Short- and long-term outcomes in Middle Eastern diabetic patients after percutaneous coronary intervention: results from The First Jordanian PCI Registry (JoPCR1)

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Abstract

Introduction Diabetes mellitus (DM) is highly prevalent among Middle Eastern patients admitted with acute coronary syndrome (ACS) or who undergo percutaneous coronary intervention (PCI). This study used data from the First Jordanian PCI Registry (JoPCR1) to determine the short- and long-term outcomes in a subgroup of diabetic patients within a large PCI population.

Methods JoPCR1, a prospective, multicenter study of consecutive patients who underwent PCI from January 2013 to February 2014, assessed the incidence of major cardiovascular events (cardiac mortality, stent thrombosis, major bleeding events and coronary revascularization) in diabetic compared with nondiabetic patients from the index hospitalization to 1 year of follow-up.

Results Of 2426 patients enrolled, 1300 (53.6 %) were diabetics. Compared with nondiabetic patients, diabetic

patients were older, more likely to be female and to have hypertension, hypercholesterolemia and chronic renal disease. Diabetic patients had higher prevalences of multivessel coronary artery disease and PCI than nondiabetic patients. Although both groups had similar proportions of patients undergoing PCI for ACS (76.3 vs. 78.4 %; $p = 0.237$), fewer diabetic patients had PCI for ST-segment elevation myocardial infarction than nondiabetics (27.5 vs. 33.7 %; $p = 0.0002$). Both groups had similar incidences of stent thrombosis (ST) during hospitalization (0.46 vs. 0.27 %; $p = 0.665$) and at 1 year (2.36 vs. 1.53 %; $p = 0.196$). Similarly, major bleeding events were not different between diabetic and nondiabetic patients during hospitalization (1.31 vs. 0.53 %; $p = 0.077$) and at 1 year (1.47 vs. 0.98 %; $p = 0.377$). Compared with nondiabetic patients, diabetic patients had a higher incidence of readmission for ACS and coronary revascularization at 1 year. Diabetic patients had higher incidences of cardiac mortality than nondiabetic patients during the index hospitalization (1.23 vs. 0.27 %; $p = 0.015$) and at 1 year (2.58 vs. 0.81 %; $p = 0.002$). In multivariate analysis, diabetic patients were four times more likely to die in the hospital compared to nondiabetic patients (odds ratio = 4.2; 95 % CI 1.2–14.8, $p = 0.025$).

Conclusions Diabetic patients, who accounted for more than half of this Middle Eastern PCI population, had a higher risk of cardiac mortality, readmission for ACS and coronary revascularization at 1 year compared with nondiabetic patients.

Keywords Diabetes mellitus · Cardiovascular outcomes · Percutaneous coronary intervention · Middle Eastern patients

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Introduction

Diabetes mellitus (DM) is a major risk factor for cardiovascular disease (CVD) [1]. In the Middle East, where CVD is the leading cause of death [2, 3], 45–70 % of patients admitted with acute coronary syndrome (ACS) have DM [4, 5]. Diabetic patients have a higher incidence of short- and long-term adverse events compared with nondiabetic patients when they are admitted for ACS or undergo percutaneous coronary intervention (PCI) [6]. The outcome of Middle Eastern diabetic patients who undergo PCI for ACS or stable coronary disease has not been well studied. There are no regional reports of clinical profiles or long-term outcome of diabetic patients admitted with ACS or who underwent PCI. Published large Middle Eastern ACS registries [7, 8] have reported the clinical profiles and prognoses of ACS populations, but did not specifically address the cardiovascular outcomes in diabetic patients, who comprised 40 % of the cohorts studied. Furthermore, patients enrolled in these registries did not receive optimal contemporary invasive therapy, and only 30 % of the ACS patients underwent PCI.

This study used data from the First Jordanian PCI Registry (JoPCR1) to assess the clinical and coronary angiographic profiles and the short- and long-term outcomes in diabetic and nondiabetic patients within a large PCI population.

