

# Risks for First Nonfatal Myocardial Infarction in Belgrade

Isidora Ratkov<sup>1</sup>, Sandra Šipetić-Grujičić<sup>1</sup>, Hristina Vlajinac<sup>1</sup>, Jelena Marinković<sup>2</sup>, Nataša Maksimović<sup>1</sup>, Dragana Matanović<sup>3</sup> and Zorana Vasiljević<sup>4</sup>

<sup>1</sup> Belgrade University, School of Medicine, Institute of Epidemiology, Belgrade, Serbia

<sup>2</sup> Belgrade University, School of Medicine, Institute for Social Medicine, Statistics and Health Research, Belgrade, Serbia

<sup>3</sup> Clinical Center Serbia Belgrade, Clinic for Physical Medicine and Rehabilitation, Belgrade, Serbia

<sup>4</sup> Urgent Center Serbia Belgrade, Clinic for Cardiovascular Diseases, Belgrade, Serbia

## ABSTRACT

*The aim of this study was to investigate which one among possible risk factors are independently related to first nonfatal myocardial infarction (MI) in Belgrade population. Case-control study was conducted in Belgrade during the period 2005–2006. Case group comprised 100 subjects 35–80 years old who were hospitalized because of first nonfatal MI at the coronary care unit in Urgent Center, Belgrade. Control group consisted of 100 persons chosen among patients treated during the same period at the Institute of Rheumatology, Institute for Gastroenterology, and Clinic for Orthopedics, Belgrade, Serbia. Cases and controls were individually matched by sex, age ( $\pm 2$  years) and place of residence (urban/rural communities of Belgrade). According to the multivariate analysis risk factors for MI occurrence were »good« socioeconomic conditions (OR=2.76), total alcohol consumption (OR=2.62) and consumption of brandy (OR=6.73), stressful life events taken together (OR=3.13) and stress because of close relative's death (OR=3.35), great financial problems (OR=31.64) and small financial problems (OR=8.47), hypertension (OR=2.39), MI among all relatives (OR=3.66), MI in father (OR=6.24), and low level of high density lipoprotein cholesterol (OR=152.41). Amateur sport activity in the past was negatively associated with MI development. The results obtained are mainly in accordance with other studies results and can be of help in development of strategy for coronary heart disease prevention in Serbia.*

**Key words:** case-control study, myocardial infarction, risk factors, alcohol, stress, hypertension, HDL-cholesterol, physical activity, genetic

## Introduction

Cardiovascular diseases (CVD) are leading causes of morbidity and mortality in majority of countries all over the world<sup>1</sup>. It is estimated that each year 3.8 million of men and 3.4 million of women in the world die from ischemic heart diseases (IHD), which is about 12% of all deaths<sup>1</sup>. This group of CVD is the leading cause of death in the world, except in Africa and West Pacific region where cerebrovascular diseases are on the first place<sup>2</sup>. IHD are responsible for nearly 50% of all CVD deaths in Europe and for 71% in USA<sup>3</sup>. In population of Belgrade (Serbia) IHD were cause of death in 33% of men and 23% of women during the period 1990–2002.

In the developed countries CVD mortality began to decrease thanks to preventive measures and early and adequate therapy<sup>1</sup>. In 2003 almost 80% of CVD deaths were registered in the developing countries<sup>1</sup>.

Data about independent risk factors for IHD are inconsistent although more than 300 risk factors have been recognized<sup>1</sup>. It is estimated that conventional risk factors are responsible for 75% of CVD diseases occurrence<sup>1</sup>.

The aim of this study was to investigate which one among possible risk factors are independently related to first nonfatal myocardial infarction in Belgrade population.

## Methods

Case-control study was conducted in Belgrade during the period 2005–2006. Case group comprised 100 subjects 35–80 years old who were hospitalized because of

first nonfatal myocardial infarction at the coronary care unit in Urgent Center, Belgrade. All cases met the World Health Organisation criteria for MI, which require typical symptoms plus either elevations in cardiac enzyme concentrations or diagnostic changes on an electrocardiogram. Cases were not included in the study if they 1) had MI in personal history, 2) had chronic medical illness that may affect risk factors for CVD, or 3) were physically or mentally unable to answer the questions. Control group consisted of 100 persons chosen among patients treated during the same period from rheumatic diseases (gonarthrosis, coxarthrosis, spondilosis), some gastrointestinal diseases (inguinal hernia, appendicitis, hemorrhoids, cholecistitis, gallstone), and light injuries (closed and open fractures of hands, legs and ribs) at the Institute of Rheumatology, Institute for Gastroenterology and Clinic for Orthopedics, Belgrade, Serbia. Controls met the same exclusion criteria as cases – those with history of CVD or chest pain were not included in the study. Cases and controls were individually matched by sex, age ( $\pm 2$  years) and place of residence (urban/rural communities of Belgrade).

