SHORT COMMUNICATION

Prevalence, characteristics, and prognostic implications of type 2 diabetes in patients with myocardial infarction

The Polish Registry of Acute Coronary Syndromes (PL-ACS) annual 2018 report

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Received: November 6, 2019.
Revision accepted: February 10, 2020.
Published online: February 12, 2020.
Kardiol Pol. 2020; 78 (3): 243-246
doi:10.33963/KP.15189

Introduction Diabetes mellitus (DM) is a common risk-factor for cardiovascular diseases. In patients without a history of cardiovascular disease, DM is associated with a higher risk of coronary artery disease (CAD), coronary death, and nonfatal myocardial infarction (MI).[1] Patients with at least a 10-year history of DM without any target organ damage and with any risk factor other than DM are categorized as high-risk individuals.[2] Diabetes may be found in 13.7% to 35.6% of patients with MI and is associated with worse clinical parameters, higher prevalence of comorbidities, and a greater extent of CAD.[2-5] These patients are also characterized by increased in-hospital mortality, both in men (11.7% in DM vs 7.8% in non-DM) and women (15.6% in DM vs 12.6% in non-DM).[3]

Proper in-hospital treatment and treatment recommended at discharge are of great importance in patients with DM. As the Polish Registry of Acute Coronary Syndromes (PL-ACS) contains data on both MI and DM treatment, as well as in-hospital and long-term outcomes, we decided to analyze the population of diabetic patients with MI. The purpose of the study was to compare baseline characteristics, treatment patterns, and in-hospital outcomes of patients with and without DM hospitalized for MI. The second aim was to compare hypoglycemic treatment in patients with DM with and without left ventricular systolic dysfunction (LVSD) during hospitalization and at discharge.

Methods The rationale and methodology of PL-ACS were described previously.[6] At the time of this analysis, the registry included 738 790 patients with acute coronary syndrome (ACS), of which 456 381 had MI. The study included patients with MI hospitalized between January 2018 and December 2018. They were divided into 2 groups: patients

with DM and those without. Diabetes was defined in the case report form of the registry as history of type 2 diabetes before the hospital admission.

Moreover, patients with DM were grouped regarding to LVSD. The cutoff for the diagnosis of LVSD was defined as left ventricular ejection fraction (LVEF) below 40% on the latest in-hospital echocardiography.

The study protocol was approved by the ethics committee, and all patients provided written informed consent to participate in the study.

Statistical analysis Categorical variables were presented as percentages. Continuous variables with normal distribution were presented as mean (SD) and those with other than normal distribution, as median and interquartile range (IQR). Comparisons between groups were carried out using the *t* test or the Mann–Whitney test where appropriate. Categorical variables were compared with the χ^2 test, with the Bonferroni correction for multiple comparisons and the Yates correction in case of small sample size.

Results and discussion We included 25 748 consecutive patients admitted to the hospital with MI between January 2018 and December 2018 who were reported to the PL-ACS registry, including 7323 individuals (28.4%) with DM. In other ACS registries, the prevalence of DM varied between 13.7% (MULTIPRAC Registry [Multinational Non-interventional Study of Patients with ST-segment Elevation Myocardial Infarction Treated with Primary Angioplasty and Concomitant Use of Upstream Antiplatelet Therapy with Prasugrel or Clopidogrel]) and 35.6% (CZECH-2 Registry).[5]

The baseline characteristics and results were presented in TABLE 1 and Supplementary material, *Table S1*. Patients with DM had higher systolic blood pressure, heart rate, body mass index, were more often women, and more often had non–ST-segment elevation myocardial infarction.[7] The prevalence of comorbidities was higher in the group with DM and more smokers were found in the nondiabetic group. These observations are consistent with other registries.[5] Patients with diabetes had higher levels of glucose, which is considered to be a risk factor regardless of the diabetic or hemodynamic status.[8,9] Moreover, patients with DM had higher levels of triglycerides, lower levels of cholesterol, worse kidney function, and lower LVEF. Patients with DM were older than those without DM, which is in line with other ACS registries, in which patients with DM were 64 to 71 years old, and without DM, 61.7 to 67.6 years old.[5] This observation may be explained by the fact that in nondiabetic patients, the registered MI was more often the first one (80.2%) compared with patients with DM (68.2%)