Materials and methods

JoPCR1 is a prospective multicenter study of patients who underwent PCI for ACS or SC in 12 tertiary care centers in Jordan (January 2013 to February 2014). During admission, clinical, laboratory, electrocardiographic, echocardiographic and coronary angiographic findings were recorded and compared in diabetic and nondiabetic subgroups. The pharmacological therapy and PCI procedure details were also compared between the two groups. All patients received dual oral antiplatelet therapy (aspirin and either clopidogrel or ticagrelor) before PCI. All PCI procedures were performed according to current standard guidelines. The arterial access site, type and number of stents, and the use of antithrombotic medications, including glycoprotein IIb/IIIa inhibitors (GPI), were left to the operator's discretion. In-hospital adverse events (cardiac mortality, stent thrombosis (ST), major bleeding events and acute PCI complications), and 1- and 12-month events (cardiac mortality, ST, major bleeding events, coronary revascularization and readmission for ACS or heart failure) were compared in diabetic and nondiabetic patients.

DM was defined according to the standard diagnostic criteria set by the concerned societies, task forces and ACS registries [1, 9–12]. The criteria included fasting serum glucose ≥ 126 mg/dl, 2-h glucose level ≥ 200 mg/dl, glycosylated hemoglobin (HbA1c) value ≥ 6.5 %, patients who have unequivocal hyperglycemia and classical symptoms of DM (polyuria, polydipsia and unexplained weight loss) with casual plasma glucose > 200 mg/dl, or fasting plasma glucose ≥ 126 mg/dl, patients with a prior diagnosis of DM or those prescribed antidiabetic medications by a physician.

ACS was classified as acute ST-segment elevation myocardial infarction (STEMI) or non-ST-segment elevation ACS (NSTEMI), which includes non-ST-segment MI (NSTEMI) and unstable angina (UA). SC was defined as chronic stable angina or silent ischemia [13]. Stent thrombosis (definite and probable) was defined according to the Academic Research Consortium definition [14], and major bleeding events were defined according to the CRUSADE (Can Rapid risk stratification of Unstable angina patients Suppress ADverse outcomes with Early implementation of the ACC/AHA guidelines) study definition [15]. The GRACE (Global Registry of Acute Coronary Events) risk score [16] and CRUSADE bleeding risk score [15] were calculated for each patient by online calculators that use certain clinical, laboratory and echocardiographic characteristics. The study protocol was approved by the institutional review board or ethics committee at each participating center.

IBM SPSS Statistics 20 (IBM Corp., 2011) was used for data entry and analysis. Data were described using means and percentages. The chi-square test was used to test differences between proportions, and the independent t test was used to test differences between the means in the two groups (diabetic and nondiabetic patients). A binary logistic regression was used to test the difference in the in-hospital death rate between diabetic and nondiabetic patients. The variables that were adjusted for included age, gender, hypertension, hypercholesterolemia, cigarette smoking, chronic renal disease and number of diseased coronary arteries. A *p* value of less than 0.05 was considered statistically significant.

Results

This study enrolled 2426 patients prospectively. DM was present in 1300 (53.6 %) patients, including type 2 DM in 91 (7 %) and type 1 DM in 1209 (93 %). Table 1 shows the baseline characteristics of the diabetic and nondiabetic patients. Diabetic patients had more prevalence of other major cardiovascular risk factors, i.e., hypertension, hypercholesterolemia and obesity. More diabetic than nondiabetic patients had comorbidities including heart

