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„Obesity Paradox“ – Fiction or a Fact?

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Key words: obesity paradox; heart rate > 80 bpm; STEMI.

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Abstract

Background: Many cardiovascular diseases are associated with obesity, but, despite this fact, obese people live longer than their normal-weight counterparts do. This phenomenon is called the „obesity paradox“.

Aim: Purpose was to investigate the impact of obesity on the final outcome; determine the connection between obesity and heart rate > 80 beats per minute and other risk factors, and presence of „obesity paradox“.

Material and Methods: Research included 140 patients with anterior wall acute STEMI treated in Coronary Unit, Clinical Center Kragujevac form January 2001-June 2006. Heart rate was calculated as the mean value of baseline and heart rate in the first 30 minutes after admission. Body mass index was calculated as the ratio of body weight in kilograms and body height in squared meters, and classified according to the WHO recomendations.

Results: More than 75% obese patients were in both groups, survivors and those who died. In the subgroup with heart rate > 80 results were similar. Obesity had no significant effect on mortality despite the fact that the large number of patients with fatal outcome was obese.

Conclusion: Correlation with acute myocardial infarction and elevated heart rate is evident, but obesity was not independent predictor for mortality which can only partly confirm presence of „obesity paradox“.

Introduction

Coronary heart disease (CHD) is the primary cause of morbidity and mortality in both developed and developing countries and its incidence is increasing rapidly worldwide [1, 2]. About 20% of acute coronary syndromes (ACS) are ST-segment elevation myocardial infarction (STEMI) and it has the highest in-hospital mortality within subtypes of ACS [2, 3]. Among patients with acute myocardial infarction, those who present with STEMI develop larger infarctions, have more in-hospital complications, and have higher short term mortality than patients without ST elevation [1, 4].

Many modifiable (hyperlipidaemia, hypertension, smoking, diabetes) and non-modifiable (gender and age) risk factors were related to the development of atherosclerosis and the risk of presenting with ACS [4]. Heart rate was not considered as a risk factor for cardiovascular diseases for a long time [1, 5], but recently there was the change of the attitude on this issue, based on the fact that heart rate is the main factor influencing cardiac efficacy and performance, causing the increase of myocardial oxygen consumption (MVO_2), and decrease of myocardial perfusion due to shortened diastole. The individuals with elevated heart rate are more likely to develop accelerated atherosclerosis and ACS, and have higher mortality risk [1, 7].

Obesity is a complex disorder characterized

by the accumulation of excess adipose tissue due to genetic, metabolic, behavioral and social factors [1, 8]. Although it is a big contributor to the higher prevalence of cardiovascular morbidity and premature mortality in developed countries, it has only recently been afforded the same level of attention as other risk factors for CHD [1, 9]. The prevalence of obesity in developed and many developing countries is estimated to range from 40% to 60% [1, 10].

Similar to other risk factor models, body weight is thought as the equation „the more, the worse“, and there is no doubt that weight gain is associated with high blood pressure, diabetes, and cardiovascular disease, in addition to several metabolic disorders and other conditions. For that reason, cut-off points have been sought to define normal or excessive weight levels, and different obesity degrees, in addition to facilitate behaviors [11].

Many measurements have been used to determine body-fat accumulation but the most often is body mass index (BMI) which is calculated by dividing the body weight (in kilograms) by height (in meters, squared). After NHANES II (National Health And Nutrition Examination Survey II) trial which defined obesity in adults as BMI greater than 27.3 kg/m^2 for women and 27.8 kg/m^2 for men [1, 12], in 1998, the National Institutes of Health (NIH) Expert Panel on the identification, evaluation and treatment of overweight and obesity in adults adopted the WHO (World Health Organization) classification which divides BMI values into 4 categories: underweight, normal, overweight and obesity [1,13].

The association between heart rate, body weight and blood pressure has been confirmed in clinical studies, denoting the increased sympathetic activity as the major link to these three disorders. A ten-year study showed that over time healthy individuals with increased heart rate and increased sympathetic activity develop increased blood pressure and weight gain [14]. It has been suggested that increased sympathetic activity may also have a major role in the relationship between high heart rate and cardiovascular mortality [15].

