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Diabetic Patients with an Acute Myocardial Infarction in Terms of Risk Factors and Comorbidities Management: Characteristics of the Highest-Risk Individuals

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A – research concept and design; **B** – collection and/or assembly of data; **C** – data analysis and interpretation; **D** – writing the article; **E** – critical revision of the article; **F** – final approval of article

Abstract

Background. Patients with diabetes mellitus (DM) and acute myocardial infarction (AMI) are heterogeneous individuals with different clinical status compared to patients without DM.
Objectives. The aim of this study was to analyze the group of diabetic patients with ST-segment elevation MI (STEMI) or non-ST-segment elevation infarction (NSTEMI) including risk factors, medical history, laboratory findings, advancement of coronary vessel atherosclerosis, and diagnostics and therapeutic modalities performed. A comparison of groups according to the type of MI was also made.
Material and Methods. The study involved all (n = 130) patients with DM and AMI, hospitalized in the Department of Cardiology, Medical University of Silesia, Katowice, in 2012. Clinical presentation, medical history, laboratory tests, imaging studies and additional tests as well as treatment management data were collected. Statistical analysis of the data obtained was performed using STATISTICA® software. Coronary angiography was performed in 120 subjects (92.3%).
Results. NSTEMI almost doubled STEMI occurrence in the study group (65.4% vs. 34.6%). Left main disease (LMD) was more often diagnosed in the NSTEMI subgroup of patients (14.1% vs. 6.7%). There were no significant differences between the compared groups as far as clinical presentation and comorbidities are concerned; more frequent previous PCI in NSTEMI patients was noticed, however (37.7% vs. 17.8%; $p = 0.0195$). The STEMI subgroup was characterized by higher leukocytosis (13.2 vs. 10.0 × 103/μL; $p < 0.001$) and serum glucose concentration (217 vs. 182 mg%; $p = 0.001$); they were also treated with invasive methods more frequently (95.5% vs. 75%; $p < 0.001$) and the left anterior descending artery was delivered with stents more frequently (63.3% vs. 48.7%; $p = 0.0426$).
Conclusions. Patients with DM and AMI are burdened with metabolic disorders and numerous risk factors. They require aggressive diagnostics and therapy including new revascularization techniques and optimal medical treatment. Regardless of the type of AMI (STEMI or NSTEMI), the study group was homogeneous in terms of complaints, comorbidities and metabolic profile (**Adv Clin Exp Med 2016, 25, 4, 655–663**).

Key words: treatment, diabetes mellitus, acute myocardial infarction.

Patients with diabetes mellitus (DM) and acute myocardial infarction (AMI) represent heterogeneous group of patients with differences in clinical status at baseline, advancement of coronary artery atherosclerosis, occurrence of comorbidities, metabolic state and previous history of percutaneous coronary interventions (PCI) and/or coronary artery bypass graft surgery (CABG).

Diabetic patients have a higher initial risk of mortality compared to patients without the coexistence of DM. Regardless of DM, the presence of hyperglycemia is an independent risk factor for poor prognosis in subjects with acute coronary syndromes (ACS) [1].

The increased risk of atherosclerosis development and further complications in patients with DM are caused by different mechanisms including endothelial dysfunction and abnormal platelet reactivity as well as coagulation-fibrinolysis balance disorders [2, 3].

A number of mechanisms in DM, some still not precisely known, are associated with disturbances of platelet function, their activity, adhesion and aggregation. Metabolic disorders result in platelet hyperreactivity [4–8].

The scale of the problem of AMI in diabetic patients is shown in the Polish Registry of Acute Coronary Syndromes. According to that registry, DM was present in 21.2% of patients with myocardial infarction with ST-segment elevation (STEMI), in 28.1% with acute myocardial infarction without ST-segment elevation (NSTEMI) and in 22.1% of individuals with unstable angina [9]. A similar observation emerges from the Swedish Coronary Angiography and Angioplasty Register (SCAAR) [10]. It has been shown that DM is associated with a significantly higher risk of ACS and of death due to MI [9, 11].

The aim of this study was to analyze the group of diabetic patients with AMI – both with STEMI and with NSTEMI, including risk factors, medical history, laboratory findings, advancement of coronary vessel atherosclerosis, and diagnostics and therapeutic modalities performed. A comparison of the groups according to the type of MI was also made.

