Original article

Kardiologia Polska
2011; 69, 4: 336–343
ISSN 0022–9032

Impact of multivessel coronary disease on one--year clinical outcomes and five-year mortality in patients with ST-elevation myocardial infarction undergoing percutaneous coronary intervention

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Abstract

Background: Multivessel coronary disease (MVD) occurs in approximately 40–65% of patients with ST-segment elevation myocardial infarction (STEMI) treated with percutaneous coronary intervention (PCI), and is associated with significantly increased morbidity and mortality rates.

Aim: To evaluate the impact of MVD on in-hospital and long-term clinical outcomes in patients with STEMI and PCI, and to compare these results with those from a group of patients with a single coronary vessel disease (SVD).

Methods: Consecutive patients with STEMI treated with PCI were included in the analysis. Patients were divided into two groups: patients with SVD (n = 828, 46.6%) and patients with MVD (n = 948, 53.4%). Clinical follow-up was performed at 12 months, and five-year mortality was assessed. Major adverse cardiac events (MACE) at 12-month follow-up were defined as death (from any cause), stroke, need for percutaneous or any surgical coronary artery revascularisation, and non-fatal myocardial infarction.

Results: The in-hospital mortality was 2.9% *vs* 9.5% ($p < 0.0001$) and the five-year mortality was 11.9% *vs* 23.8% ($p < 0.0001$), for SVD *vs* MVD patients, respectively. The cumulative incidence of MACE during 12-month follow-up was significantly higher in patients with MVD (32.5% *vs* 14.5%, $p < 0.0001$). Moreover, multivariate analysis revealed that after a correction for baseline differences, the presence of MVD was a strong and independent predictor for five-year mortality in patients treated with PCI (hazard ratio 1.45, 95% confidence interval 1.13–1.88, $p = 0.004$).

Conclusions: The presence of MVD in patients with STEMI is a strong and independent risk factor for higher long-term mortality.

Key words: multivessel coronary artery disease, myocardial infarction

Kardiol Pol 2011; 69, 4: 336–343

INTRODUCTION

Although enormous progress has been made over the past few decades in the diagnosis and treatment of acute coronary syndromes (ACS), they remain one of the most frequent causes of hospitalisation and mortality. The estimated annual incidence of ACS in Poland is approximately 140,000, of which 35% are ST-segment elevation myocardial infarctions (STEMI) [1].

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Received: 09.08.2010 **Accepted:** 26.01.2011

Multivessel coronary disease (MVD) occurs in approximately 40–65% of patients with STEMI [2–5] and is associated with reduced success of myocardial reperfusion and significantly increased morbidity and mortality, regardless of the reperfusion method employed [2, 6–8]. Neither abciximab nor the use of stents have ameliorated the adverse clinical implications of MVD [9].

According to current guidelines, primary angioplasty for STEMI should be limited to the culprit vessel [10]. Despite prompt and successful restoration of epicardial blood flow by percutaneous coronary intervention (PCI), a significant proportion of patients with STEMI remain at increased risk for death and other adverse outcomes. Clinical identification of these patients before hospital discharge is warranted.

Despite the limited information concerning the influence of MVD on long-term outcomes in STEMI-patients treated with PCI, there is a growing trend towards additional revascularisation and other strategies. The objective of this investigation was to evaluate the impact of MVD on in-hospital and long-term clinical outcomes in patients with STEMI who underwent PCI limited to the infarct-related artery (IRA), as well as to compare these results with those from a group of patients with single coronary vessel disease (SVD). We hoped to identify differences in patient characteristics and clinical course, based on the findings at a large interventional cardiology centre in Poland. Furthermore, we analysed the factors affecting the long-term prognosis.

METHODS

Study population

We conducted a single-centre analysis of 1,776 consecutive patients with STEMI who underwent immediate coronary intervention at our centre between January 1998 and December 2003. The SVD was diagnosed in 828 (46.6%) patients, while MVD, defined as > 70% diameter stenosis of at least one major epicardial coronary artery or its major branch, remote from the IRA, as determined by visual assessment, was diagnosed in 948 (53.4%) patients. Patients with STEMI after coronary artery bypass grafting (CABG) were excluded from analysis. Included in the analysis were patients with cardiogenic shock on admission, defined as the presence of both of the following criteria: clinical (symptoms of shock, peripheral hypoperfusion) and haemodynamic (systemic systolic pressure < 90 mm Hg or systemic systolic pressure 90–110 mm Hg during intra-aortic balloon pumping [IABP] or while using inotropic drugs).