All participants were interviewed by two physicians during the first five days after the diagnosis of disease. Data were collected on basic demographic characteristics (sex, age, place of residence, nationality, education, occupation, marital status), some habits (smoking and alcohol, coffee and tea consumption), diet (daily number of meals, type and quantity of grease consumed, consumption of milk and dairy products, meat, vegetables, fruits, mixed dishes, bread, sweets, spices, etc.), anthropometric characteristics (body height, body weight, waist and hip circumference), stressful life events (severe accident, hospitalization, death or removal from the house of a relative, change or loss of job, birth of a sibling, and other stressful events), personal and family history.

Degree of obesity was estimated on the basis of body mass index (BMI), waist circumference and the ratio of waist and hip circumference. According to WHO classification, subjects with BMI  $\geq 30.00$  are obese. According to waist circumference (WC), women have the first degree of obesity when WC is 80–87 cm, and the second degree of obesity when WC is  $\geq 88$  cm. Men have the first degree of obesity when WC is 94–101 cm, and the second degree of obesity when WC is  $\geq 102$  cm. According to waist/hip ratio, men are obese when this ratio is greater than 1, and women are obese when this ratio is greater than 0.85. Data on personal history of participants were obtained from medical documentation. Current smokers were defined as subjects who smoked any quantity of tobacco in the previous 12 months. Former smokers were defined as subjects who smoked in the past and quit more than a year earlier. The ethic committee of hospitals approved the study. All participants provided informed consent before participating in the study.

In the analysis of data, conditional univariate and multivariate logistic regressions were used.

In the present work only part of the study results are presented.

## Results

In Table 1–5 only variables for which differences between cases and controls were at significance level of  $p \leq 0.100$  are presented. Differences at level of  $p < 0.050$  were considered as statistically significant.

Cases and controls did not differ by sex, age and place of residence since they were matched on these variables (Table 1). Among participants about one third were men, 52% were younger than 60 years, and 86% were from urban communities of Belgrade. Compared groups also did not differ in nationality, marital status, education and occupation. Significantly more cases (34%) than controls (6%) reported »good« socio-economic conditions.

Some lifestyle characteristics of compared groups are presented in Table 2. Cases were significantly more frequently current smokers, but they did not differ from controls in the frequency of former smokers, passive smoking at home and at working place, as well as in frequency of coffee and tea consumption. Alcohol consumption was significantly more frequent among cases than controls. Out of alcoholic beverages cases more frequently consumed brandy and wine in comparison with controls, but there were no differences in consumption of beer and hard liquor. Well water and salt were significantly more frequently used by cases than controls. In comparison with controls cases were less physically active (occupational activity, present and past amateur sport activity). Cases significantly more frequently than controls consumed fatty meat.

During the year preceding the diagnose of disease, cases, in comparison with controls, more frequently experienced as stressful the following life events: death of a close relative, death of a close friend, hospitalization of

**TABLE 1**  
DEMOGRAPHIC CHARACTERISTICS OF CASES WITH FIRST NONFATAL MYOCARDIAL INFARCTION AND THEIR CONTROLS

Characteristic	Cases (N=100)	Controls (N=100)	p-value <sup>a</sup>
Sex			
Men	62 (62%)	62 (62%)	matched
Women	38 (38%)	38 (38%)	
Age			
$\leq 60$	52 (52%)	52 (52%)	matched
61–70	25 (25%)	27 (27%)	
$\geq 71$	23 (23%)	21 (21%)	
Place of residence			
Urban	86 (86%)	86 (86%)	matched
Rural	14 (14%)	14 (14%)	
Marital status			
Married	71 (71%)	81 (81%)	0.099
Single, divorced, widowed	29 (29%)	19 (19%)	
Socio-economic conditions			
Poor	17 (17%)	18 (18%)	0.001
Average	49 (49%)	76 (76%)	
Good	34 (34%)	6 (6%)	