Material and Methods

The study involved all patients (n = 130) hospitalized in 2012 in the Department of Cardiology, Medical University of Silesia in Katowice with previously diagnosed DM and coexisting AMI. STEMI and NSTEMI subgroups were distinguished and subjected to further analysis. Statistical analysis was performed using STATISTICA® software. The results are presented as numbers and percentages or as mean values and standard deviations (SD). The chi-square (χ^2) test of independence was used to assess relationships between qualitative variables and, in the case of a small size of the tested groups, two-tailed Fisher's exact test was used. The Mann-Whitney U test was used to compare quantitative parameters. P-value below 0.05 was considered statistically significant.

All individuals underwent physical examination, had a 12-lead electrocardiogram (ECG), transthoracic echocardiography (TTE) and laboratory tests (complete blood count, electrolytes, creatinine, lipid profile, glucose and markers of myocardial necrosis) performed. In the next step, the results of the coronary angiography, percutaneous coronary interventions and the qualification for further treatment (conservative or invasive) were analyzed. The optimal medical therapy for ACS was administered in every patient during hospitalization, according to the current guidelines.

Results

The characteristics of patients with DM and ACS, taking into consideration their demographic data, previous medical history and type of chronic treatment, are presented in Table 1.

An analysis of patients with DM and AMI showed that NSTEMI was more often diagnosed than STEMI. Patients with NSTEMI had more PCI with stent implantation and/or CABG procedures previously performed compared to the STEMI individuals. The difference was statistically significant.

The clinical presentation of the studied patients (on admission) and their complaints are shown in Table 2.

There were no significant differences on clinical presentation between the studied groups of patients regarding the type of AMI. The frequency of chest pain, dyspnea, sudden cardiac arrest, cardiogenic shock, pulmonary edema or complete AV block were similar.

Type and frequency of comorbidities in the study group is presented in Table 3.

There were no significant differences in the clinical presentation and occurrence of comorbidities between the compared groups of patients with DM and AMI.

The characteristics of patients taking into account the type of infarction and the results of laboratory findings are shown in Table 4.

The mean serum glucose concentration, cardiac markers, leukocytosis, the number of red blood cells and hematocrit were considerably higher in STEMI patients than in NSTEMI subjects. There was no significant difference between the groups regarding lipid profile, serum creatinine and hemoglobin concentrations or the number of platelets.

The left ventricular ejection fraction (LVEF) measured echocardiographically using the Simpson's method at admission in the NSTEMI patients was slightly higher than in the STEMI subjects (45% ± 12 vs. 40% ± 11). The difference; however, was not statistically significant.

Diagnostic coronary angiography was performed in 120 patients (92.3%) of the studied group. Left main disease (narrowing of artery lumen ≥ 50%) was found in 15 patients including 3 patients with STEMI (6.7%) and 12 (14.1%) with NSTEMI. Lumen stenosis of at least 70% in native coronary arteries and narrowing of 50% or greater in the case of stents previously implemented were considered significant. The findings from the coronary angiography (state before PCI) in the studied group of patients with DM and AMI are presented in Table 5.

Table 1. Characteristics of patients with diabetes mellitus and acute myocardial infarction

Study group No. of patients n = 130 (100%)							
Type of myocardial infarction			STEMI (n = 45; 34.6%)		NSTEMI (n = 85; 65.4%)		p-value
Age (mean ± SD; range)			66.4 ± 11.3 (47–88)		69.4 ± 7.3 (52–88)		ns.
Number of patients and percentage			**n**	(%)	**n**	(%)	
Men			24	53.3	44	51.8	ns.
Women			21	46.7	41	48.2	ns.
History of previous myocardial infarction	STEMI		8	17.8	18	21.2	ns.
	NSTEMI		4	8.9	18	21.2	ns.
	unknown type		1	2.2	8	9.4	ns.
Smoking	active smokers		11	24.4	14	16.5	ns.
	past smokers		10	22.2	15	17.7	ns.
History of previous stroke or TIA			8	17.8	11	12.9	ns.
Previous percutaneous coronary interventions	PCI		8	17.8	32	37.7	0.0195
	type and number of stents	1 BMS	6	13.3	17	20	ns.
		2 or more BMS	1	2.2	8	9.5	
		1 DES	1	2.2	8	9.5	
		2 or more DES	0	0	0	0	
	POBA		0	0	0	0	ns.
	PCI and CABG		0	0	10	11.8	0.0166
	CABG		1	2.2	10	11.8	ns.
Treatment of DM	insulin therapy		10	22.2	24	28.2	ns.
	insulin therapy and oral hypoglycemic drugs		6	13.3	9	10.6	
	oral hypoglycemic drugs		18	40	39	45.9	
	only diabetic diet		11	24.4	13	15.3	

STEMI – ST-segment elevation myocardial infarction; NSTEMI – non-ST-segment myocardial infarction; PCI – percutaneous coronary intervention; CABG – coronary artery bypass grafting; BMS – bare-metal stent; DES – drug-eluting stent; POBA – plain old balloon angioplasty; TIA – transient ischemic attack; p – statistical significance; ns. – not statistically significant; DM – diabetes mellitus.

