and duration (days) of hospital stay. However there was a trend for increasing rate of MI and major bleeding in diabetics compared with nondiabetics, but the difference did not reach a statistically significant value. There was no report of stroke or mortality among both groups.

In accordance with the results of the present study, Fujiwara and colleagues also reported that significant difference had occurred only in the incidence of TVR (P=0.04) in diabetics than in nondiabetics.

In Sayed and colleagues study there were no significant difference in in-hospital outcomes except for in-hospital stay which was longer in diabetic patients compared with nondiabetic patients.

The GUSTO IIb substudy showed that there were higher incidence in both in-hospital heart failure and cardiogenic shock among diabetic patients compared with nondiabetic patients (P=0.001 and 0.04, respectively).

Three months clinical follow-up

At 3 months follow-up, diabetic patients were significantly more likely to experience rehospitalization, revascularization, and had a trend toward higher recurrent MI despite being insignificant statistically than nondiabetics.These results matched the results of Fujiwara and colleagues by the end of 6 months follow-up. While in the study of Syed and colleagues by the end of 1 year follow-up, there was significant difference in mortality (P=0.001) and less event-free survival in diabetics (especially revascularization) than nondiabetics.

In Aronson *et al.* [10] there was significant difference toward higher mortality (P=0.001) and higher incidence of readmission by heart failure in diabetics compared with nondiabetics (P=0.003) but these results had included in-hospital and subsequent follow-up for 14 months. On the contrary, in the GUSTO IIb substudy within 6 months of follow-up after acute MI, there was no significant difference in the cumulative incidence of death/reinfarction between diabetic and nondiabetic patients.

Diabetes and the factors before reperfusion therapy

The present study highlighted many important pretreatment factors that may partly explain the worse outcome of diabetics.

The first is the significant delay from symptom onset to first medical contact in diabetic patients compared with nondiabetic patients in the present study resulted in a significant delay in reperfusion.

A similar finding was also recorded in the study by Fujiwara and colleagues and GUSTO IIb substudy.

In the study by Fujiwara and colleagues there was relative delay in mean time from the onset of symptoms to device in diabetics which was 4.3±2.2 versus 4.3±2.5 h in nondiabetics.

In GUSTO IIb substudy the significant delay for the diabetic patients was 3.51±2.50 h than in nondiabetics (3.20±2.35).

The relative delay in the presentation of symptoms in diabetic patients may be explained by diabetic neuropathy, vague symptoms, and difficulty in interpreting the ECG of diabetic patients due to common prevalence of nonspecific ECG changes (Fujiwara and colleagues)

The second is the significant higher prevalence of coronary risk factors in diabetic patients compared with nondiabetic patients, current smoking, hypertension, and dyslipidemia

In accordance with the results of the present study, Fujiwara and colleagues, Sayed and colleagues, and GUSTO IIb substudy found a higher prevalence of hyperlipidemia, associated hypertension and history of renal insufficiency in diabetics compared with nondiabetics.

The third, diabetic patients in this study had large infarct size than nondiabetics as reflected by the higher mean of CK-MB and higher prevalence of extensive anterior MI than nondiabetics. In previous studies, the difference between diabetic and nondiabetic patients as regards enzyme release was not reported.

The fourth, as regards echocardiographic parameters, there was a trend toward an increase in left ventricular end diastolic dimension and left ventricular end systolic dimension, lower ejection fraction, higher diastolic dysfunction grade III than that in the nondiabetic group.

Study limitations

(1) The study was underpowered to detect the difference in major adverse events between both groups due to its small sample size with small variability range and due to the multivariables involved.
(2) DES was used in few patients instead of their indications because of financial and/or other causes not related to clinical judgment.
(3) Long delay before presentation which affect the clinical outcome of all patients.
(4) Short follow-up period and difficult communication.
(5) Higher percentage of patients who refused to enter the study.
(6) Only two centers of Egypt included.

According to this study we can conclude the following:

(1) Compared with nondiabetics, diabetic patients are more likely to have early post-MI heart failure, TVR, and hospital stay.
(2) Diabetic patients are significantly more likely to experience revascularization and are more likely to be hospitalized for ACS or decompensated heart failure
(3) Multicenters, larger study population, and longer period of follow-up are highly recommended to highlight this issue.

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Conflicts of interest

There are no conflicts of interest.

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