The clinical data from all patients with STEMI were prospectively recorded in a computerised database as part of a single-centre ACS registry. Follow-up information was obtained by direct phone call, outpatient visits or from the National Health Fund database.

Procedure

At our centre, an interventional cardiologist is on duty 24 hours a day. All patients with acute STEMI were treated with 300–500 mg of aspirin, 300 mg clopidogrel (since 2001) and 75 mg daily thereafter or ticlopidine 250 mg twice daily for a period of at least eight weeks. The 5,000–10,000 units of unfractionated heparin, and 2.5–5 mg of morphine intravenously was administrered. Depending on the patient's condition, other medications were also used, and the patients were referred for urgent coronary angiography.

Standard guidewires, balloon catheters and coronary stents were used. In some patients with MI complicated by cardiogenic shock, depending on their clinical status, IABP was performed. Vascular sheaths were removed upon normalisation of blood coagulation parameters (i.e. activated partial thromboplastin time). After the intervention, apart from thienopiridynes, all patients received 150 mg of aspirin daily indefinitely, as well as beta-blockers, angiotensin-converting enzyme inhibitors, and statins, unless otherwise contraindicated.

Definitions and end-points

Acute STEMI was diagnosed based on stenocardial pain lasting ≥ 30 min, with electrocardiographic features of an evolving MI, i.e. ST segment elevation ≥ 0.1 mV in two or more limb leads or ≥ 0.2 mV in two or more precordial leads, or a newly-formed left bundle branch block, with time since onset not exceeding 12 hours (or in the case of cardiogenic shock, 18–24 h).

Clinical follow-up was performed at 12 months, and five-year mortality was assessed. Mortality over the five-year follow-up period was obtained for 1,738 patients (98%). Angiographic success of IRA angioplasty was defined as thrombolysis in myocardial infarction (TIMI) grade 3 flow and less than 30% residual stenosis.

Major adverse cardiac events (MACE) at 12-month follow-up were defined as death (from any cause), stroke, need for percutaneous or any surgical coronary artery revascularisation, and non-fatal MI.

Statistical analysis

Continuous parameters with a normal distribution are presented as mean ± SD. The significance of differences between mean values was tested with the Student's *t*-test. Qualitative parameters were analysed with the χ^2 test (where numbers were anticipated to be less than 5, Yates' correction for continuity was implemented). Mortality curves up to five years after STEMI were constructed using the Kaplan-Meier method and compared using the log-rank test. To assess the impact of individual parameters on mortality, a multivariate analysis was performed using step-down Cox proportional hazards regression modelling and expressed as a hazard ratio (HR), with a 95% confidence interval (CI). All clinical and angiographic variables were used in the risk-adjusted models. The level of statistical significance was set at $p < 0.05$ (two-tailed). Calculations and statistical analyses were performed with Statistica PL, version 7.0 (StatSoft Inc.).

Table 1. Baseline clinical characteristics of the study groups

	SVD (n = 828)	MVD (n = 948)	P
Age [years]	55.1 ± 10.8	60.1 ± 10.4	< 0.0001
Male	614 (74.2%)	693 (73.1%)	0.62
Duration of pain [h]	4.5 ± 3.2	5.2 ± 4.3	< 0.0001
Thrombolysis before PCI	257 (31.0%)	291 (30.7%)	0.88
Anterior myocardial infarction	380 (45.9%)	344 (36.3%)	< 0.0001
Arterial hypertension	382 (46.3%)	542 (57.5%)	< 0.0001
Diabetes	132 (16.0%)	220 (23.4%)	0.0001
Hyperlipidaemia	483 (58.4%)	536 (56.8%)	0.51
Current smoker	563 (68.2%)	569 (60.6%)	0.001
Prior myocardial infarction	86 (10.4%)	257 (27.1%)	< 0.0001
Cardiogenic shock on admission	50 (6.1%)	125 (13.2%)	< 0.0001

SVD — singlevessel coronary artery disease; MVD — multivessel coronary artery disease; PCI — percutaneous coronary intervention