Multivessel CAD and left main CAD were diagnosed more often on coronary angiography in DM patients. No difference in the number of patients treated with PCI was found, while patients with DM had coronary artery bypass grafts and inotropes administered more often and glycoprotein IIb / IIIa inhibitors less often. Although there was no difference in the second (other than acetylsalicylic acid) antiplatelet drug use, clopidogrel was used more often in patients with DM, while ticagrelor, in those without DM. This finding is in contrary to the results of the PLATO (Platelet Inhibition and Clinical Outcomes) study, which showed that ticagrelor use was associated with less adverse events in patients with DM and with better survival, with no increase in bleeding.[10] This paradox of treating sicker patients with the less effective drug was described before.[11] The latest European Society of Cardiology guidelines recommended that patients with and without DM should be treated according to the same antiplatelet strategy, and dual antiplatelet therapy with prasugrel or ticagrelor in patients with ACS was superior to dual antiplatelet therapy with clopidogrel in both DM and non-DM groups.[2]

Patients with DM received at discharge more often: β-blockers, renin-angiotensin-aldosterone system blockers, mineralocorticoid receptor antagonists, diuretics, statins, and nitrates. This might be associated with more advanced age, higher blood pressure, heart rate and lower LVEF. The use of antiplatelet drugs at discharge was similar in both groups.

In our study patients with DM had higher occurrence of all in-hospital adverse events, including in-hospital death. This observation is consistent with previous studies, in which in-hospital mortality varied between 1.43% (MULTIPRAC) and 9.42% (Belgian STEMI) in patients with DM and ACS and between 0.34% (MULTIPRAC) and 6.63% (Belgian STEMI) in those with ACS but no DM.[3,5]

Comparing the hospital treatment of DM in patients with and without LVSD, patients with LVSD received insulin treatment more often, while patients without LVSD, oral antidiabetic drugs. Similar observations were done at discharge. During hospitalizations no differences in the classes of oral antidiabetic drugs between the groups were found. Surprisingly, patients with DM and LVSD were more often discharged without any treatment of DM. Some patients with DM were also treated with thiazolidinediones or dipeptidyl peptidase 4 inhibitors, which are suspected to play a role in LVSD after MI and are contraindicated in patients with reduced LVEF or at high risk of heart failure.[2,12] Patients with DM and LVSD had higher in-hospital mortality than those without LVSD (9.5% vs 2% respectively; P <0.0001).

According to the Polish summary of product characteristics of metformin, it is contraindicated in patients with heart failure. However,

TABLE 1 Baseline characteristics, treatment, and outcomes of patients with myocardial infarction and diabetes (continued on the next page)

Parameter		DM (n = 7323)	No DM (n = 18425)	*P* value
Baseline characteristics				
Age, y, mean (SD)		70.6 (10.0)	66.8 (11.7)	<0.001
Male sex		4254 (58.1)	12463 (67.6)	<0.001
Body mass index, kg/m^2, median (IQR)		29.4 (6.8)	27.2 (5.7)	<0.0001
Main symptom of myocardial infarction	Chest pain	6093 (83.2); 7321	16290 (88.5); 18417	<0.001
	Dyspnea	682 (9.3); 7321	995 (5.4); 18417	
	Other	546 (7.5); 7321	1132 (6.1); 18417	
ST-elevation myocardial infarction		2234 (30.5)	7040 (38.2)	<0.001
Killip class	1	5669 (77.4)	15701 (85.3)	<0.001
	2	1134 (15.5)	1975 (10.7)	
	3	312 (4.3)	334 (1.8)	
	4	204 (2.8)	398 (2.2)	
Systolic blood pressure, mm Hg, median (IQR)		140 (38)	135 (30)	<0.001
Diastolic blood pressure, mm Hg, median (IQR)		80 (20)	80 (20)	0.09
Heart rate, bpm, median (IQR)		78 (20)	75 (19)	<0.001
Sinus rhythm on admission		6412 (87.7); 7313	16933 (92); 18399	<0.001
History of arterial hypertension		6290 (87.4); 7197	11702 (65.3); 17920	<0.001
History of hyperlipidemia		3850 (57.3); 6722	7071 (41); 17245	<0.001
History of coronary artery disease		2435 (34.5); 7057	3506 (19.6); 17885	<0.001
History of myocardial infarction		2267 (31.8); 7128	3724 (19.8); 18807	<0.001
History of PCI		2085 (29.3); 7117	3254 (18); 18075	<0.001
History of CABG		570 (8); 7119	723 (4); 18081	<0.001
History of atrial fibrillation		1308 (18.4); 7095	2043 (11.3); 18050	<0.001
History of stroke		624 (8.8); 7093	849 (4.7); 18055	<0.001
History of heart failure		1143 (17.7); 7024	1600 (8.9); 17973	<0.001
History of chronic kidney disease		1121 (15.8); 7095	1155 (6.4); 18040	<0.0001
Smoking		3404 (55.4); 6149	10469 (64.1); 16332	<0.001
History of peripheral artery disease		785 (11.2); 7006	965 (5.4); 17874	<0.001
History of cardiac arrest		191 (2.6); 7310	463 (2.5); 18389	0.66
Glucose at admission, mmol/l, median (IQR)		9 (5.7)	6.4 (2.2)	<0.001
Hemoglobin A_{1c}, %, median (IQR); total		7.2 (2.1); 744	5.7 (0.7); 1187	<0.001
Total cholesterol, mmol/l, mean (SD)		4.4 (1.3)	4.9 (1.4)	<0.001
LDL cholesterol, mmol/l, median (IQR)		2.4 (1.6)	2.9 (1.6)	<0.001
HDL cholesterol, mmol/l, median (IQR)		1.1 (0.4)	1.2 (0.5)	<0.001
Triglycerides, mmol/l, median (IQR)		1.5 (1)	1.2 (0.9)	<0.001
eGFR, ml/min/1.73 m^2, median (IQR)		73.2 (47.4)	82.2 (44.6)	<0.001
LVEF, %, median (IQR)		47 (15)	50 (15)	<0.001
LVEDD, mm, median (IQR)		51 (7)	50 (8)	<0.001
LVESD, mm, median (IQR)		37 (10)	35 (9)	<0.001
NYHA	I	3477 (50.3)	10556 (59.9)	<0.001
	II	2948 (42.6)	6217 (35.3)	
	III	423 (6.1)	743 (4.2)	
	IV	68 (1)	115 (0.6)	