The left anterior descending (LAD) branch of the left coronary artery was significantly more often the culprit vessel in STEMI patients compared to those with NSTEMI.

The type, number and site of implantation of stents in the studied patients with DM and AMI are shown in Fig. 1 and 2.

The analysis showed that in the case of STEMI, the left anterior descending artery (LAD) was the more frequent target vessel for PCI. There was no significant difference between the two types of AMI as far as other coronary arteries were concerned. The analysis also revealed that PCI was unsuccessful in 9 patients: 3 (6.7%) of the STEMI and 6 (7.1%) of the NSTEMI group. More bare-metal stents were implanted in the target vessel in patients with STEMI compared to NSTEMI ($p = 0.002$).

Figure 3 summarizes treatment management in the studied group of patients with DM and AMI.

PCI was performed more often in patients with STEMI compared to NSTEMI subjects ($p < 0.001$).

Table 2. Characteristics of patients with DM and AMI regarding reported complaints and abnormalities on physical examination and additional studies (on admission)

Parameter	Type of MI				p-value
	NSTEMI n = 85		STEMI n = 45		
Number of patients and percentage	n	%	n	%	
Chest pain	67	78.8	38	84.4	ns.
Dyspnea	9	10.6	3	6.7	ns.
Cardiac arrest	3	3.5	3	6.7	ns.
Syncope	3	3.5	0	0	ns.
Atypical chest pain	0	0	1	2.2	ns.
Without symptoms	3	3.5	0	0	ns.
Cardiogenic shock	5	5.9	6	13.3	ns.
Pulmonary edema	8	9.4	3	6.8	ns.
Third-degree atrioventricular block	2	2.3	0	0	ns.
Killip classification ≥ II	10	10.8	2	4.4	ns.
Evidence of congestive heart failure	3	3.5	0	0	ns.

AMI – acute myocardial infarction; STEMI – ST-segment elevation myocardial infarction; NSTEMI – non ST-segment elevation myocardial infarction; DM – diabetes mellitus; p – statistical significance; ns. – not statistically significant.

Table 3. Characteristics of patients with DM and AMI including comorbidities

Comorbidities		Study group, n = 130				p-value
		STEMI n = 45		NSTEMI n = 85		
		n	%	n	%	
Atrial fibrillation	persistent/permanent	5	11.1	10	11.8	ns.
	paroxysmal	6	13.3	9	10.6	
Chronic kidney disease		6	13.3	14	16.5	
Peripheral artery disease		5	11.1	19	22.4	
Lipid disorders		33	73.3	60	70.6	
Obesity		23	51.1	35	41.2	
Arterial hypertension		37	82.2	78	91.8	

DM – diabetes mellitus; AMI – acute myocardial infarction; STEMI – ST-segment elevation myocardial infarction; NSTEMI – non ST-segment elevation myocardial infarction; p – statistical significance; ns. – not statistically significant.

Following coronary angiography, only conservative treatment was more frequently administered in NSTEMI (p = 0.0083). On the other hand, after initial treatment with PCI, more NSTEMI patients were qualified for invasive treatment compared to STEMI individuals (p = 0.0075).

Thirteen patients died during hospitalization: 7 in the STEMI group (15.6%) and 6 in the NSTEMI group (7.1%). The difference between the groups was not statistically significant. All these patients had diagnostic coronary angiography performed, and in 11 (84.6%) subjects PCI was performed as well. In two cases, PCI failed due to unfavorable anatomy of the lesions. Also, in all these patients, AMI was complicated with cardiogenic shock.

Discussion

The Euro Heart Survey registry shows that DM occurs in about 30% patients with coronary artery disease [1, 12, 13].