Table 2. Baseline angiographic characteristics of the study groups

	SVD (n = 828)	MVD (n = 948)	P
Infarct related artery:			< 0.0001
LM	4 (0.5%)	12 (1.3%)	
LAD	396 (47.8%)	347 (36.6%)	
RCA	321 (38.8%)	444 (46.8%)	
CX	107 (12.9%)	145 (15.3%)	
Baseline TIMI flow grade			0.029
0–1	548 (66.2%)	673 (71.0%)	
2–3	280 (33.8%)	275 (29.0%)	
Number of significantly stenosed vessels:			–
1	828 (100%)	0 (0%)	
2	0 (0%)	619 (65.3%)	
3	0 (0%)	314 (33.1%)	
4	0 (0%)	15 (1.6%)	
Stent implantation	581 (70.2%)	618 (65.2%)	0.025
Abciximab	36 (4.4%)	33 (3.5%)	0.35
Final TIMI flow grade: 0–2	69 (8.3%)	102 (10.8%)	0.084
Angiographic success	759 (91.7%)	846 (89.2%)	0.084

LM — left main; LAD — left anterior descending; RCA — right coronary artery; CX — circumflex; TIMI — thrombolysis in myocardial infarction; rest abbreviation as in Table 1

RESULTS

Baseline clinical and angiographic characteristics

Clinical and angiographic characteristics of the study groups are presented in Table 1. Compared to patients with SVD, MVD patients were older and had a higher prevalence of hypertension, diabetes, previous MI, cardiogenic shock on admission and a longer duration of myocardial pain, as well as a lower frequency of anterior wall MI and current smoking.

The groups differed significantly in most of the angiographic parameters analysed, including the distribution of coronary arteries responsible for infarction and baseline flow in the IRA. Patients with SVD had a higher frequency of stent implantation during angioplasty. Furthermore, a trend was observed towards higher angiographic success in patients with SVD, although this result did not reach statistical significance. Detailed results of the angiographic analysis are shown in Table 2.

The in-hospital parameters differed significantly in the two groups. Patients with MVD had a lower left ventricular ejection fraction (LVEF), much more frequently underwent CABG before discharge and planned PCI in non-IRA vessels, and their hospital stay was significantly longer. Detailed data concerning the in-hospital period are presented in Table 3.

Table 3. In-hospital outcomes of the study groups

	SVD (n = 828)	MVD (n = 948)	P
Creatinine kinase max [IU]	2,504 ± 2,077	2,552 ± 2,350	0.68
Left ventricular ejection fraction [%]	45.8 ± 7.9	43.6 ± 8.7	< 0.0001
Re-occlusion angiographically confirmed (urgent PCI required)	37 (4.5%)	52 (5.5%)	0.33
CABG during hospitalisation	5 (0.6%)	80 (8.4%)	< 0.0001
Elective PCI in a non-IRA vessel during hospitalisation	0 (0%)	187 (19.7%)	< 0.0001
Hospital stay [days]	8.3 ± 4.7	9.4 ± 5.5	< 0.0001

CABG — coronary artery bypass grafting; IRA — infarct related artery; rest abbreviation as in Table 1

Table 4. In-hospital, 12-month risk analysis and five-year mortality

	SVD (n = 828)	MVD (n = 948)	P
In-hospital mortality	24 (2.9%)	90 (9.5%)	< 0.0001
12-month follow-up:			
Death	50 (6.0%)	148 (15.6%)	< 0.0001
Myocardial infarction	43 (5.2%)	46 (4.9%)	0.74
Stroke	15 (1.8%)	12 (1.3%)	0.35
Revascularisation (PCI)	24 (2.9%)	48 (5.1%)	0.021
Revascularisation (CABG)	13 (1.6%)	137 (14.5%)	< 0.0001
Cumulative MACE	120 (14.5%)	308 (32.5%)	< 0.0001
Five-year mortality*	96 (11.9%)	221 (23.8%)	< 0.0001

*Five-year follow-up was obtained for 1,738 patients (810 in SVD group, and 928 in MVD group); CABG — coronary artery bypass grafting; MACE — major adverse cardiac events; rest abbreviation as in Table 1

Short- and long-term outcomes

The in-hospital, 12-month risk analysis and the five-year mortality in the two groups are presented in Table 4. A total of 9.5% of MVD patients and 2.9% of SVD patients died during hospitalisation. A significant difference in the mortality rate was also found during the 12-month follow-up: 6.0% of SVD patients and 15.6% of MVD patients. The cumulative incidence of MACE during the 12-month follow-up was significantly higher in patients with MVD. No differences were found between the two groups in the 12-month observation with regard to MI or stroke, but MVD patients more frequently underwent target vessel revascularisation (re-PCI or CABG) during the follow-up period.