Several epidemiological studies showed a positive relationship between obesity and mortality, in particular cardiovascular mortality. However, several cross-sectional, retrospective database studies, including one from a clinical US Veterans Administration population in the issue of Mayo Clinic Proceedings, have found an inverse correlation between body mass index and mortality, often termed the „obesity paradox“. Validation of this paradox requires that the inverse correlation between adiposity and mortality persist even when appropriate corrections for confounding variables are added to the analysis. Conversely, if the paradoxical association between body weight and mortality can be dissipated or eliminated by appropriate correction of confounding variables such as the presence of chronic disease, then there is little or no paradox [16].

Despite claims that obesity is not harmful in older individuals, several large-scale studies indicated that both overweight and obesity, at all ages and in both sexes, particularly no-smokers and without history of disease, are linked to increased mortality. Although the relative escalation in risk associated with a high BMI may decline with advancing age, the absolute rise is still much greater in elderly subjects, simply due to increased death rates in this age range [17].

Materials and Methods

This study included 140 patients with anterior wall acute myocardial infarction with ST-segment elevation treated in Coronary Unit, Center for Cardiology, Clinical Center Kragujevac for 5.5 years (January 2001 – June 2006). The aim of this retrospective, and mostly prospective, population-type, longitudinal study was to determine what the predictors of a bad outcome are in the observed group, with defining the intrahospital mortality in the Coronary Unit as a bad outcome. By a random choice we included patients with the following criteria: (1) Patients older than 30 years; (2) Without diabetes mellitus; (3) Without prior myocardial infarction; (4) With no malignant diseases; (5) Without haematologic diseases; (6) Without systemic autoimune diseases; (7) Patients with thrombolitic therapy aplied; (8) EF on admission according to Simpson greater than 35%; (9) KILLIP class I and II. Patients with acute coronary syndrome and significant LV dysfunction have lower, but relatively stable stroke volume, and their heart output depends on heart rate levels. In several studies, including GISSI 2 and 3, it was confirmed that mortality is greater in patients with heart rate >80 beats per minute and without significant LV dysfunction. Since the thrombolitic terapy was highly indicated to be applied in these patients, due to acute myocardial infarction, and since it was already demonstrated in several studies that patients with KILLIP III and IV have less benefits than KILLIP I and II patients when this therapy is applied, we decided to exclude patients with severe heart failure from the research. We considered that inclusion of patients with severe heart failure and LV dysfunction could influence the results and mortality rate, and since many studies were already conducted in these groups of patients we wanted to investigate the influence in patients with less severe heart damage.

Acute myocardial infarction was diagnosed according to criteria for diagnosing acute coronary syndromes. Mandatory term for including patients in this study was the presence of typical ECG changes for myocardial infarction: ST-segment elevation ≥1 mV, longer than 0.08 s from J spot in two contiguous leads; and one of the following criteria: 1) typical anginal pain lasting longer than 20 minutes; 2) characteristic elevation of cardiospecific enzymes (CK), at least twice as normal; 3) increased troponin

(TnIU) levels according to the referent values of a local laboratory, with the following of AST, ALT and LDH levels. As an independent variables we examined the following parameters:

1. Gender, age, smoking habbit, body mass index (BMI), KILLIP class, dyslipidemias, history of hypertension, angina pectoris, prior cardio-vascular therapy. For age and gender risk factors, we considered male patients older than 50, and female patients older than 60 years. Anamnestic data on heart attack in patient's father before the age of 55, and mother before the age of 65 were considered as a positive family history for cardiovascular diseases, especially for myocardial infarction.
2. Hemodinamic status of patients on the admission to the Coronary Unit: (1) Heart rate was calculated as the mean value of baseline and heart rate in the first 30 minutes after admission, recorded on monitor and electrocardiogram. Patients were constantly monitored in the intensive care unit and ECG was done two times daily. Based on results of many previously conducted studies, experimental and clinical, with different patient groups, including hypertensives, with 24 hour ambulatory monitoring, with acute coronary syndrome, with or without heart failure, we took heart rate greater than 80 beats per minute as a cut-off point. Most of the studies already proved that morbidity and mortality rates increase when heart rate exceeds the threshold of 80 beats per minute, so the selection of heart rate values was empirical. (2) Blood pressure levels were measured in a lying position after 5 minutes of rest, and classified according to the recommendations of the VII U.S. National Committee on Prevention, Detection, Monitoring and Treatment of High Blood Pressure: normal (systolic <120; diastolic <80 mmHg); prehypertension (systolic 120-139; diastolic 80-89 mmHg); I degree hypertension (systolic 140-159; diastolic 90-99 mmHg); II degree hypertension (systolic ≥160; diastolic ≥100 mmHg).
3. ECG was analyzed daily, cardiospecific enzymes were followed (CK, AST, ALT, LDH, troponin TnIU); End-diastolic and end-systolic left ventricle volumes, as well as ejection fraction were detected in 2D-echocardiography mode and classified according to Simpson's criteria.
4. Body mass index was calculated as the ratio of body weight in kilograms and body height in squared meters, and classified in five cathegories according to the WHO classification from 1998: underweight BMI as less than 18.5 kg/m^2, normal BMI as 18.5 to 24.9 kg/m^2, overweight BMI as 25.0 to 29.9 kg/m^2, and obese BMI greater than or equal to 30 kg/m^2. After classification of patients according to these guidelines we divided them in only two categories: those with normal weight (< 25 kg/m^2) and those with higher body weight (> 25 kg/m^2).

For statistical analysis we used the methods of descriptive (tabular and graphical representation, measures of central tendency and measures of variability) and analytical statistics. With univariate statistical analysis, we analyzed the influence of each independent variable on the observed outcomes: mortality, and heart rate. Factors that in univariate model showed statistically significant entered into multivariate model, which selected the independent prognostic factors. For analyzing the influence of predictors of mortality logistic regression analysis was used, and for analyzing their effects on heart rate multivariate regression model.

Results

Considering the mean age of the patients with anterior wall STEMI there was a difference between survivors and respondents with the fatal outcome, with statistically significant younger age among the survivors. There was no significant gender-related difference in these two groups, although in both groups there was a slightly higher distribution of male patients (Table 1).

Table 1: Basic characteristics (age and gender) of patients with anterior wall acute myocardial infarction with ST-segment elevation.

Patient characteristics		Fatal outcome		Significance
		No	Yes	
Number of patients (N)		100	40	
Age (X±SD (Med, min-max))		63.02 ± 11.34 (65.5; 27-83)	69.60 ± 8.68 (70; 46-83)	[a]p=0.002*
Gender n (%)	Male – 60%	63 (63%)	21 (52.5%)	[b]p=0.252
	Female – 40%	37 (37%)	19 (47.5%)	

*statistically significant difference; [a] Mann Whitney U test; [b]χ 2-test; SD – standard deviation.

Heart rate on admission in patients with anterior wall STEMI was significantly different between survivors and patients with fatal outcome, with higher levels in patients with fatal outcome. Mean heart rate was for about 20 beats per minute higher in patients who had a fatal outcome comparing to those who survived (Table 2).

Table 2: Haemodynamic characteristics of patients with anterior wall acute myocardial infarction with ST-segment elevation – differences between survivors and patients who died.

Parameters		Fatal outcome		Significance
		No	Yes	
Heart rate on admission (X ±SD (Med, min-max))		87.97 ± 16.70 (86; 46-132)	102.05 ± 23.16 (95.5; 50-182)	[b]p=0.000*
Heart rate: ≥80 / <80 bpm n (%)	Yes	72 (72.0%)	37 (92.5%)	[c]p=0.008*
	No	28 (28.0%)	3 (7.5%)	
History of hypertension	Yes	68 (68.0%)	35 (87.5%)	[b]p=0.018*
	No	32 (32.0%)	5 (12.5%)	
Systolic blood pressure (X ± SD (Med, min-max))		139.60 ± 22.64 (140.0; 90-200)	130.95 ± 22.44 (130.0; 80-180)	[a]p=0.043*
Diastolic blood pressure (X ± SD (Med, min-max))		87.19 ± 1.99 (89.0; 60-130)	84.25 ± 14.53 (90; 50-110)	[a]p=0.292

*statistically significant difference; [a]t-test; [b]χ 2-test; [c]Mann Whitney U test; SD – standard deviation.