Table 4. Characteristics of patients with DM and AMI regarding laboratory findings

Parameter	STEMI (n = 45)		NSTEMI (n = 85)		p
	n	result ± SD	n	result ± SD	
CPK (U/L)	40	1286 ± 1616	78	436 ± 854	< 0.001
CK-MB (U/L)	43	135 ± 149	83	55 ± 84	< 0.001
Blood glucose (mmol/L)	43	12 ± 4.6	83	10.1 ± 6.9	0.0011
HbA1c (%)	18	7.7 ± 1.6	36	7.4 ± 1.2	ns.
Total cholesterol (mg/dL)	41	182 ± 51	80	164 ± 40	ns.
LDL cholesterol (mg/dL)	39	108 ± 42	77	96 ± 34	ns.
HDL cholesterol (mg/dL)	41	39 ± 43	80	42 ± 13	ns.
Triglycerides (mg/dL)	41	171 ± 153	79	136 ± 76	ns.
Creatinine (mg/dL)	45	1.09 ± 0.72	84	1.16 ± 0.74	ns.
White blood cells ($\times 10^3/\mu L$)	45	13.2 ± 3.87	83	10.03 ± 3.37	< 0.001
Red blood cells ($\times 10^6/\mu L$)	45	4.76 ± 0.55	83	4.48 ± 0.62	0.0259
Hemoglobin (g/L)	45	143 ± 17	83	136 ± 17	ns.
Hematocrit (%)	45	42.4 ± 4.2	83	40.4 ± 4.7	0.0356
Platelets ($\times 10^3/\mu L$)	45	218 ± 76	83	202 ± 73	ns.

HbA1c – glycosylated hemoglobin A1c; CPK – creatinine phosphokinase; CK-MB – MB isoform of creatinine kinase; ns. – statistically not significant; n – number; SD – standard deviation.

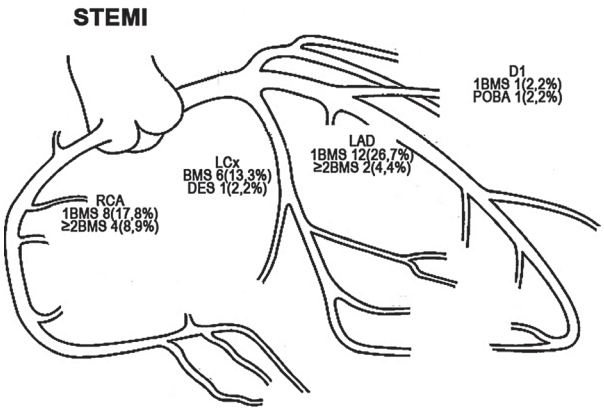

Fig. 2. Number and location of percutaneous coronary interventions with stent implantation (BMS or DES) and the plain old balloon angioplasty performed in patients with diabetes mellitus and STEMI

RCA – right coronary artery; LCx – left circumflex coronary artery; LAD – left anterior descending coronary artery; D1 – first diagonal branch of the left anterior descending coronary artery; BMS – bare-metal stent; DES – drug eluting stent; POBA – plain old balloon angioplasty; STEMI – ST-segment elevation myocardial infarction.

From the PRAIS-UK Registry it emerged that patients with ACS without persistent ST-segment elevation and a coexistence of DM more frequently had arterial hypertension, congestive heart failure,

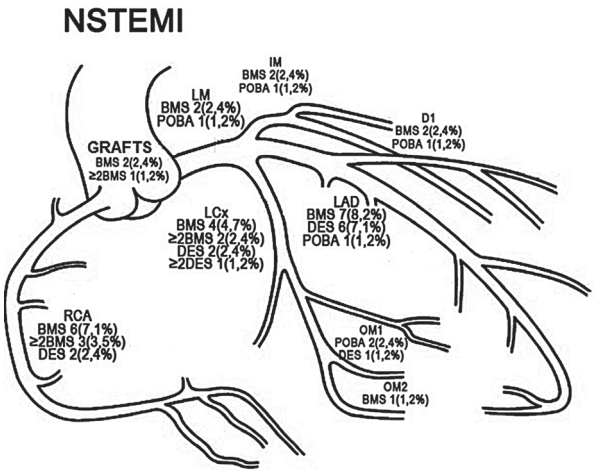

Fig. 1. Number and location of percutaneous coronary interventions with stent implantation (BMS or DES) and plain old balloon angioplasty performed in patients with diabetes mellitus and NSTEMI

RCA – right coronary artery; LCx – left circumflex coronary artery; OM1 and OM2 – obtuse marginal branches of circumflex coronary artery; LAD – left anterior descending coronary artery; D1 – first diagonal branch of the left anterior descending coronary artery; IM – intermedius branch of the left coronary artery; BMS – bare-metal stent; DES – drug eluting stent; POBA – plain old balloon angioplasty; NSTEMI – non-ST-segment elevation myocardial infarction; Grafts – coronary bypass graft.

