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THE INFLUENCE OF METABOLIC SYNDROME ON THE QUALITY OF LIFE IN PATIENTS WITH ACUTE MYOCARDIAL INFARCTION WITH ST SEGMENT ELEVATION

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Metabolic syndrome (MetS) is a cluster of several risk factors that may indicate worse outcome after myocardial infarction with ST segment elevation (STEMI). The aim of this study was to determine the impact of MetS on quality of life among patients with STEMI.

A prospective study was performed among all STEMI patients who were treated with primary percutaneous coronary intervention in Clinical Centre of Serbia. During the three-year follow up, the occurrence of new cardiovascular events was followed. After 36 months the valid data were collected for 507 patients. At the end of the follow up, all alive and capable patients completed the Short Form 36 (SF-36) questionnaire.

The prevalence of MetS was 42.80%. An increased appearance of new myocardial infarction ($p = 0.004$), new unexpected revascularizations ($p = 0.014$) and the increased number of hospitalizations because of heart failure ($p = 0.050$) were recorded in the group of patients with MetS during a follow-up. Multiple regression analysis revealed that MetS was a predictor for lower scores of: physical functioning (OR 2.684; $p < 0.001$), role physical functioning (OR 2.121; $p = 0.001$), bodily pain (OR 2.559; $p = 0.005$), general health (OR 2.522; $p < 0.001$) and physical component score (OR 2.516; $p < 0.001$). Among mental components, MetS was a predictor of lower scores of vitality (OR 1.999; $p = 0.002$) and mental health (OR 2.142; $p = 0.016$).

Patients with MetS are at high risk for the appearance of new cardiovascular events, and the presence of this syndrome is associated with poorer quality of life after surviving STEMI.

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Key words: *metabolic syndrome; myocardial infarction with ST segment elevation; quality of life; new cardiovascular events*

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Introduction

Metabolic syndrome (MetS) is defined as a group of interrelated factors that significantly increase the risk of coronary artery disease, other forms of atherosclerotic cardiovascular disease, type 2 diabetes mellitus, cardiovascular mortality, and all-cause mortality. These factors are: hypertrigliceridemia, low level of HDL cholesterol, hypertension, abdominal obesity and insulin resistance (1, 2).

Myocardial infarction with ST-elevation (STEMI) remains to be a significant cause of morbidity and mortality throughout the world among CVD (3, 4). Conventional treatment focuses mainly on functional outcomes, survival and extending life. However, morbidity and mortality rates are incomplete measures of outcome, since they do not reflect all aspects of health. Many patients consider the quality of the additional life years gained equally important as the length of life. Indeed, the goal of today's medicine should be to increase both patients' quantity and quality of life (5). In response, assessment of health-related quality of life (HRQoL) has been increasingly integrated in daily clinical practice. HRQoL is a subjective measure of overall well-being and reflects how a disease and its symptoms are perceived by a patient. Although there is no universal agreement on what constitutes HRQoL, current assessment focuses on the domains of social functioning, physical functioning and psychological functioning (6). It is known that acute cardiovascular events, such as myocardial infarction and stroke, influence on the HRQoL. MetS is a chronic, progressive and multi-complex health

problem that can trigger physical, emotional and psychosocial problems. The impact of MetS on health-related quality of life is yet to be clearly established, although obesity, diabetes and hypertension have obvious consequences of HRQoL (7, 8). However, little is known about how MetS influences the appearance of new cardiovascular events and HRQoL in patients with STEMI treated with primary percutaneous coronary intervention (pPCI). Therefore, our objective was to estimate the influence of MetS to new cardiovascular events and HRQoL among patients with STEMI.

Material and methods

This prospective study included 507 consecutive patients having suffered acute STEMI and treated with primary percutaneous coronary intervention (pPCI) in Clinical Center of Serbia, Belgrade Serbia, between December 2009 and June 2010. The diagnosis of STEMI was established and pPCI performed using guidelines for the management of acute myocardial infarction in patients presenting with ST-segment elevation of European Society of Cardiology (9). In brief, patients with an episode of chest pain within the last 12 hours and ST-elevation on electrocardiography (ECG) in at least two consecutive leads were included.