According to the outcome in the total sample there was significant difference in the incidence of heart rate levels lower / greater or equal to 80 beats

per minute, with 72% of respondents having the heart rate greater than 80 bpm in the group of patients who survived, and 92.5% of respondents with these heart rate levels in the group of patients who died (Table 2).

When we used the mortality of patients as criteria to analyze the incidence of obesity, we got no statistically significant difference in the prevalence of obese patients. In both subgroups, patients with fatal outcome and among the survivors, there were more than 75% of obese subjects (Table 3). The same results were obtained after a dividing the patients into the categories of normal and higher body weight (less/higher than 25 kg/m^2). Between patients with a fatal outcome and survivors, there was significant difference in the frequency of those with BMI lower and higher than 25 kg/m^2. In both of the above-mentioned groups, subjects with BMI values greater than 25 kg/m^2 were more significantly represented, making more than 75% of analyzed total sample of patients.

Table 3: Prevalence of obesity and low HDL-cholesterol in a total sample and in subgroup of patients with heart rate greater than 80 beats per minute.

Total number of patients		Fatal outcome		Significance
		No	Yes	
Obesity n (%)	Yes	76 (76%)	33 (82.5%)	[a]p=0.403
	No	23 (23%)	7 (17.5%)	
HDL < 1.03 –man; < 1.29 - woman n (%)	Yes	56 (56%)	27 (62.5%)	[a]p=0.492
	No	44 (44%)	13 (37.5%)	
HDL (X ± SD (Med, min-max))		1.15 ± 0.32 (1.14; 0.33-2.10)	1.00 ± 0.30 (0.99; 0.34-1.58)	[b]p=0.011*
Subgroup of patients with heart rate > 80 beats per minute		Fatal outcome		Significance
		No	Yes	
Obesity n (%)	Yes	56 (77.8%)	30 (81.1%)	[a]p=0.689
	No	16 (22.2%)	7 (18.9%)	
HDL < 1.03 –man; < 1.29 - woman n (%)	Yes	37 (51.4%)	25 (67.6%)	[a]p=0.106
	No	35 (48.6%)	12 (32.4%)	
HDL (X ± SD (Med, min-max))		1.17 ± 0.33 (1.20; 0.33-2.10)	1.00 ± 0.31 (0.99; 0.34-1.58)	[b]p=0.011*

*statistically significant difference; [a]χ 2-test; [b]Mann Whitney U test; SD – standard deviation; HDL- high density lipoprotein.

After analyzing the total number of subjects, we divided them into subgroups according to the heart rate levels to those who had heart rate lower and those with greater than 80 beats per minute. The aim was to investigate whether there was a difference in distribution of normal-weight and obese patients when heart rate is elevated so we could see if there is a connection between these two risk factors.

This analysis showed similar results as previous. No significant difference was shown in the prevalence of obesity in patients with high heart rate, although more than 3/4 (75%) of patients were obese in the group with fatal outcome and among the survivors, in this subgroup (Table 3). According to the mortality of patients, BMI values were not significantly different, and there was also no difference in the frequency of patients with BMI values lower and higher than 25 kg/m^2. In the group of survivors there was 76%, whereas in the group with a fatal outcome BMI higher than 25 was present in 81.1% of patients.

Hypertension had the significant influence on mortality (χ2-test; p=0.018). Patients with a prior hypertension were more exposed to the risk of dying and had the fatal outcome more often. This risk factor was present on admission in 68% of respondents in the group of survivors and 87.5% in the group of patients who died during the study (Table 2).

Beside the anamnestic data on the existence of prior hypertension in patients included in this research, we also measured blood pressure levels on the admission in Coronary Unit so we could confirm or reject the presence of hypertension, and the influence on the outcome in these patients. We also wanted to make the difference between the influence of systolic and diastolic blood pressure levels on the outcome. Results showed that when the mortality of the respondents was observed as a category for differentiate the patients, those who survived had higher levels of systolic blood pressure with the statistically significant difference. Mean systolic blood pressure in patients who died was 130.95 ± 22.44 (130.0; 80-180), comparing to 139.60 ± 22.64 (140.0; 90-200) in those who survived. There was no significant difference in the mean values of diastolic blood pressure between survivors and patients who died from acute myocardial infarction. In both groups, mean diastolic blood pressure was about 85 mmHg (Table 2).