Table 5. Type and location of culprit lesions in patients with DM and AMI

Type and location of diseased vessels	Type of myocardial infarction				p-value
	STEMI (n = 45)		NSTEMI (n = 85)		
	n	(%)	n	(%)	
RCA	20	44.4	37	43.5	ns.
In-stent restenosis in RCA	1	2.2	1	1.2	
LM	3	6.7	12	14.1	
In-stent restenosis in LM	0	0	1	1.2	
LAD	28	62.20	37	43.5	p = 0.0426
In-stent restenosis in LAD	0	0	5	5.9	ns.
Stenosis in LAD and in-stent restenosis	1	1.1	2	2.4	
Stent thrombosis in LAD	0	0	1	1.2	
LCx	20	44.4	24	28.2	
In-stent restenosis in LCx	0	0	1	1.2	
D1	3	6.7	9	10.6	
OM1	5	11.1	7	8.2	
In-stent restenosis in OM1	0	0	1	1.2	
OM2	0	0	2	2.4	
IM	3	6.7	4	4.7	
Bypass graft stenosis	0	0	6	7.1	
PDA	1	2.2	1	1.2	
PLV	0	0	2	2.4	

DM – diabetes mellitus; AMI – acute myocardial infarction; RCA – right coronary artery; LM – left main coronary artery; PDA – posterior descending artery; PLV – posterolateral ventricular branch; LCx – left circumflex coronary artery; OM – obtuse marginal branch of circumflex coronary artery; LAD – left anterior descending coronary artery; D1 – the first diagonal branch of the left anterior descending coronary artery; IM – intermedius branch of the left coronary artery; p – statistical significance; ns. – not statistically significant.

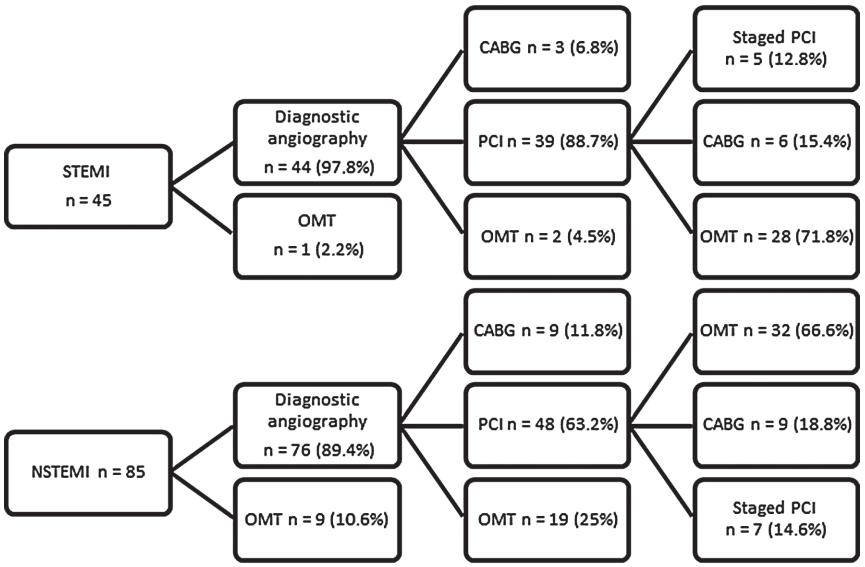

Fig. 3. Management of patients with diabetes mellitus and STEMI or NSTEMI

STEMI – myocardial infarction with ST-segment elevation; NSTEMI – myocardial infarction without ST-segment elevation; OMT – optimal medical therapy; CABG – coronary artery bypass graft surgery; PCI – percutaneous coronary intervention.

history of previous stroke and myocardial infarction. Mortality was also higher in diabetic patients [14]. Likewise, patients with ACS, DM and arterial hypertension have a higher risk of death compared to patients without DM and/or arterial hypertension [15]. In our study group, the prevalence of arterial hypertension was not dependent on the type of AMI.

Diabetic patients have greater atherosclerosis advancement and there are also more cases of multivessel coronary artery disease [16].