Table 1 Baseline features in diabetic and nondiabetic patients

Features	Diabetic patients (<i>N</i> = 1300)	Nondiabetic patients (<i>N</i> = 1126)	<i>p</i> value
Age in years, mean $\pm$ SD	59.5 $\pm$ 7.9	57.0 $\pm$ 7.1	<0.0001
Age $\leq$ 50 years	19.8 %	31.7 %	<0.0001
Females	26.8 %	13.5 %	<0.0001
Hypertension	72.1 %	48.3 %	<0.0001
Systolic BP on admission, mean $\pm$ SD (mmHg)	135.6 $\pm$ 22.0	130.9 $\pm$ 21.6	0.42
Diastolic BP on admission, mean $\pm$ SD (mmHg)	78.2 $\pm$ 13.1	76.2 $\pm$ 12.6	0.50
Cigarette smoking	35.9 %	52.2 %	<0.0001
Hypercholesterolemia	57.0 %	36.1 %	<0.0001
Lipid profile, mean $\pm$ SD (mg/dl)			
Total cholesterol	169.7 $\pm$ 24.6	171.3 $\pm$ 26.1	0.02
LDL-C	105.3 $\pm$ 15.2	129.5 $\pm$ 19.4	0.0004
HDL-C	36.7 $\pm$ 11.1	36.5 $\pm$ 11.4	0.76
Triglycerides	192.5 $\pm$ 33.4	166.2 $\pm$ 26.4	<0.001
Past PCI	27.2 %	29.8	0.170
BMI $\geq$ 30 kg/m ²	30.6 %	26.8 %	0.044
Known heart failure	1.3 %	0.3 %	<0.0001
Past stroke	2.5 %	1.5 %	<0.0001
Known PAD	1.5 %	0.2 %	<0.0001
Chronic renal disease	3.8 %	1.7 %	0.01
Estimated CrCl <60 ml/min	13.7 %	10.4 %	0.009
ST-segment deviation	46.9 %	50.8 %	0.061
Elevated serum cardiac biomarkers	37.2 %	43.3 %	0.002
LVEF <45 %	13.9 %	10.7 %	0.020

Chi-square test was used to test differences between proportions, and independent *t* test was used to assess the differences between the means in diabetic and nondiabetic patients

BMI body mass index, *BP* blood pressure, *CrCl* creatinine clearance *HDL-C* high-density lipoprotein cholesterol, *LDL-C* low-density lipoprotein cholesterol, *LVEF* left ventricular ejection fraction, *PAD* peripheral arterial disease, *PCI* percutaneous coronary intervention

failure, past stroke, peripheral arterial disease and chronic kidney disease.

Mean systolic and diastolic blood pressures on admission in diabetic patients were not different from those in nondiabetic patients. Diabetic patients had lower mean serum total cholesterol and low-density lipoprotein cholesterol and higher mean triglycerides levels.

The rate of use of cardiovascular medications prior to hospitalization was higher in diabetic than nondiabetic patients, including beta blockers (BBs) (51.5 vs. 42.8 %; *p* < 0.001), renin angiotensin aldosterone inhibitors (RAASBs) (47.5 vs. 33.0 %; *p* < 0.001) and statins (58.3 vs. 45.2 %; *p* < 0.001). Low-molecular-weight heparin and/or unfractionated heparin were used in 99 % of diabetic and nondiabetic patients.

Diabetic patients also had higher past CV burden (past stroke, peripheral arterial disease and heart failure). However, fewer diabetic patients had elevated serum levels of cardiac biomarkers and STEMI compared with nondiabetic patients.

Table 2 depicts the coronary angiographic findings, indications for PCI and in-hospital complications of the procedure. About three-fourths of diabetic and nondiabetic patients had ACS as an indication for PCI. More diabetic than nondiabetic patients had multivessel coronary artery disease (CAD) and PCI. Although PCI for the left main coronary artery was done in a minority of patients, it was performed more in diabetic than nondiabetic patients. The majority of stents used in diabetic and nondiabetic patients were second-generation drug-eluting stents (DES). Diabetic patients did not experience more peri-procedural complication than nondiabetic patients.

Prior to admission, the majority (79 %) of the diabetic patients were using antidiabetic medications including 25.0 % who were using insulin alone or in combination with oral agents (Table 3). During hospitalization, insulin was used in about one-half of diabetic patients. At 1 year, 23.1 % of diabetic patients were using insulin, and 35.1 % were using oral agents.

Table 2 Coronary angiographic features and PCI procedural details and complications

Features	Diabetic patients (<i>N</i> = 1300) (%)	Nondiabetic patients (<i>N</i> = 1126) (%)	<i>p</i> value
Coronary artery disease			
One vessel	55.4	61.8	0.002
Multivessel	42.7	37.0	0.005
LM	1.9	1.2	0.22
PCI performed for			
One vessel	68.6	74.5	0.002
Multivessel	29.7	25.0	0.011
LM	1.7	0.5	0.014
Indication for PCI			
ACS	76.3	78.5	0.214
STEMI	27.5	33.7	0.001
NSTEACS	48.8	44.8	0.054
Chronic stable disease	23.7	21.5	0.214
Types of stents			
BMS	8.6	10.8	0.078
Second-generation DES	90.6	88.1	0.053
BVS	0.8	1.1	0.58
PCI complications			
Ventricular tachyarrhythmia	0.8	1.0	0.760
Heart failure	9.2	6.7	0.029
Cardiogenic shock	0.8	0.3	0.173
Coronary dissection	0.6	1.3	0.113
Emergency CABG	0	0.3	0.153