As far as the concern of lipoprotein profile components, only low HDL-cholesterol levels had significant incidence. HDL-cholesterol showed statistically significant difference between survivors and patients with fatal outcome, with lower values of this parameter in patients with fatal outcome. There was no significant difference in distribution of HDL-cholesterol lower than 1.03 mmol/l for male and <1.29 mmol/L – female patients according to mortality. In both groups there was more than 55% of patients with lower than above-mentioned levels. In subgroup of patients with heart rate greater than 80 beats per minute HDL-cholesterol also showed statistically significant difference between survivors and patients with fatal outcome, with significantly lower values in those who died. Still there was no significant difference in distribution of HDL-cholesterol lower than 1.03 mmol/l for male and <1.29 mmol/L–female patients according to mortality. In both groups there was more than 50% of patients with lower than above mentioned levels (Table 3).

Logistic regresion was used to investigate what are the predictors or independent risk factors for mortality. Univariate logistic regresion analyzed the influence on mortality of each observed factor in the presence of all others risk factors and those that showed significance in this analysis were included in multivariate regresion model to examine what risk factors have independent influence on mortality.

Univariate model singled out heart rate on admission greater than 80 beats per minute, but not the obesity (BMI higher than 25 kg/m^2) as statistically significant risk factor for mortality, among other risk factors. When they were included in multivariate model, heart rate on admission greater than 80 beats per minute remained significant and was singled out

as strong and independent risk factor with a high influence on mortality. Obesity remained with no significant influence on mortality in the subgroup also. We can consider obesity as one of the important risk factors for morbidity, considering the fact that more than 75% of subjects in total sample and in subgroup with high heart rate were obese, but not the independent one, and with no independent mortality rate influence. Hypertension and HDL-cholesterol were singled out in univariate analysis as important risk factors but not as independent predictors for mortality (Table 4).

Table 4: Univariate and multivariate analysis of risk factors influencing the mortality of patients with anterior wall STEMI and heart rate greater than 80 bpm.

Risk factors	Univariate		Multivariate	
	#expB (95%CI)	Significance	expB (95%CI)	Significance
Heart rate on admission≥ 80 bpm	1.040 (1.017-1.063)	p=0.000*	1.076 (1.006-1.151)	p=0.033*
Hypertension	0.304 (0.109-0.848)	p=0.023*	0.588 (0.069-4.987)	p=0.626
Systolic blood pressure	0.994 (0.986-1.003)	p=0.170	/	/
Diastolic blood pressure	0.987 (0.962-1.012)	p=0.291	/	/
Obesity	0.672 (0.263-1.712)	p=0.405	/	/
Subgroup of patients with heart rate > 80 beats per minute				
HDL-cholesterol	0.194 (0.052-0.717)	p=0.014*	8.078 (0.115-10.192)	p=0.327
Hypertension	0.379 (0.130-1.107)	p=0.076	/	/
Systolic blood pressure	0.982 (0.965-1.000)	p=0.052	/	/
Diastolic blood pressure	0.986 (0.960-1.014)	p=0.319	/	/
Obesity	0.817 (0.303-2.204)	p=0.689	/	/
HDL-cholesterol	0.194 (0.052-0.717)	p=0.014*	8.078 (0.115-10.192)	p=0.327

Analysis of heart rate refers to a total sample, and other risk factors were analyzed in the subgroup with heart rate > 80 bpm as well in a total sample; HDL – high density lipoprotein; *statistically significant difference; #exponentiation of the B coefficient, which is an odds ratio; CI-confidence interval.

Discussion

Controversy about obesity as an independent risk factor for cardiovascular disease still exists, with many authors associating obesity and cardiovascular diseases, and others have denying this relationship. Some authors consider obesity as a condition characterized by an amplified cardiovascular risk, through a concomitant association with hypertension, diabetes mellitus and dyslipidemia. This point of view was partly confirmed in this research considering the fact that the majority of our patients had hypertension and low HDL-cholesterol as a form of dyslipidemia as the most common risk factors. We have no results for patients with diabetes mellitus because the existence of this metabolic disorder was one of the criteria for excluding patients from the research. In contrast, others report that obesity is an independent risk factor, especially if it is characterized by central fat distribution [8]. We could not confirm or reject this hypothesis because our patients were divided according to BMI levels, we did not measure waist circumference or waist-to-hip ratio to estimate the presence of central adiposity.