The significant difference in mortality rate was also maintained during the five-year follow-up: 11.9% in SVD group and 23.8% in MVD group ($p < 0.0001$; Fig. 1). In the multivariable analysis of the entire study population, the presence of MVD was an independent factor affecting mortality risk during the five-year follow-up period (HR = 1.45, 95% CI 1.13–188, $p = 0.004$; Fig. 2).

An additional multivariable analysis of the MVD subpopulation identified cardiogenic shock, final TIMI flow < 3, the presence of chronic total occlusion (CTO) in a non-IRA, diabetes, hypertension, anterior wall infarction and lower LVEF as independent predictors of death in the five-year follow-up in this group of patients (Fig. 3).

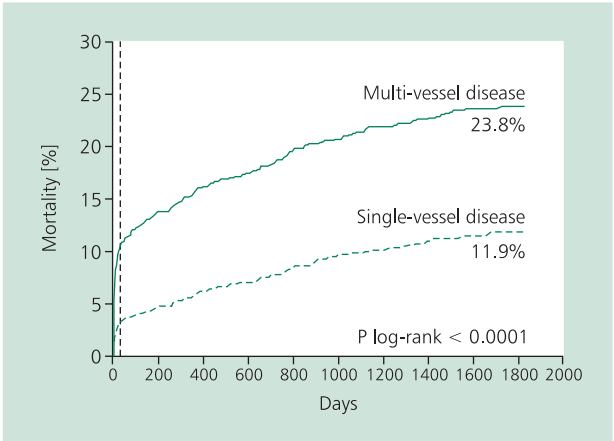

Figure 1. Five-year mortality in patients with single- and multivessel coronary artery disease

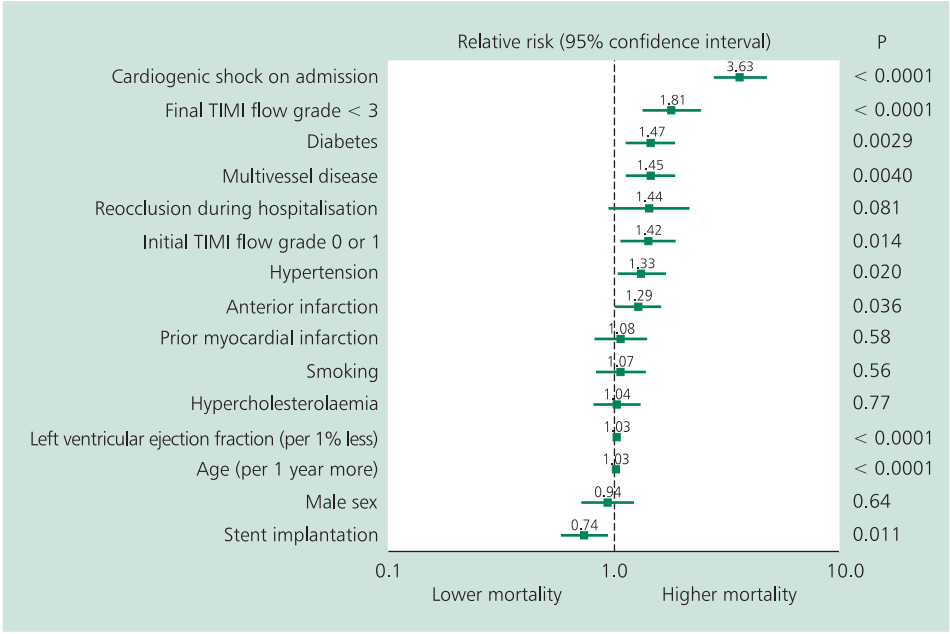

Figure 2. Predictors of five-year mortality in the entire study population (Cox proportional hazards model results). Variables are shown in descending order of Wald X^2 values; TIMI — thrombolysis in myocardial infarction