Chi-square test was used to test differences between proportions in diabetic and nondiabetic patients

ACS acute coronary syndrome, BMS bare metal stent, BVS bioresorbable scaffold, CABG coronary artery bypass graft surgery, DES drug-eluting stent, LM left main coronary artery, NSTEACS non-ST-segment elevation ACS, PCI percutaneous coronary intervention, STEMI ST segment elevation myocardial infarction

Table 3 Use of antidiabetes medications in the diabetic patients

Medication	Pre-admission (1300 patients) <i>N</i> (%)	During admission (1300 patients) <i>N</i> (%)	At 1 year (1260 patients) <i>N</i> (%)
Insulin	223 (17.2)	593 (45.6)	244 (19.4)
Oral antidiabetic medications	701 (53.9)	289 (22.2)	396 (31.4)
Insulin and oral medications	101 (7.8)	63 (4.8)	47 (3.7)
Neither	275 (21.1)	355 (27.4)	573 (45.5)

Use of evidence-based medications during hospitalization and at 1 year in diabetic and nondiabetic patients is shown in Table 4. During hospitalization, similar percentages of diabetic and nondiabetic patients received dual oral antiplatelet agents, BB and statins, and more diabetics received RAASB than nondiabetics.

During the index hospitalization and at 1 year, diabetic patients had a higher incidence of cardiac mortality compared with nondiabetic patients (Table 5). The most common three causes of in-hospital death in diabetic (*N* = 16) and nondiabetic patients (*N* = 3) were cardiogenic shock (8 diabetic and 1 nondiabetic patients), ventricular arrhythmias (4 diabetic

and one nondiabetic patients) and stent thrombosis (2 diabetic and no nondiabetic patients).

In multivariate analysis, and after adjusting for age, gender, hypertension, hypercholesterolemia, cigarette smoking, chronic renal disease and number of diseased coronary arteries, diabetic patients were four times more likely to die in the hospital compared to nondiabetic patients (odds ratio = 4.2; 95 % CI 1.2–14.8, *p* = 0.025). There were no differences in the incidence of ST, major bleeding events or readmission for ACS in both groups; however, more diabetic than nondiabetic patients were readmitted at 1 year for ACS and coronary revascularization.

Table 4 Use of secondary cardiovascular prevention medications in diabetic and nondiabetic patients

Group	Medications during hospitalization					Medications at 1 year				
	Number of patients	DAPT (%)	BB (%)	RAASB (%)	Statins (%)	Number of patients	DAPT (%)	BB (%)	RAASB (%)	Statins (%)
All patients	2426	99.9	79.8	62.3	97.8	2348	96.8	74.3	57.2	92.3
Diabetics	1300	99.1	74.8	62.2	93.6	1255	93.0	80.1	68.7	94.7
Nondiabetics	1126	99.1	74.6	51.1	94.8	1093	85.7	76.9	61.7	93.3
<i>p</i> value (diabetics vs. nondiabetics)		0.829	0.947	<0.0001	0.242	–	<0.001	0.066	<0.0001	0.179

Chi-square test was used to test differences between proportions in diabetic and nondiabetic patients

BB beta blockers, DAPT dual antiplatelet therapy, RAASB renin angiotensin aldosterone system blockers