<sup>a</sup> according to univariate logistic regression analysis

**TABLE 2**  
LIFESTYLE CHARACTERISTICS OF CASES WITH FIRST NONFATAL MYOCARDIAL INFARCTION AND THEIR CONTROLS

Characteristic	Cases (N=100)	Controls (N=100)	p-value <sup>a</sup>
Current smoker	52 (52%)	34 (34%)	0.011
Alcohol consumption	41 (41%)	16 (16%)	<0.001
Consumption of brandy	31 (31%)	10 (10%)	<0.001
Consumption of beer	13 (13%)	6 (6%)	0.099
Consumption of wine	12 (12%)	0 (0%)	0.010
Well water consumption <sup>b</sup>	36 (36%)	21 (21%)	0.020
Consumption of salt			
Little	46 (46%)	20 (20%)	0.062
Moderate	40 (40%)	76 (76%)	
Much	14 (14%)	4 (4%)	
Physically active at working place <sup>c</sup>	52 (52%)	64 (64%)	0.091
Degree of physical activity at working place:			
Easy	68 (68%)	52 (52%)	0.049
Moderate	12 (12%)	25 (25%)	
Heavy	20 (20%)	23 (23%)	
Amateur sport activity in the past	11 (11%)	32 (32%)	<0.001
Present amateur sport activity	57 (57%)	84 (84%)	<0.001
Frequent consumption of fatty meat <sup>d</sup>	50 (50%)	35 (35%)	0.002

<sup>a</sup> according to univariate logistic regression analysis; <sup>b</sup> in comparison with consumption of faucet drinking water; <sup>c</sup> in comparison with physically inactive; <sup>d</sup> in comparison with those who do not consume fatty meat or consumed it rarely

**TABLE 3**  
LIFE EVENTS REPORTED AS STRESSFUL BY CASES WITH FIRST NONFATAL MYOCARDIAL INFARCTION AND THEIR CONTROLS

Variable	Cases (N=100)	Controls (N=100)	p-value <sup>a</sup>
Death of a close relative	3 (3%)	1 (1%)	0.023
Great financial problems	10 (10%)	1 (1%)	0.024
Hospitalization of the family member	14 (14%)	4 (4%)	0.020
Death of a close friend	12 (12%)	1 (1%)	0.013
Serious disease or hospitalization of participant	3 (3%)	14 (14%)	0.011
Small financial problems	24 (24%)	5 (5%)	<0.001
»Other« stressful events <sup>b</sup>	10 (10%)	2 (2%)	0.032
Total number of stressful events:			
0	19 (19%)	50 (50%)	<0.001
1	47 (47%)	42 (42%)	
2	23 (23%)	7 (7%)	
3+	11 (11%)	1 (1%)	

some family members, great and small financial problems, and »other« stressful events. Controls more frequently reported their own disease and hospitalization as stressful events. The number of stressful events was significantly greater in cases than in controls (Table 3).

In personal history, cases significantly more frequently than controls, reported abdominal obesity, essential hypertension, cardiovascular diseases (arrhythmia, palpitations), and high values of total cholesterol, triglycerides and LDL cholesterol and low values of HDL cholesterol (Table 4). Cases and control did not significantly differ in the frequency of endocrine, rheumatic, malignant and infectious diseases.

In comparison with controls cases had significantly more relatives (mother, father, brother, sister, grandmother, grandfather) with myocardial infarction and some other cardiovascular diseases (Table 5). Out of individual relatives, in comparison with controls, mothers of cases had significantly more frequently MI and fathers of cases had significantly more frequently »other« CVD (hypertension, stroke, angina pectoris, cardiac insufficiency, aortal aneurisms, arrhythmia).

Multivariate logistic regression analysis was performed in two steps. First, we used four separate models including all variables that, according to univariate logistic regression analysis, were related to MI at a significance

**TABLE 4**  
PERSONAL HISTORY OF CASES WITH FIRST NONFATAL MYOCARDIAL INFARCTION AND THEIR CONTROLS

Variable	Cases (N=100)	Controls (N=100)	p-value <sup>a</sup>
Obesity according to waist circumference (women $\geq 80$ cm and men $\geq 94$ cm)	69 (69%)	82 (82%)	0.079
Essencial hypertension ( $\geq 140$ mmHg / $\geq 90$ mmHg)	63 (63%)	41 (41%)	0.003
Diabetes mellitus	21 (21%)	12 (12%)	0.090
Total cholesterol $\geq 5.20$ mmol/L	42 (42%)	22 (22%)	0.003
HDL cholesterol $\leq 1.00$ mmol/L	40 (40%)	0 (0%)	0.047
LDL cholesterol $\geq 3.40$ mmol/L	40 (40%)	2 (2%)	<0.001
Tryglicerides $\geq 1.70$ mmol/L	43 (43%)	13 (13%)	<0.001
CVD <sup>b</sup>	4 (4%)	12 (12%)	0.047