After pPCI patients were hospitalized in the Cardiology Department with continuous monitoring including clinical, ECG, laboratory and echocardiography. Echocardiography was performed in the first week of myocardial infarction, on the ultrasonic unit Vivid 4 according to the clinical standard and in accordance with recommendations related to current echocardiography guidelines (10).

Diagnosing of metabolic syndrome

To set up the diagnosis of MetS we used AHA /NHLBI (American Heart Association and the National Heart, Lung and Blood Institute) criteria: central obesity, waist circumference 102/88 cm (M/F); tryglycerides ≥ 1.7 mmol/L; HDL < 1.03/1.3 mmol /L (M/F); systolic blood pressure ≥ 130 mmHg and / or diastolic blood pressure ≥ 85 mmHg or an antihypertensive therapy; fasting blood glucose values greater than 5.6 mmol/L or the use of glucose lowering treatment (11). Parameters according to which the diagnosis was set had been determined in the following way:

Venous blood samples were collected for the biochemical measurements after 48 hours of hospitalization. Serum glucose, HDL cholesterol, triglycerides, LDL cholesterol, total cholesterol and C-reactive protein (CRP) were measured with standard enzymatic colorimetric techniques.

Systolic and diastolic blood pressure was measured with aneroid sphygmomanometer in a sitting position and the average of three consecutive measurements at five minutes intervals was used as final values.

Body weight was measured on a calibrated electronic scale, and height was measured using a standard wall-mounted stadiometer. Body mass index (BMI) was calculated as body weight in kilograms divided by height in squared meters (kg/m^2).

Waist circumferences were obtained using a flexible steel metric tape according to standard procedures. Male patients with waist circumferences more the 102 cm and female more than 88 cm were considered to be obese. All anthropometric variables were measured by the same trained physician, during the hospitalization after the stabilization of vital parameters.

Follow up

During the 3 year follow up period, the authors collected data on mortality, cardiovascular mortality, new myocardial infarction, new revascularization (CABG and PCI), stroke and appearance of heart failure. For patients who died during the follow up, hospital records and necrophy data were reviewed. At the end of 36 month follow up, all alive patient were called for the final examination in order to fill in the questionnaire, the Short Form 36 (SF-36).

Health status

Since we wanted to determine the influence of MetS on HRQoL among the patients with STEMI, we chose to use generic questionnaire, the Short form 36 (SF-36). The reliability, validity and responsiveness of the SF-36 is well documented in patients with coronary artery disease (12). The SF-36 assesses eight health status domains: physical functioning, role physical functioning, role emotional functioning, mental health, vitality, social functioning, bodily pain and general health. Scale scores are obtained by summing the items together within a domain, dividing this outcome by the range of scores and then transforming the raw scores to a scale of 0 to 100 (13). A higher score on the SF-36 sub domains represents a better functioning; a high score on the bodily pain scale indicates freedom from pain. Based on the eight sub domains, physical and mental component summary scores can be calculated according to an algorithm, with the sub domains physical functioning, role physical functioning, bodily pain and general health being the primary contributors to the physical component score and role emotional functioning, vitality, social functioning, and mental health being the primary contributors to the mental component score (14).

Statistical analysis

Statistical analysis was performed with the SPSS 18.0 statistical package. Continuous data were expressed as mean ± SD and categorical data as percentage. Comparisons of prevalence between groups were made using the chi square test or Fisher' s exact test (in case the expected value of the variable was < 5 in at least one group). Mean comparisons were performed using Student's t test. Multivariate analysis model with adjustment for differences at

baseline was used to determine the impact of MetS on HRQoL, and the individual impact of MetS components on HRQoL after 36 month after myocardial infarction. A p value < 0.05 was considered statistically significant.

Ethical considerations

All studies on humans described in the present manuscript were carried out with the approval of the responsible ethics committee and in accordance with national law and the Helsinki Declaration of 1975. (in its current revised form.) Informed consent was obtained from all patients included in the study.

Results

After diagnosing MetS, we formed a group of 217 patients with MetS (Mets+) and another group of 290 patients without the presence of Mets (MetS (-)). Patients with MetS were older, more likely to be women and had a significant prevalence of MetS components. Among the patients with MetS, the most frequent risk factor was hypertension followed by high triglycerides, abnormal fasting glucose level, obesity and low HDL.