TABLE 1 Baseline characteristics, treatment, and outcomes of patients with myocardial infarction and diabetes (continued from the previous page)

Parameter	DM (n = 7323)	No DM (n = 18 425)	*P* value
In-hospital outcomes			
Pulmonary edema	139 (1.9); 7265	162 (0.9); 18 267	<0.001
Cardiogenic shock	166 (2.3); 7265	313 (1.7); 18 267	<0.001
Cardiac arrest	223 (3.1); 7263	380 (2.1); 18 267	<0.001
Stroke / transient ischemic attack	34 (0.5); 7263	59 (0.3); 18 265	0.1[a]
Major bleeding	142 (2); 7264	234 (1.3); 18 267	<0.001
In-hospital mortality	370 (5.1); 7323	625 (3.4); 18 425	<0.001

Data are presented as number (percentage); total number of patients for whom data were available unless otherwise indicated.

a Yates correction

Abbreviations: CABG, coronary artery bypass graft; DM, diabetes mellitus; eGFR, estimated glomerular filtration rate; HbA1C, glycated hemoglobin; HDL, high-density lipids cholesterol; LDL, low-density lipids cholesterol; LVEF, left ventricular ejection fraction; LVEDD, left ventricular end diastolic diameter; LVESD, left ventricular end systolic diameter; NYHA, New York Heart Association functional classification

according the international summary of product characteristics, metformin may be used in patients with stable chronic heart failure with a regular monitoring of cardiac and renal function, while it is contraindicated in patients with acute and unstable heart failure. According to the current European Society of Cardiology guidelines, metformin is safe at all stages of heart failure with estimated glomerular filtration rate greater than 30 ml/min.[2] In our study, 51.6% of diabetic patients with MI and LVEF less than 40% had biguanides administered during hospital stay and 24.4% at discharge. Metformin may reduce the risk of cardiovascular events and all-cause mortality in patients with MI, as well as heart failure.[13] Those benefits are not associated with the hypoglycemic effects of metformin.[14]

To conclude, patients with DM were older, had more comorbidities, greater CAD extent, and more in-hospital events. They received the same (PCI, antiplatelet drugs) or more intensive (other drug classes) treatment than patients without DM. Patients with DM and LVSD less often received oral antidiabetic drugs and more often had insulin or no antidiabetic treatment administered compared with diabetic patients without LVSD.

SUPPLEMENTARY MATERIAL

Supplementary material is available at www.mp.pl/kardiologiapolska.

ARTICLE INFORMATION

CONFLICT OF INTEREST None declared.

HOW TO CITE Niedziela JT, Hiczkiewicz J, Kleinrok A, et al. Prevalence, characteristics, and prognostic implications of type 2 diabetes in patients with myocardial infarction: the Polish Registry of Acute Coronary Syndromes (PL-ACS) annual 2018 report. Kardiol Pol. 2020; 78: 243-246. doi:10.33963/KP.15189

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