<sup>a</sup> according to univariate logistic regression analysis; <sup>b</sup> CVD/Cardiovascular diseases (arrhythmia, palpitations)

**TABLE 5**  
FAMILY HISTORY OF CASES WITH FIRST NONFATAL MYOCARDIAL INFARCTION AND THEIR CONTROLS

Variable	Cases (n=100)	Controls (n=100)	p-value <sup>a</sup>
Miocardial infarction among relatives	34 (34%)	11 (11%)	<0.001
Myocardial infarction in/of mother	9 (9%)	3 (3%)	0.089
Myocardial infarction in/of father	14 (14%)	3 (3%)	0.011
Other CVD among relatives <sup>b</sup>	68 (68%)	50 (50%)	0.013
Other CVD – mother	39 (39%)	24 (24%)	0.023
Other CVD – father	31 (31%)	20 (20%)	0.076
Other CVD – brother	23 (23%)	13 (13%)	0.069

<sup>a</sup> according to univariate logistic regression analysis; <sup>b</sup> Other CVD/Other cardiovascular diseases (hypertension, stroke, angina pectoris, cardiac insufficiency, aortal aneurisms, arrhythmia)

level  $p \leq 0.100$ . Model 1 included demographic and life-style characteristics; model 2, stressful life events; model 3, personal history; and model 4, family history. Present and past amateur sport activities were not included in the second model of multivariate logistic regression since they highly correlated with HDL cholesterol. Variables significantly related to type 1 diabetes according to these four multivariate regression analyses were put together in two models (Table 6).

The following variables were included in the final model A: current smokers, alcohol consumption, well water consumption, »good« socioeconomic conditions, present and past amateur sport activity, fatty meat consumption, abdominal obesity, total number of stressful life events, personal history of essential hypertension, CVD and total cholesterol, and history of MI and »other« CVD in relatives. According to multivariate analysis risk factors for MI occurrence were »good« socioeconomic conditions (OR=2.76), alcohol consumption (OR=2.62), one or more of stressful life events (OR=3.13), hypertension (OR=2.39) and MI in relatives (OR=3.66). Amateur sport activity in the past was negatively associated with MI development.

The following variables were included in the final model B: current smokers, consumption of brandy, well

water consumption, »good« socioeconomic conditions, present and past amateur sport activity, fatty meat consumption, abdominal obesity, individual stressful life events, that is death of a close relative, death of a close friend, hospitalization of some family members, great and small financial problems, and »other« stressful events, personal history of essential hypertension, CVD and low values of HDL cholesterol, and history of MI in father and history of »other« CVD in mother. According to multivariate analysis risk factors for MI were »good« socioeconomic conditions (OR=5.16), consumption of brandy (OR=6.73), low values of HDL cholesterol (OR=152.41), history of MI in father (OR=6.24), death of close relative (OR=3.35), great financial problems (OR=31.64) and small financial problems (OR=8.47).

## Discussion and Conclusions

According to the results of the present study risk factors for MI occurrence were »good« socioeconomic conditions, alcohol consumption, one or more of stressful life events, hypertension, low values of HDL cholesterol and MI in relatives. Recreational sport activity in the past had protective effect on MI development.

**TABLE 6**  
FACTORS RELATED TO FIRST NONFATAL MYOCARDIAL INFARCTION ACCORDING TO MULTIVARIATE LOGISTIC REGRESSION ANALYSIS

MODEL A			
Variable	OR	95% CI	p
Alcohol consumption	2.62	1.17–5.90	0.020
»Good« socioeconomic conditions	2.76	1.49–5.11	0.001
Amateur sport activity in the past	0.27	0.11–0.68	0.005
Stressful life events <sup>a</sup> 1+2+3/0	3.13	1.89–5.16	<0.001
Essential hypertension in personal history	2.39	1.17–4.85	0.016
Myocardial infarction among relatives	3.66	1.51–8.88	0.004