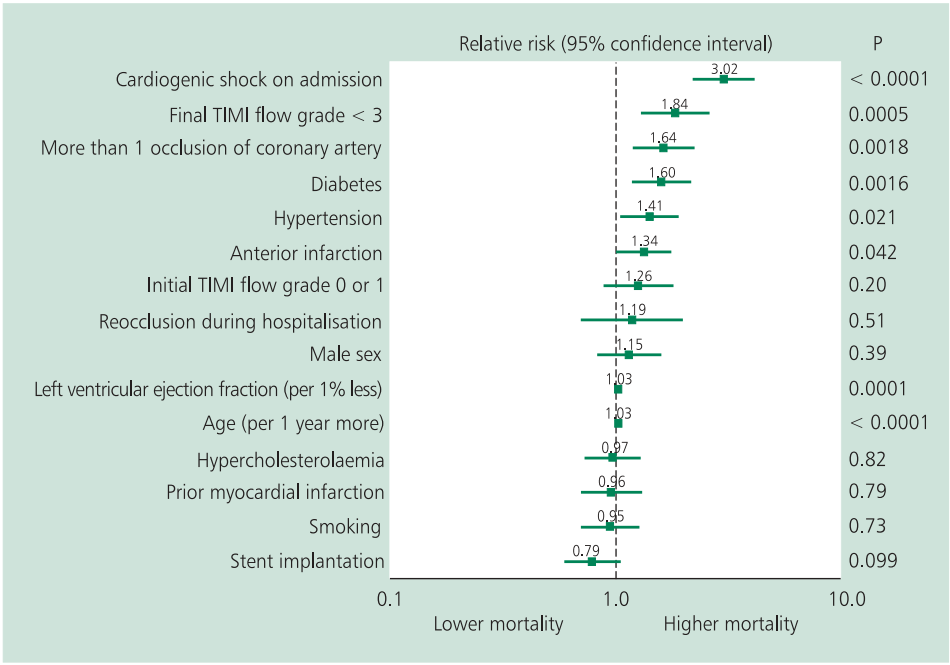

Figure 3. Predictors of five-year mortality in the multivessel coronary artery disease group (Cox proportional hazards model results). Variables are shown in descending order of Wald X^2 values; TIMI — thrombolysis in myocardial infarction

DISCUSSION

There are a number of principal findings of this investigation. Firstly, the presence of significant stenoses in vessels remote from IRA increased early and long-term mortality and MACE during 12-month follow-up after PCI for STEMI. Secondly, after adjusting for differences in baseline clinical characteri-

stics, the presence of MVD remained a powerful independent predictor of higher mortality. Finally, MVD patients with cardiogenic shock on admission, diabetes, hypertension, final TIMI flow < 3, CTO, anterior wall infarction and lower LVEF had worse long-term prognosis.

In approximately 50% of cases, urgent coronary angiography in the setting of PCI in STEMI patients identifies significant lesions in vessels not related to the acute event [2–5]. The presence of MVD is associated with poorer clinical outcomes [9, 11, 12]. There is only limited information on the effects of MVD on long-term outcomes in patients with STEMI undergoing PCI.

The direct mechanism of how MVD so seriously worsens the prognosis, although widely investigated, remains unknown. Patients with MVD have more risk factors and a greater incidence of co-morbidities, worse LV function, and a higher rate of ischaemia before MI, all of which may contribute to a poor prognosis [13].

In our study, as in previously reported investigations, patients with MVD were older, and had higher rates of hypertension, diabetes and previous MI [9, 12]. Furthermore, a longer duration of pain was observed in MVD patients, which undoubtedly affected the prognosis. This was probably related to a higher pain threshold in the older population of patients who more frequently had concomitant diabetes complicated by visceral neuropathy and sensory disorders, associated with significantly more frequent painless MI in this population [15–17].

A significantly higher stent implantation rate in the SVD patients was observed. This probably results from the nature of their lesions, which generally carried a higher thrombus burden. Furthermore, MVD patients had more severe coronary disease and more frequently required urgent surgical revascularisation. For these patients, balloon angioplasty was sometimes used as a bridge before CABG [14].

Cardiogenic shock remains one of the most important factors affecting the mortality rate of patients with STEMI. In populations of patients with MI complicated by cardiogenic shock, the presence of MVD is reported in approximately 70% [18], which is consistent with our data. The presence of significant lesions in vessels other than the IRA decreases perfusion throughout the coronary tree and results in a global deterioration of the LV function, which, in 75% of cases, is a direct cause of cardiogenic shock [19, 20].

Furthermore, van der Schaaf et al. [21, 22] demonstrated that the presence of a CTO in non-IRA was is an independent predictor of mortality in patients with STEMI as well as in patients with STEMI complicated by cardiogenic shock treated with PCI. Additionally, in our analysis of MVD patients, more than 30% had three-vessel coronary disease, which correlates with adverse prognosis [14, 23].