The PROSPECT (Providing Regional Observations to Study Predictors of Events in the Coronary Tree) study showed that diabetic patients and those with metabolic syndrome presenting with ACS treated with PCI have an increased 3-year incidence of major coronary events [17]. Also the SCAAR Registry indicates that the mortality of patients (with stable angina, STEMI or NSTEMI) after diagnostic angiography and PCI is higher in subjects with DM [10].

It was demonstrated that patients with DM and glucose levels above 8.5 mmol/L (154 mg/dL) presenting with STEMI and subjected to PCI have worse response to anti-platelet therapy with clopidogrel [18].

Patients presenting with STEMI are of benefit with regard to primary PCI [19]. Our analysis shows that STEMI patients more frequently were referred to diagnostic angiography and PCI than NSTEMI individuals and it was statistically significant ($p < 0.001$).

A strategy of early revascularization also improves clinical outcomes in NSTEMI patients [19]. NSTEMI patients were referred to CABG more often than STEMI patients after diagnostic coronary angiography. 1/5 of NSTEMI patients had a history of previous CABG, which made it difficult to choose the optimal modality of revascularization. Patients with DM and AMI have worse prognosis than subjects without DM despite the introduction of drug-eluting stents [20]. But still, we have to remember that the higher risk the patient is (as in the case of DM), the more benefits can be achieved.

The presence of hyperglycemia on admission in patients with DM and AMI is undoubtedly associated with a significantly higher mortality and morbidity [13, 21]. Patients presenting with STEMI had significantly ($p = 0.0011$) higher levels of serum glucose on admission than patients with NSTEMI. The intensity of hyperglycemia treatment remains an open issue because of the risk of increasing mortality in patients with intensively controlled glycaemia [22, 23]. Hypoglycemia during hospitalization worsens prognosis and increases the risk of complications including cardiovascular events and even death. Moderate control of glycaemia is advised currently. In the latest ESC guidelines, it is emphasized that insulin should be considered in patients presenting with ACS and with hyperglycemia (> 10 mmol/L or > 180 mg/dL), taking into account the comorbidities [1, 21, 24–28].

Glycated hemoglobin A1c (HbA1c) has been associated with cardiovascular risk factors and the incidence of death from any cause [29, 30]. Our analysis shows that the average value of HbA1c was significantly increased, indicating a lack of optimal DM control in the last few months regardless of the AMI type.

Atherogenic dyslipidemia is often found in diabetic patients [31]. In our study group, there were no statistically significant differences in the concentrations of lipoprotein cholesterol and triglyceride levels between STEMI and NSTEMI patients, but lipid disorders still had been seen in a majority of subjects. Special attention in diabetic patients should be paid to lipid profile assessment and ordering aggressive treatment of dyslipidemia. In the group of patients with diabetes developing AMI, elevated levels of LDL cholesterol and of triglycerides prove ineffective lipid lowering therapy in these individuals.

Atrial fibrillation in diabetic patients and coexisting with AMI was diagnosed in 1/5 of the subjects in the study group. Those patients are of high risk of stroke and have indications for oral anticoagulant therapy. Importantly, there is also a higher risk of bleeding complications due to the triple anticoagulation/antiplatelet therapy. The selection of the stent type (BMS or DES) should be made individually, taking into account the risk of stroke and bleeding complications.

The group of patients with DM and AMI is burdened with metabolic disorders and numerous cardiovascular risk factors. These patients require intensive diagnostic procedures and aggressive treatment including percutaneous and surgical revascularization. Preventive strategies, especially the elimination of modifiable risk factors, should be implemented in every subject. The presented data suggests special attention in diabetic patients should be paid to lipid disorders. The elevated level of LDL-cholesterol shown is a crucial target as far as risk factors for cardiovascular events are considered.

The analysis of patients with DM and AMI shows that, regardless of the type of myocardial infarction (STEMI or NSTEMI), they are a homogeneous group as far as clinical presentation, comorbidities and metabolic profile assessed by glycated hemoglobin A1c are concerned.

Diabetic patients presenting with NSTEMI, compared to STEMI, more often had a history of previous PCI or CABG. In STEMI subjects, the left anterior descending artery was the infarct-re-

lated artery more often. STEMI patients had higher mean concentrations of glucose and higher leukocytosis.

Patients with DM and AMI require an individual management strategy due to the history of previous revascularization (PCI and CABG or CABG alone), which may limit the options of later coronary revascularization and increase the risk of intervention (e.g. re-CABG or PCI in venous grafts) and, as a consequence, worsen their prognosis.

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