<sup>a</sup> During 12 month before the diagnosis of disease, that is during 12 months before interviewing controls

MODEL B			
Variable	OR	95% CI	p
»Good« socioeconomic conditions	5.16	226–11.75	<0.001
Consumption of brandy	6.73	2.44–18.55	<0.001
Low values of HDL – cholesterol	152.41	16.44–1412.95	<0.001
Myocardial infarction – father	6.24	1.25–31.08	0.025
Death of a close relative	3.35	1.01–11.13	0.048
Great financial problems	31.64	1.92–521.86	0.016
Small financial problems	8.47	2.33–30.78	0.001

In the global case-control INTERHEART study the following nine modifiable risk factors were responsible for 90.4% of acute MI development: raised lipoprotein apoB/apoA1 ratio, smoking, diabetes mellitus, hypertension, abdominal obesity, psychosocial factors, low consumption of vegetables and fruits, physical inactivity and less regularly alcohol consumption<sup>4</sup>. The INTERHEART investigators found that these risk factors are the same in almost every geographic region and every racial/ethnic group worldwide and are consistent in men and women<sup>5–7</sup>. But in case-control study conducted in Costa Rica the most important factors associated with MI are abdominal obesity, smoking and caffeine intake, whereas intake of alcohol, consumption of healthy diet, and increased physical activity are inversely associated with risk of MI<sup>8</sup>.

At the beginning of the 20th century, cardiovascular diseases were more frequent in the upper socio-economic class<sup>9</sup>, but from the middle of the 20th century, especially in developed countries, cardiovascular diseases have become more frequent in lower socio-economic groups<sup>10</sup>. This changing pattern is not yet fully understood. The recognition of cardiovascular risk factors and adoption of proposed preventive measures mostly by higher socio-economic groups does not seem to provide complete explanation<sup>9</sup>. In the black African INTERHEART study, MI risk was increased with higher income and education in contrast to Arabs and white<sup>5</sup>.

Although moderate alcohol consumption could have beneficial effect on cardiac diseases<sup>4,5,8</sup>, it is considered

that excessive alcohol consumption, more than four alcoholic drinks per day in men and more than two in women, has direct toxic effect on heart and increase mortality of CVD<sup>11</sup>. In native South Asians the majority of AMI risk was explained by 9 potentially modifiable risk factors, as in the global INTERHEART study, but alcohol consumption did not appear to be protective<sup>6</sup>. This may be related to lower prevalence of alcohol consumption or to differences in drinking pattern.

The role of stressful events in the occurrence of acute myocardial infarction (AMI) is well known<sup>12–14</sup>. Sexual activity and excessive grieve can also provoke AMI<sup>12</sup>. Acute intensive stress and stressful life events such as earthquakes, war, threat of attack, and fear of death may precipitate AMI<sup>13</sup>. Pertinent pressure and stress at work can cause six time increase of risk for AMI during the following 24 hours<sup>14</sup>. According to data from INTERHEART study conducted in Latin America, subject who have been exposed to permanent stress have 2.8 time higher risk for MI in comparison with subjects who were never exposed to stress<sup>7</sup>.

In comparison with physically active subjects physically inactive have two times higher risk to develop AMI or to die from AMI<sup>15</sup>. According to some studies beneficial effect has only intensive physical activity<sup>16</sup>, but according to some other studies the similar effect has also moderate physical activity<sup>17</sup>.

Hypertension contributes to AMI occurrence in 20% women and in 15% of men<sup>4</sup>. According to global INTERHEART study, subjects who smoked and who have hy-

pertension and diabetes were at 13 times higher risk of AMI in comparison with persons without any of these three risk factors<sup>4</sup>. It is considered that smoking, hypertension and diabetes are responsible for 53% of all acute myocardial infarctions<sup>4</sup>. During the last two decades MI mortality decreased due to increased use of hypertension therapy.

Increased total cholesterol is considered to be a risk factor for MI mortality<sup>18</sup>, but level of HDL cholesterol seems to be more specific and better predictor of IHD mortality<sup>19</sup>. Although high level of HDL cholesterol is considered as protective for IHD, in 20% of women IHD occurred in spite of high level of HDL cholesterol<sup>20</sup>. Increased LDL cholesterol has been found to be a risk factor for IHD in many studies, and decrease of LDL cholesterol level by the use of statins is followed by decreased IHD morbidity and mortality<sup>21</sup>. In the present study, MI cases had increased triglycerides and LDL cholesterol and low values of HDL cholesterol, in comparison with controls, but only HDL cholesterol was independently related to MI.