In the group of patients without MetS the most frequent risk factor for CVD was smoking, whose presence was significantly higher in this group. In patients with MetS the presence of previous infarction, stroke, PCI and CABG were recorded in a higher percentage but without significant statistical difference (Table 1).

Parameters obtained during hospitalization are shown in Table 2. The parameters according to which the MetS was diagnosed were significantly higher in the group of patients with MetS with the exception of HDL, which was significantly lower in the group of patients with MetS. It can also be observed that marker of inflammation (C-reactive protein) was increased in the group of patients with MetS. Between the examined groups, there was no significant difference in ejection fraction of the left ventricle, as well as extensity of coronary artery disease and localization of infarct-related artery.

The appearance of new adverse events during the three-year follow-up is shown in Table 3. At the end of the follow-up, among the examined groups, a significantly higher percentage of new myocardial infarction was recorded (p = 0.004); and new, unexpected revascularization (p = 0.014). Patients with MetS had a higher percentage of all cause of death, cardiovascular death and strokes but without significant statistical difference. In patients with MetS there was significantly greater percentage of the recorded cases of hospitalization because of heart failure (p = 0.050). Figure 1 shows the mean scale SF-36 in the examined groups. It can be noticed that the middle value scale SF- 36 is significantly lower in the group of patients with metabolic syndrome in all domains.

The results of multivariate logistic regression that we used to examine the impact of MetS on the quality of life, as well as individual influence of MetS components on the quality of life are shown in Tables 4 and 5. The presence of MetS carried a significant risk for low HRQoL; it especially referred to physical components. Among mental components, MetS was a predictor of lower scores of vitality and mental health (Table 4). In the second multivariate model, we analyzed the individual influence of MetS components adjusted for sex, age and smoking. Multivariate logistic regression showed that only elevated blood pressure adversely affected physical functioning, general health and physical component score. Other MetS components individually did not carry a significant risk for low HRQoL (Table 5). There was no association between smoking and HRQoL in both models.

Table 1. Baseline characteristics of analyzed patients

	MetS (+) (N = 217)	MetS (-) (N = 290)	p
Female sex n	59 (27.19%)	54 (18.62%)	0.022
Age, years (± SD)	60.71 ± 11.52	57.50 ± 10.95	0.002
FBG ≥ 5.6mmol/L or th	158 (72.81%)	77 (26.55%)	< 0.001
TG ≥ 1.7 mol/L or th	126 (58.06%)	103 (35.52%)	< 0.001
HDL < 1.03/1.3mol/l (M/F) or th	114 (52.53%)	116 (40.00%)	0.005
BP > 130/85 or th	173 (79.72%)	156 (53.79%)	< 0.001
Obesity*	136 (62.67%)	56 (19.31%)	< 0.001
Family history of CAD	103 (47.47%)	126 (43.44%)	0.368
History of smoking	144 (66.36%)	221 (76.20%)	0.015
Previous M.I.	32 (14.75%)	31 (10.68%)	0.171
Previous stroke	12 (5.53%)	11 (3.79%)	0.073
Previous PCI	13 (5.99%)	9 (3.10%)	0.114
Previous CABG	2 (0.92%)	1 (0.34%)	0.402

FBG –fasting blood glucose; th- therapy; TG tryglicerides; BP- blood pressure *- waist circumference > 102/88 cm (M / F);
M.I. - myocardial infarction; CAD- coronary artery disease; PCI – Percutaneous coronary intervention; CABG-coronary arteries bypass surgery