Table 5 In-hospital, 1- and 12-month major cardiovascular events

Events and timing	Diabetic patients <i>N</i> = 1300	Nondiabetic patients <i>N</i> = 1126	<i>p</i> value
In hospital			
Stent thrombosis	0.46 %	0.27 %	0.665
Major bleeding events	1.31 %	0.53 %	0.077
Cardiac mortality	1.23 %	0.27 %	0.015
Cardiogenic shock	0.62	0.09	0.072
Ventricular tachyarrhythmia	0.31	0.09	0.46
Stent thrombosis	0.15	0	0.56
Major bleeding	0.08	0.09	0.27
Stroke	0.08	0	0.97
One month	<i>N</i> = 1272 (%)	<i>N</i> = 1115 (%)	<i>p</i> value
Stent thrombosis	1.64	1.08	0.320
Major bleeding events	1.39	0.80	0.240
Cardiac mortality	1.54	0.81	0.148
Target vessel revascularization	1.49	0.99	0.363
Readmission for			
Acute coronary syndrome	2.36	0.99	0.016
Heart failure	0.71	0.36	0.369
One year	<i>N</i> = 1255	<i>N</i> = 1093	<i>p</i> value
Stent thrombosis	2.36	1.53	0.196
Major bleeding events	1.47	0.98	0.377
Cardiac mortality	2.58	0.81	0.002
Target vessel revascularization	3.80	2.26	0.042
Readmission for			
Acute coronary syndrome	6.57	3.53	0.001
Heart failure	1.43	0.90	0.321

Chi-square test was used to test differences between proportions in diabetic and nondiabetic patients

Discussion

The major findings of this study are (1) diabetic patients accounted for about half of this contemporary Middle Eastern PCI population and (2) compared with nondiabetic patients, diabetics had worse baseline cardiovascular risk profiles and were at increased risk of in-hospital and 1-year

cardiac mortality as well as readmission for ACS and coronary revascularization.

In the Middle East, the incidence of DM is rising especially in younger age groups [17]. The majority of the diabetic patients in our study had type 2 DM. Prevalence of DM among ACS and PCI populations in the west is about 25–35 % [18–20]. These rates are lower than those

observed in Middle Eastern ACS populations, where diabetic patients account for 45–70 % of these populations [4, 5, 7, 8, 21].

Patients with diabetes have worse baseline cardiovascular risk profiles and more comorbidities than nondiabetics [22]. We share these findings with other large ACS registries and studies from this region [7, 8, 12]. Diabetics in our study were older, more likely to be females and had a higher prevalence of hypertension, dyslipidemia, heart failure, chronic renal disease, past stroke and peripheral arterial disease.

Despite the higher prevalence of hypertension in diabetic patients, blood pressure readings on admission were not different in both groups, most likely due to the fact that more diabetic patients were prescribed BB and RAASB on admission than nondiabetics. Likewise, the higher rate of use of statins among diabetic patients on admission explains the finding of lower serum levels of total cholesterol and low-density lipoprotein cholesterol in these patients.

The PCI population in our study consisted of one-fifth of patients with chronic stable coronary disease and four-fifths of patients with ACS. PCI populations in western studies recruited CAD patients that consisted of approximately one-third of stable patients and two-thirds of ACS patients [1, 10, 12]. Recent epidemiological studies indicated that cardiac patients in developing countries tend to present with more acute complications than with stable disease compared with patients in the west [22].

DM, by virtue of myriad processes, is associated with severe atherothrombotic CAD [23, 24]. It is also associated with a deleterious cardiovascular outcome that is observed when these patients are treated medically or when they undergo percutaneous or surgical coronary revascularization. This is related to several clinical and pathological factors associated with DM [23, 25, 26]. Diabetic patients are more often females, older and have a higher prevalence of comorbid disease than nondiabetics [27], similar to our findings. They also tend to have smaller coronary artery size, longer complex lesions, often unstable and accelerated disease, higher on-treatment platelet reactivity and higher risk of in-stent restenosis [28–30]. Diabetic patients are particularly at higher risk of recurrent cardiovascular events than nondiabetic patients even with the adoption of advanced pharmacological and technological aspects of PCI [31, 32]. Despite all of these features, diabetic patients with ACS derive a greater benefit from an early invasive and revascularization strategy than nondiabetic patients [33, 34].