Usually, obesity is defined as a risk factor, whereas overweight has been associated with favourable prognosis when compared with normal weight. This protective effect of overweight and even obesity has been shown especially in studies involving older people. Recently, this „obesity paradox“ has arisen much interest and several explanations have been presented. Because the obesity paradox is usually encountered in cohorts involving older people, it is possible that the development of fragility- with possible links to cardiovascular diseases- could contribute to worse prognosis [18].

In this research, we confirmed the results of many previous studies, referring to a high incidence of obesity in patients with cardiovascular diseases, especially with acute myocardial infarction. More than 75% of our patients were obese (had BMI greater than 25 kg/m^2). But we couldn't confirm also the presence of „obesity paradox“ because there was more obese than normal-weight patients who died during the research. When we used the mortality as criteria to analyze the incidence of obesity, there was no important difference in the obesity prevalence [1].

Obesity produces an increment in total blood volume and cardiac output that is caused in part by the increased metabolic demand induced by excess body weight. Thus, at any given level of activity, the cardiac workload is greater for obese subjects. Obese subjects have higher cardiac output and a lower total peripheral resistance than do lean individuals [19].

One of the most interesting aspects of recent investigations in cardiovascular epidemiological studies is the realization that increased heart rate is frequently associated with high blood pressure, obesity, dyslipidemia, and elevated hematocrit. It has been argued that the interrelationship between the above-mentioned risk factors reflects persistant sympathetic stimulation [1, 20].

The results of this research that could confirm the facts about association between high heart rate, hypertension and obesity through sympathetic overactivity as a major link, are those that are showing the higher prevalence of hypertension and obesity in subgroup of our patients with heart rate greater than 80 beats per minute.

Although there was no difference in the prevalence of obesity in the subgroup with high heart rate, we can say that there is a strong connection between obesity and high heart rate. More than 3/4 (75%) of patients were obese in the group with fatal outcome and in survivors in this subgroup.

Hypertension had the significant influence on mortality in patients with anterior wall STEMI (χ2-test; p=0.018) in a total sample. Patients with a prior hypertension were more exposed to the risk of dying and had the fatal outcome more often. This risk factor was present on admission in 68% of respondents in the group of survivors and 87.5% in the group of patients who died during the study. Results were

similar in the subgroup with high heart rate [1].

Several theories are attempting to explain the association between obesity and heart rate. Some authors believe that increased caloric intake leads to higher values of insulin, which acts on the central nervous system increasing sympathetic activity and thus the heart rate [1, 21]. In contrast, the Framingham and Tecumseh trials have shown that obesity may be a consequence rather than a cause of increased sympathetic activity. The same pathophysiological mechanism by which increased sympathetic tone causes hypertension could be responsible for obesity. Thermogenic effect of sympathetic activity is a physiological compensatory mechanism against the increase in body weight [1, 22].

Obesity has a strong effect on lipoprotein metabolism, regardless of ethnic group. Increased weight is a determinant of higher levels of triglycerides, elevated LDL-cholesterol, and low HDL-cholesterol. Conversely, weight loss is associated with a healthier lipoprotein profile in both men and women: triglycerides decrease, HDL-cholesterol increases, and LDL-cholesterol decreases. Changes in HDL-cholesterol levels are more pronounced in women than in men. The association between obesity and LDL-cholesterol is more complex. LDL-cholesterol concentrations increase with BMI in men, but such increases are not as pronounced in women, the elderly, and some ethnic groups. Increasing BMI is associated with small, atherogenic LDL-cholesterol [1, 23-25].

This research confirmed above mentioned when we take into account that low HDL-cholesterol had statistically significant incidence as the most important lipid profile disorder. (t-test, p=0.011), with lower values in patients who died. In both groups there was more than 55% of patients with lower than above-mentioned levels. Results were similar in the subgroup with high heart rate. LDL-cholesterol was mostly desirable or normal which also concurs to a previous data [1].