Table 2. Clinical characteristics of the analyzed patients

		MetS (+) (N = 217)	MetS (-) (N = 290)	p
Systolic blood pressure (mmHg)		138.33 ± 24.30	129.15 ± 21.31	< 0.001
Diastolic blood pressure (mmHg)		88.01± 12.88	82.77± 11.83	< 0.001
Waist circumference (cm)		104.77± 9.98	95.01 ± 14.06	0.001
BMI (kg/m^2)		28.41 ± 3.70	25.61 ± 3.60	< 0.001
Glycemia (mmol/L)		7.46 ± 2.31	6.38 ± 1.96	< 0.001
HDL cholesterol (mmol/L)		1.07 ± 0.25	1.17 ± 0.27	0.001
Triglycerides (mmol/L)		2.20 ± 1.09	1.73 ± 1.00	< 0.001
LDL cholesterol (mmol/L)		3.57 ± 1.06	3.60 ± 1.00	0.180
Total cholesterol (mmol/L)		5.50 ± 1.30	5.69 ± 1.24	0.594
C- reactive protein (mg/L)		5.10 ± 2.02	4.60 ± 1.96	< 0.001
LVEF (%)		49.67 ± 9.55	49.51 ± 10.14	0.865
Localization of M.I.	Anterior	87 (40.09%)	133 (45.86%)	0.163
	Inferior	125 (57.60%)	148 (51.03%)	
	Other	5 (2.30%)	9 (3.10%)	
Infarct vessel	LAD	88 (40. 55%)	134(46. 21%)	0.148
	CX	34 (15.67%)	47 (16.21%)	
	RCA	95 (43.78%)	109 (37.59%)	
One vessel disease		65 (29.95%)	113 (38.97%)	0.089
Two vessel disease		69 (31.80%)	90 (31.03%)	
Three vessel disease		83 (38.25%)	87 (30.00%)	

LVEF - left ventricular ejection fraction; EDD - end diastolic diameter; ESD - end systolic diameter; M.I. - myocardial infarction; LAD - left anterior descending artery; Cx - circumflex artery; RCA - right coronary artery

Table 3. Adverse outcomes during the 36-th month follow up

	MetS (+) n (%)	MetS (-) n (%)	p
All cause of death	35 (16.35)	38 (13.10)	0.336
Cardiovascular death	30 (13.82)	34 (11.72)	0.480
New myocardial infarction	17 (7.83)	7 (2.41)	0.004
New stroke	6 (3.22)	2(0.69)	0.055
New unexpected revascularization (PCI/CABG)	33 (15.20)	24 (8.28)	0.014
Dyspnea	35 (16.13%)	28 (9.66%)	0.028
Hospitalization due to heart failure	9 (4.15)	4 (1.38)	0.050

PCI- percutaneous coronary intervention; CABG-coronary artery bypass surgery

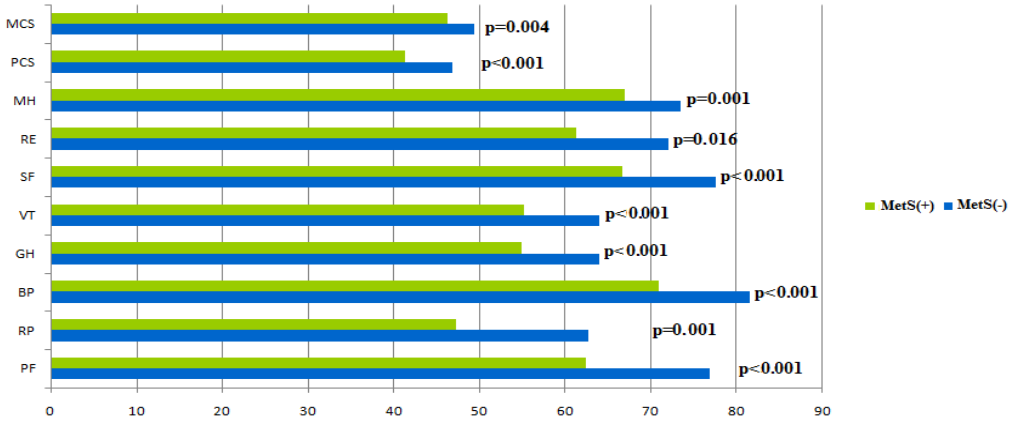

Figure 1. Mean scores (SD) for SF-36 subscales in examined patients at the end the follow-up: mental component summary (MCS); physical component summary (PCS); mental health (MH); role emotional functioning (RE); social functioning (SF); vitality (VT); general health (GH); bodily pain (BP); role physical functioning (RP) and physical functioning (PF)

Table 4. Influence of MetS on HRQoL in multivariate logistic model adjusted for age, sex and smoking