Another factor that may contribute to adverse outcomes in MVD patients is the lack of a compensation mechanism for the decrease in the LVEF in acute MI. Grines et al. [24] demonstrated that among patients who underwent immediate angiography after reperfusion treatment, those with SVD had enhanced regional wall motion of the non-infarct zone, and therefore better LVEF and lower mortality, compared to patients with MVD. Patients with MVD had lower residual LVEF, and this strongly influenced survival. Although in this investigation, enzymatic infarct size did not differ between groups, it is likely that patients with STEMI had LV dysfunction before MI as a consequence of the greater extent of their coronary artery disease. Additionally, MVD patients not only had lower LVEF at discharge but also less improvement in LV systolic function [25].

Due to the paucity of data regarding optimal treatment for patients with STEMI and MVD, the need for, and timing of, subsequent revascularisation of diseased non-IRA vessels remains controversial. Although some investigators have reported that incomplete revascularisation in patients with acute MI is a strong and independent risk factor for death and MACE [26], current practice guidelines in the acute setting recommend revascularisation of diseased non-IRA vessels only in the presence of haemodynamic or electrical instability [10]. Goldstein et al. [27] have shown that the pathological process in STEMI involves the entire coronary tree and may lead to the destabilisation and rupture of multiple atherosclerotic plaques, resulting in significantly increased risk of death and repeated ischaemic events. The dynamics of this specific inflammatory process are highest in the first month following acute MI [28], possibly explaining the increase in mortality rate in the first 30 days observed in our investigation (Fig. 1).

With this in mind, a complete analysis of each individual case with respect to total revascularisation is warranted. We believe that the assessment of vulnerability of other lesions by cardiac computed tomography or virtual histology could be useful. To evaluate the effectiveness of such a procedure will require further prospective, randomised trials.

Limitations of the study

The main limitation of our study is that it is not a prospective, randomised trial, but a single-centre registry. This could affect the results.

CONCLUSIONS

The presence of MVD in patients with acute MI is an independent factor that results in a poorer long-term prognosis. It seems reasonable that total revascularisation should be considered in every clinical case. The assessment of this treatment method, especially with regard to the timing and extent of revascularisation, requires further, prospective studies.

Conflict of interest: *none declared*

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Wpływ wielonaczyniowej choroby wieńcowej na jednoroczne wyniki kliniczne i śmiertelność 5-letnią u pacjentów z zawałem serca z uniesieniem odcinka ST leczonych przezskórną interwencją wieńcową

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Streszczenie

Wstęp: Wielonaczyniowa choroba wieńcowa (MVD) występuje u ok. 40–65% chorych z zawałem serca z uniesieniem odcinka ST (STEMI) leczonych przezskórną interwencją wieńcową (PCI). Jej obecność znacznie pogarsza rokowanie.

Cel: Celem pracy było oszacowanie wpływu MVD na wyniki okresu wewnątrzszpitalnego i rokowanie odległe u chorych z STEMI leczonych PCI oraz porównanie ich z wynikami uzyskanymi u osób z jednonaczyniową chorobą wieńcową (SVD).

Metody: Kolejni pacjenci z STEMI leczeni za pomocą PCI zostali poddani analizie i podzieleni na dwie grupy: grupa I — pacjenci z SVD (n = 828; 46,6%), grupa II — pacjenci z MVD (n = 948; 53,4%).

Wyniki: To jednoośrodkowe badanie obserwacyjne objęło 1776 kolejnych chorych z STEMI leczonych za pomocą PCI. Śmiertelność wewnątrzszpitalna wyniosła 2,9% i 9,5% ($p < 0,0001$), natomiast 5-letnia — 11,9% i 23,8% ($p < 0,0001$) odpowiednio w grupie I i II. Częstość dużych niekorzystnych zdarzeń sercowych (MACE) w okresie 12-miesięcznej obserwacji była istotnie wyższa u chorych z MVD (14,5% w grupie I *v.* 32,5% w grupie II; $p < 0,0001$). Ponadto w analizie wieloczynnikowej, po korekcji różnic w wyjściowej charakterystyce, wykazano, że obecność MVD jest silnym i niezależnym czynnikiem ryzyka zgonu w obserwacji 5-letniej (wskaźnik ryzyka: 1,45; 95-procentowy przedział ufności: 1,13–1,88; $p = 0,004$).

Wnioski: Obecność wielonaczyniowej choroby wieńcowej u osób z STEMI jest silnym i niezależnym czynnikiem ryzyka wyższej śmiertelności w obserwacji odległej.

Słowa kluczowe: wielonaczyniowa choroba wieńcowa, zawał serca

Kardiol Pol 2011; 69, 4: 336–343

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Praca wpłynęła: 09.08.2010 r. **Zaakceptowana do druku:** 26.01.2011 r.