The lower incidence of NSTEMI among the diabetic group in our study is another finding that concurs with studies from other regions [7, 8, 21, 22] and is related to the fact that diabetic patients are more likely be older, with

more diffuse multivessel CAD, as we indicated earlier. This profile favors the presentation with NSTEMI more than with STEMI, which occurs at a higher frequency in nondiabetics who tend to be younger, males and smokers with a higher prevalence of single-vessel disease, as shown in Tables 1 and 2. We also observed a lower rate of elevated serum cardiac biomarkers in diabetic compared with nondiabetic patients (37 vs. 43 %). The 6 % difference is almost equal to the 6.6 % difference in the diagnosis of more cases of unstable angina (where serum cardiac enzymes are not elevated) among diabetic than nondiabetic patients (37.7 vs. 30.1 %, $p < 0.001$).

Although DM is an independent predictor of mortality among ACS and PCI patients, studies that compared outcome in diabetic and nondiabetic patients admitted for ACS or those who undergo PCI showed mixed results [35]. The in-hospital and 1-year cardiac mortality rates in diabetic patients in this registry were higher than those in nondiabetics, and DM was found to be an independent predictor of cardiac mortality. However, the mortality rate we reported was lower than the rates reported by other local studies where less than one-third of enrolled patients underwent PCI [7, 8, 21].

Contrary to studies that found DM to be an independent predictor of ST and major bleeding events [36, 37], diabetic patients in our study did not have a higher rate of these two major adverse events during index hospitalization or at 1 year. Second-generation DESs were used in the majority of diabetic and nondiabetic patients in this registry. Implanting DES has demonstrated superiority in reducing the need for repeat revascularizations compared with bare metal stents in diabetic patients [38]. Nonetheless, DM is still among the most important risk factors for adverse clinical events, including ST, even in the DES era [39]. Different types of the second-generation DESs, which have almost completely replaced first-generation DESs, showed comparable clinical outcomes in the diabetic patients up to 1 year of follow-up [25].

Registries have consistently shown that patients with ACS and DM are suboptimally treated with the recommended medications compared with nondiabetic patients with a clear impact on in-hospital and long-term mortality [1, 40]. Our data indicate that, except for GPI, parenteral anticoagulant medications, oral dual antiplatelet therapy and secondary cardiovascular prevention medications were used in diabetic patients in similar or higher rates compared with nondiabetic patients. At 1 year, more than 90 % of diabetics were still using dual antiplatelet agents and statins, with more than 80 % using BB and approximately 70 % using RAASB. GPIs are recommended for diabetic patients admitted with ACS or undergoing PCI [14, 41]. These medications were underused in this study, especially in diabetic patients, possibly because of the high rate of

pretreatment with potent dual oral antiplatelet agents, which obviates the need for a third antiplatelet agent.

Some studies have indicated that glycated hemoglobin (HbA1c) levels were correlated with cardiovascular outcomes in diabetic patients [42, 43], while others failed to demonstrate any correlation of periprocedural HbA1c levels with the incidence of cardiac events at 1 year in diabetic patients with ACS undergoing PCI with second-generation DES [42]. We did not assess the potential presence of such a correlation because HbA1c was only measured in 36 % of diabetic patients during the index hospitalization and in 21 % at 1 year. This “real life” practice has to be addressed, and physicians caring for diabetic patients after PCI should check their HbA1c blood levels regularly. The fact that approximately 60 % of diabetic patients were using antidiabetic agents at 1 year (23.1 % insulin and 35.1 % oral agents) without adequate HbA1c guidance is another area in the care of these patients that needs to be improved.

Our study has few limitations worth discussing. This was a nonrandomized comparison of two different groups of patients; thus, it cannot be free from the inherent limitations of observational registries such as allocation bias and collection of nonrandomized data. Although there was a prospective enrollment of consecutive patients, participation was voluntary, and inclusion of all comers was not verified. Additionally, ACS patients who died before or shortly after admission and those who did not undergo angiography or PCI were not represented in this study. The participating hospitals are high-volume tertiary care centers; thus, the results cannot be generalized to the whole region.

Despite these limitations, this study is unique in that it evaluated the short- and long-term outcomes in diabetic patients who underwent PCI in the Middle East, a region that is not well represented in cardiovascular interventional studies and registries.

Conclusions

In this contemporary prospective Middle Eastern PCI registry, diabetic patients accounted for about one-half of the studied population. DM was an independent predictor of worse cardiovascular outcome, and diabetic patients had a higher incidence of in-hospital and 1-year cardiovascular events compared with nondiabetic patients.

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Compliance with ethical standards

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