		OR	95%CI	p
PF	Metabolic syndrome	2.684	1.572 - 4.581	< 0.001
	Gender	1.821	1.010 - 3.320	0.050
	Age	1.051	1.021 - 1.081	0.001
RP	Metabolic syndrome	2.121	1.374 - 3.274	0.001
	Age	1.022	1.000 - 1.044	0.050
BP	Metabolic syndrome	2.559	1.318 - 4.966	0.005
GH	Metabolic syndrome	2.522	1.318 - 4.966	< 0.001
PCS	Metabolic syndrome	2.516	1.557 - 4.065	< 0.001
		1.029	1.006 - 1.052	0.012
VT	Metabolic syndrome	1.999	1.284 - 3.113	0.002
	Gender	1.687	1.093 - 2.866	0.043
SF	-	-	-	-
RE	Age	1.021	1.008 - 1.044	0.048
MH	Metabolic syndrome	1.766	1.121 - 2.782	0.016
MCS	Gender	1.955	1.133 - 3.373	0.016

Physical functioning (PF); role physical functioning (RP); bodily pain (BP); general health (GH); physical component summary (PCS); vitality (VT); social functioning (SF); role emotional functioning (RE); mental health (MH) and mental component summary (MCS).

Table 5. Individual influence of MetS components (elevated blood pressure, abnormal fasting glucose level, obesity,elevated triglycerides, low HDL (according to the criteria for MetS)) on HRQoL in multivariate logistic model adjusted for age, sex and smoking

		OR	95%CI	p
PF	Elevated blood pressure	2.418	1.245 - 4.695	0.009
	Gender	2.306	1.220 - 4.358	0.010
	Age	1.047	1.016 - 1.078	0.002
RP	-	-	-	-
BP	-	-	-	-
GH	Elevated blood pressure	1.921	1.141 - 3.233	0.014
PCS	Elevated blood pressure	1.700	1.059 - 2.729	0.028
	Gender	2.040	1.093 - 3.805	0.025
VT	Gender	1.940	1.119 - 3.363	0.018
SF	-	-	-	-
RE	-	-	-	-
MH	-	-	-	-
MCS	Gender	2.066	1.165 -3.665	0.013

Physical functioning (PF); role physical functioning (RP); bodily pain (BP); general health (GH); physical component summary (PCS); vitality (VT); social functioning (SF); role emotional functioning (RE); mental health (MH) and mental component summary (MCS).

Discussion

MetS is a major cause of myocardial infarction, with a rapidly increasing tendency in prevalence (15). This claim was confirmed by the findings of several studies. Namely, Lee et al., Yilmaz et al. and Zeller et al. reported that the prevalence of MetS in patients with STEMI varied from 46% to 59,4% (16-18). Also, a study originating from our region demonstrated a high prevalence of MetS among STEMI patients (19). Our study also confirmed a high prevalence of MetS in these patients; the incidence of MetS in our study was 42.80% which is in accordance with the above mentioned studies. Our study also revealed that female sex was more frequent among MetS patients. Similar to our findings are the findings of two studies that also found higher prevalence of females among MetS in patients with myocardial infarction (18, 19).

During the follow-up period, we found that among patients with MetS, there were a significantly higher number of myocardial infarctions and repeated revascularizations. These findings are in accordance with the results of Mente A. et al. and Takeno

M. et al. (20, 21). Moreover, MetS is connected with the presence of pro-inflammatory condition that is confirmed by the increased presence of inflammatory markers suggesting an increased risk for new cardiovascular events (22, 23). Our study confirms that patients with MetS had significantly increased marker of inflammation (CRP) compared to the group of patients without MetS. In their study, Takeno M. et al. showed that MetS was associated with high CRP level and that it was a significant predictor for the appearance of new cardiovascular events in patients who survived STEMI (21). All these claims suggest that MetS is significantly associated with the development of new coronary stenosis or restenosis during the follow-up period, which increase the need for new coronary revascularization (24) and the occurrence of heart failure (18). Our study confirmed these claims because patients with MetS have a significantly higher percentage of new revascularizations and the hospitalization due to heart failure.

It is well known that a myocardial infarction has a significant impact on HRQoL (25, 26), but little is known about what kind of impact MetS has on HRQoL among patients who survive STEMI. Several studies have shown the adverse impact of MetS on HRQoL. These are mainly studies that have investigated the general population (27). This is the first study that investigated the impact of MetS on HRQoL in a group of patients with STEMI. And we found that MetS was associated with lower HRQoL of the physical components of the SF-36. In addition, participants with MetS scored significantly lower on the PCS score than did persons without the syndrome. By contrast, no association was observed between MetS and the mental component summary score. Our results showed that MetS had an extremely adverse effect on the physical component of SF-36 and physical component score; but it had no impact on mental component score.