The negative impact of high BMI on all-cause mortality is now well established, but there is an apparent decline in the relative added risk of obesity with increasing age. This has led some experts to conclude that obesity should not necessarily be viewed as a disease in individuals older than 55 years. Re-examination of the impact of obesity on health in older individuals disclosed two potential benefits of weight excess: decreased osteoporosis and better survival of obese subjects with certain health hazards, known as „obesity paradox“. This paradox refers to the unexpected findings that obese subjects seem to fare better than, or at least as well as, their normal- or low-weight counterparts in terms of mortality rates in the context of coronary artery disease in hypertensive subjects, congestive heart failure, and some instances of non-ST-segment elevation myocardial infarction.

In this research we couldn't confirm the presence of „obesity paradox“ because the majority of patients with fatal outcome were obese. In addition, we did not include patients with non-ST-segment elevation myocardial infarction in this research, which can be a potential reason for the absence of the paradox. Whether or not all these different conditions that share some common, yet unidentified, underlying mechanism are related to obesity itself, or rather reflect nutritional status or reserve, and/or possibly coexisting medical therapy [1, 26].

This interesting and potentially critical phenomenon remains presently enigmatic, requiring case- and age-specific in-depth examination. Some 20 years ago, obesity in the elderly was actually linked to the twofold increase of postmyocardial infarction and intrahospital mortality in subjects older than 65 years [17]. The results of this study are consistent with these data because the average age of patients with anterior wall acute myocardial infarction with ST-segment elevation in survivors was about 63 and about 69 years in those who died during the study period [1].

This could be one of the possible explanations why „obesity paradox“ wasn't present or pronounced in patients in this research. The majority of them had high heart rate, hypertension and were obese but they did not have lower mortality as it could be expected if phenomenon existed. All parameters that can be disturbed with increased sympathetic activity, as we mentioned before, were there, those risk factors were present in almost all patients but there was no paradox. Can the age of the subjects be the most important determinant of the paradox, or is it something else? Answers to this question should be reached through future studies, but until then we can just assume what is the key for this mistery.

In addition, Clara Carpeggiani and associates at more than 10 000 patients with ischemic and non-ischemic heart disease patients hospitalized during the past three decades in the CNR Institute of Clinical Physiology in Pisa could find some, but not all answers in the study. This study estimated the effect of BMI on long-term mortality. The correlation between BMI and total cardiovascular mortality was evaluated first in the overall population and then after dividing the patients into groups based on age: less than 45, from 45-55, 55-65 and more than 65 years.

The results showed that BMI was inversely related to mortality, but the association is lost in the group of patients younger than 65 years after the division by age. These results are explained by the fact that in older, obese and overweight patients, aggressively implement of treatment methods than in under- and normal-weight patients can mask the negative impact of elevated BMI on mortality [27].

Conclusion: Study of the „obesity paradox“ is difficult because there are so many limitations. All previous studies have been retrospective analyses;

therefore, each has been limited by an inability to adjust for all confounding variables. None of the databases used were specifically designed to study the obesity paradox as a primary goal, thus the researchers are limited to analyze only the available data and covariates. Data on recent weight change, in particular, unintentional weight loss in the period preceding the collection of weight data was also one of the problems. Other limitations are that: none of the studies examined patients of all ages, usually patients were elderly; BMI was the most often used measurement, waist circumference and waist-hip ratio were used rarely, and detailed medical treatment haven't been considered, so the valid information couldn't be afforded.