Family history positive on AMI has been found as an important risk factor for MI occurrence<sup>22</sup>. In a case-control study comprising women 18–44 years old, cases with MI had two times more frequently first-degree relatives with MI in comparison with controls<sup>23</sup>. In the same study, positive history of MI among all relatives, not only among first-degree relatives, was also found as a risk factor for MI<sup>23</sup>.

Smoking is a major risk factor for patients with cardiovascular disease<sup>24</sup>. In the global INTERHEART study, smoking and increased ApoB/ApoA1 ratio were main risk factors for MI<sup>4</sup>. According to the same study subjects who are current smokers have 2.95 times higher risk of MI than subjects who never smoked<sup>25</sup>. It is considered that current smoking is responsible for MI occurrence in 46.3% of men and in 15.4% of women<sup>25</sup>.

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In some studies, consumption of red meat increases risk for IHD<sup>26</sup>. In an Australian study MI was significantly related to trans-fatty acid<sup>27</sup>. In the present study association between fatty meat and AMI was significant, but not independent of other factors observed.

Association between CVD and drinking water hardness (depending primarily of calcium and magnesium concentration) was suggested in some epidemiological studies. Rylander et al. found that deaths by ischaemic cardiopathies were inversely associated with the concentrations of calcium and magnesium in drinking water<sup>28</sup>. However, this relation was not found by Yang et al.<sup>29</sup> who suggested that magnesium in drinking water may have a protective effect. In the present study, cases in comparison with controls, significantly more frequently consumed well water which usually has high Ca and Mg concentration, but this association was not independent.

In our study selection bias was reduced by including as cases only patients who had MI for the first time, and as controls only those patients who did not have diseases related to cardiovascular risk factors. Measurement bias was reduced by using standardized method for data collection. The main limitation of the present investigation is small number of cases and controls, the fact which probably can explain why some established risk factors for AMI occurrence, such as smoking and diabetes, are not found to be independently related to AMI. Other findings are in line with the results of other studies.

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*S. B. Sipetić*

*Belgrade University, School of Medicine, Institute of Epidemiology, Višegradaska 26, 11000 Belgrade, Serbia  
e-mail: ssipetic@yahoo.com*

## **FAKTORI RIZIKA ZA NASTANAK PRIMARNOG NEFATALNOG INFARKTA MIOKARDA U BEOGRADU**

### **SAŽETAK**

Cilj ove studije je bio da ispita koji su nezavisni faktori rizika za nastanak primarnog nefatalnog infarkta miokarda (IM) u populaciji Beograda. U Beogradu je, u periodu 2005–2006. godine, sprovedena anamnestička studija. Grupu obolelih činilo je 100 osoba uzrasta 35–80 godina koji su usled primarnog nefatalnog IM po prvi put hospitalizovani u koronarnu jedinicu Urgentnog centra u Beogradu. Kontrolnu grupu činilo je 100 osoba koji su lečeni tokom istog perioda na Institutu za reumatologiju, Institutu za gastroenterologiju i na Klinici za ortopediju. Oboleli i kontrole su bili individualno mečovani u odnosu na pol, uzrast ( $\pm 2$  godine) i mesto stanovanja (urbana/ruralna sredina Beograda). Prema rezultatima multivarijantne analize faktori rizika za IM su: »dobri« socio-ekonomski uslovi (OR=2,76), ukupno konzumiranje alkohola (OR=2,62), konzumiranje rakije (OR=6,73), svi stresni događaji posmatrani zajedno (OR=3,13), stres usled smrti bliskog rođjaka (OR=3,35), veliki finansijski problemi (OR=31,64), mali finansijski problemi (OR=8,47), hipertenzija (OR=2,39), pozitivna porodična anamneza za IM medju srođnicima (OR=3,66), pozitivna porodična anamneza za IM kod oca (OR=6,24) i niske vrednosti HDL-holesterola (OR=152,41). Amatersko bavljenje sportom u prošlosti je negativno povezano sa nastankom IM. Naši rezultati su slični rezultatima drugih studija i mogu da budu od pomoći za razvoj strategije za prevenciju ishemijske bolesti srca u Srbiji.