These findings can be explained by the fact that MetS can severely inhibit many of the normal physical functions that patient would have. Patients with MetS have increased subjective health complaints of musculoskeletal, neurological, and gastrointestinal pains. An impairment of circulation underlies all of these conditions, and results in pain with physical activity, promoting a sedentary lifestyle and a debilitating cycle ensues (28). In addition, MetS features like obesity and elevated blood pressure increase the work of the heart, while consistently increased insulin levels have macro and micro vascular complications inciting discomfort caused by decreased circulation. Thus, when these conditions are combined in MetS, the consequences can be assumed to be cumulative.

As we already mentioned, the individual components of MetS, such as obesity, elevated blood pressure and abnormal fasting plasma glucose have been shown in several studies to adversely affect the quality of life. Quovadis study, which included 1,822 obese patients, showed that patients with MetS have a poorer quality of life in physical terms, which is in accordance with our study. Individually, obesity, increased blood pressure and fasting plasma glucose had an extremely adverse effect on PCS and no impact on MCS (29). Interestingly, our results indicate that the individual MetS components except high blood pressure had no significant impact on HRQoL in study population. We found that increased blood pressure had a significant adverse impact on physical functioning, general health and physical component scores. These results coincide with the findings of individual studies (30, 31) which indicated that increased blood pressure adversely affected physical functioning. Also, our findings correlate with the findings of Chedraui et al. since they concluded that hypertension had an impact on the physical domains, while hyperglycemia was not found to have any major impact on the physical domain (32). These results may suggest that the metabolic syndrome represented to some degree the cumulative contributions of the individual components.

Conclusion

To our knowledge, the association between MetS and HRQOL has never been addressed among patients who survived STEMI. We conclude that patients with STEMI with MetS have significantly impaired HRQOL even after controlling for confounding variables. Our MetS subjects presented lower QOL in terms of physical health. These findings strongly suggest that HRQOL should be considered in the management of subjects with MetS.

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UTICAJ METABOLIČKOG SINDROMA NA KVALITET ŽIVOTA BOLESNIKA SA AKUTNIM INFARKTOM MIOKARDA SA ST SEGMENT ELEVACIJOM

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Metabolički sindrom (MetS) je skup više faktora rizika koji ukazuju na lošu prognozu nakon infarkta miokarda sa elevacijom ST segmenta (STEMI). Cilj ovog istraživanja bio je da se utvrditi uticaj MetS na kvalitet života kod bolesnika sa STEMI.

Ova prospektivna studija je sprovedena među STEMI bolesnicima koji su lečeni primarnom perkutanom koronarnom intervencijom u Kliničkom centru Srbije. Tokom tri godine, praćena je pojava novih velikih kardiovaskularnih događaja. Nakon 36 meseci prikupljeni su podaci za 507 bolesnika. Na kraju praćenja svi živi i sposobni bolesnici pozvani su kako bi popunili upitnik 36 (SF-36).

Prevalencija MetS je bila 42,80%. Tokom praćenja je zabeležen povećan broj novih infarkta miokarda (p = 0,004), novih neplaniranih revaskularizacija (p = 0,014) i povećan broj hospitalizacija zbog srčane isuficijencije (p = 0,050) u grupi bolesnika sa MetS. Višestruka logistička regresijska analiza je pokazala da je MetS prediktor za lošije vrednosti: fizičkog funkcionisanja (OR 2,684; p <0,001), fizičku ulogu (OR 2,121; p = 0,001), telesnu bol (OR 2,559; p = 0,005), opšte zdravlje (OR 2,522; p < 0,001) i skor fizičkih komponenti (OR 2,516; p < 0,001). Među komponentama koje utiču na mentalni status, Mets je prediktor lošije vitalnosti (OR 1,999; p = 0,002) i mentalnog zdravlja (OR 2,142; p = 0,016).

Bolesnici sa Mets su u visokom riziku za pojavu novih kardiovaskularnih događaja, a prisutnost ovog sindroma povezana je s lošijim kvalitetom života onih koji su preživeli STEMI.

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Ključne reči: *metabolički sindrom; infarkt miokarda sa elevacijom ST segmenta; kvaliteta života; novi kardiovaskularni događaj*