References

1. Davidovic G. Influence of risk factors combiation and high heart rate on mortality of patients with anterior wall acute myocardial infarction. University in Kragujevac; Medical faculty. 2011. Dissertation.
2. World Health Organization. The World Health Report 2002 – Reducing risks to health, promothing healthy life. Available at: URL: http://www.who.int/whr/en (11.04.2013.; 18:10h).
3. Braunwald E, Fauci AS, Kasper DL, et al.: Harrison's Principles of Internal Medicine. 15 ed. New York, Mc-Graw-Hill, 2001: pp 1386-8.
4. Rosengren A, Wallentin L, Simoons M, et al. Cardiovascular risk factors and clinical presentations in acute coronary syndromes. Heart. 2005; 91:1141-1147.
5. Nabel EG, Selwyn AP, Ganz P. Paradoxical narrowing of atherosclerotic coronary arteries induced by increases in heart rate. Circulation. 1990; 81:850-859.
6. Caguioa ES. When should resting heart rate be taken into account in the treatment of CAD? Medicographia. 2008; 30-3:255.
7. Paillard F, Tardif JC. Potential benefits of pure heart rate reduction. Medicographia, 2008. 30, 3:222-3.
8. Scaglione R, Argano C, Di Chiara T, Licata G. Obesity and cardiovascular risk: the new public health problem of worldwide proportions. Expert Rev Cardiovasc Ther. 2004; 2(2): 203-212.
9. Poirier P, Eckel RH. Obesity and Cardiovascular Disease. Current Atherosclerosis Reports. 2002; 4:448-453.
10. World Health Organization. Obesity: preventing and managing the global epidemic – report of a WHO consultation on obesity. World Health Organisation, Geneva, Switzerland. 1998.
11. Tajer CD. RAC director's letter. The Obesity Paradox. Intention of Making a Reasonable Suggestion for Secondary Prevention. Revista Argentina de Cardiologia. 2012; 80(2): 195-204.
12. Najjar MF, Rowland M. Antropometric reference data and prevalence of overweight. United States, 1976-1980. Vital Health Stat. 1987; 11(238): 1-73.
13. National Heart and Blood Institute. Clinical guidelines on the identification, evaluation and treatment of overweight and obesity in adults – Executive Summary. National Institute of Health, Bethesda, MD. 1998.
14. Valentini M, Parati G. Variables influencing heart rate. Progress in Cardiovascular disease. 2009; 52:11-19.
15. Benetos A., Bean K. Prognostic significance of heart rate in the general population. Medicographia, 2002. 24, 3:194.
16. Ades PA, Savage PD. The Obesity Paradox: Perception vs. Knowledge. Mayo Clinic Proceedings. 2010; 85(2):112-114. Available on: www.mayoclinicproceedings.com. (11.04.2013.; 18:30).
17. Osher E, Stern N. Obesity in Elderly Subjects. In sheep's clothing perhaps, but still a wolf! Diabetes Care. 2009; 32(2): S398-S402.
18. Strandberg TE, Strandberg AY, Salomaa VV, Pitkala KH, Tilvis RS, Sirola J, Miettinen TA. Explaining the obesity paradox: cardiovascular risk, weight change, and mortality during long-term follow-up in men. Eur Heart J. 2009; 30:1720-1727.
19. Poirier P, Giles TD, Bray GA, Hong Y, Stern JS, Pi-Sunyer FX, Eckel RH. Obesity and Cardiovascular Disease: Pathophysiology, Evaluation, and Effect of Weight Loss: An Update of the 1997 American Heart Association Scientific Statement on Obesity and Heart Disease From the Obesity Committee of the Council on Nutrition, Physical Activity, and Metabolism. Circulation. 2006; 113:898-918.
20. Palatini P., Julius S. Pathophysiology of the association between increased heart rate and cardiovascular morbidity and mortality. Medicographia, 2002;24(3):204-5.
21. Landsberg L, Kriger DR. Obesity, metabolism and the sympathetic nervous sistem. Am J Hypertension. 1989; 2(3 pt 2): 125s-132s.
22. Julius S, Valentini M, Palatini P. Overweight and hypertension: a two-way street? Hypertension. 2000; 35:807-813.
23. Krauss RM, Winston M, Fletcher BJ, Grundy SM. Obesity: Impact on Cardiovascular Disease. Circulation. 1998; 98:1472-1476.
24. Anderson JW, Konz EC. Obesity and disease management: effects of weight loss on comorbid conditions. Obesity Res. 2001; 9 (suppl. 4): 326S-334S.
25. Denke M. Connections between obesity and dyslipidaemia. Curr Opin Lipidol. 2001; 12:626-628.
26. Uretsky S, Messerli FH, Bangalore S, Champion A, Cooper-Deholf RM, Zhou Q, Pepine CJ. Obesity paradox in patients with hypertension and coronary artery disease. Am J Med. 2007; 120:863-870.
27. Fricker J, ESC Congress News. Time to forget obesity paradox? (29. August 2011.) http://www.escardio.org/congresses/esc-2011/congress-news/Pages/obesity-paradox.aspx (11.04.2013.; 19:05h).