IMPACT OF SOME MODIFIABLE CARDIOVASCULAR RISK FACTORS ON THE EARLY PROGNOSIS AFTER ACUTE MYOCARDIAL INFARCTION

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ABSTRACT

Introduction*: Arterial hypertension (HTN), dyslipidemias, diabetes mellitus (DM) and smoking are accepted to be major modifiable risk factors (RF) for cardiovascular morbidity and mortality worldwide. Nevertheless their role for the prognosis of patients early after an acute cardiovascular event has not been fully elucidated.*

The aim of our study was to evaluate the impact of HTN, dyslipidemia, DM and smoking on the early prognosis of patients with acute myocardial infarction (AMI).

Materials and methods*: We included 682 consecutive patients with AMI, mean age 66.6 ± 12.9 years. Detailed information was collected about the cardiovascular RF of the patients, concomitant diseases, demographic and socio-economic data.*

Results*: Acute myocardial infarction with persistent ST-elevation was diagnosed in 344 (50.4%) patients. Arterial hypertension was present in 589 (86.4%), dyslipidemia - 347 (50.9%), active smoking - 178 (26.1%), type 2 DM - 171 (25.1%). In-hospital mortality was 13.6% (n=89): 14.1% (n=46) for ST-elevation AMI and 12.7% (n=38) for non-ST-elevation AMI, p=N.S. The impact of the analyzed RF on the early prognosis, demonstrated by the odds ratio (OR) for lethal outcome was as follows: HTN - OR = 3.19, p<0.0001, DM - OR = 2.20, p = 0.003, dyslipidemia – OR = 1.80, p=0.03, active smoking - OR = 0.35, p = 0.005.*

Conclusion*: Prevalence of HTN, dyslipidemia, type 2 DM and active smoking in patients with AMI in our study was high with HTN being the most influential RF in regard to the early post-infarction prognosis. While the first three RF were associated with increased early mortality, surprisingly active smoking reduced the risk for unfavourable outcome.*

Keywords*: hypertension, dyslipidemia, diabetes, smoking, infarction, mortality.*

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Introduction

Cardiovascular diseases (CVD) remain the main cause of death in most parts of the world - 47% of all deaths in Europe are due to CVD[1-4]. In addition to being the largest contributor to mortality in Europe, CVD also makes a very large contribution to morbidity - 2500 per 100 000 population[1-5]. Coronary artery disease (CAD) is currently the most devastating CVD with incidence varying between 1/80 to 1/170 in the European countries and almost 1.8 million deaths, or 20% of all deaths in Europe annually (12.8% of all deaths worldwide)[2-4].

Coronary artery disease could be presented in different clinical forms and acute myocardial infarction (AMI) is the most life-threatening one[1, 5, 6]. Although there is a decline in death rates following AMI for the last three decades due to improved treatment and secondary prevention, mortality still remains substantial[1, 4, 5]. Approximately 12% of the patients die within 6 months of the acute coronary event and the in-hospital mortality is estimated to be 6-14%[1, 4, 5].

Development of CVD including CAD and AMI is strongly connected to lifestyle, unhealthy diet, physical inactivity, psychosocial stress and insufficient control of other diseases/risk factors

(RF)[1, 7-10]. Arterial hypertension (HTN), dyslipidemias, diabetes mellitus (DM) and smoking are traditionally accepted as strong cardiovascular RF with high prevalence in many regions of the world: HTN affects 30-45% of the European population and dyslipidemias - up to 54% of the Europeans aged ≥25 years[1, 8-10]. There are about 60 million people with DM in the European Region (~10% of people aged 25 years and over). Europe has also the highest prevalence of tobacco smoking among adults (28%) and some of the highest prevalence of tobacco use by adolescents[1, 3, 5].

Despite the general opinion about the negative influence of these RF on cardiovascular health, it is still uncertain what impact they exert on the clinical outcome of patients with an acute cardiovascular event[1, 11-15]. This gave us a reason to investigate the role of HTN, dyslipidemias, DM and active smoking, specifying their influence on the early prognosis of patients experiencing AMI.

Materials and methods

A prospective study, including 682 consecutive patients with AMI, hospitalized for the period May, 2008 - December, 2014. Of all patients 431 (63.2%) were males, the mean age of the entire group was 66.6 ± 12.9 (43-92) years: 63.4 ± 12.9 (43-87) years of the males and 72.2 ± 10.7 (49-92) years of the females, p<0.0001. The presented scientific research was a sub-study of a larger study, aiming to specify the causes for pre-hospital and in-hospital delay of medical care for patients with AMI and the opportunities for its optimization.

Detailed medical history was taken from each patient about clinical symptoms, presence of cardiovascular risk factors, concomitant diseases, demographic and socio-economic data, and physical examination was performed with focus on the cardiovascular system. All patients signed an informed consent before their enrolment in the study and an approval of the study was obtained from the local ethics committee. The study was performed in accordance with the ethical standards laid down in the 1964 Declaration of Helsinki and its later amendments.

Instrumental examinations included standard 12-lead electrocardiography, X-ray, transthoracic echocardiography, coronary angiography. The laboratory examinations included full blood count, K+, Na+, high-sensitive troponin T, creatine kinase - total and MB-fraction, blood glucose, creatinine, total cholesterol, HDL- cholesterol, LDL-cholesterol and VLDL-cholesterol, triglycerides, alanine and aspartate aminotransferase.

Statistical analysis

Statistical analysis was made using SPSS (Statistical Package for the Social Sciences) 16 (IBM SPSS Statistics 16, SPSS Inc., an IBM Co., Somers, NY). The data were summarized by frequencies and percentages for the categorical variables and by a mean value ± standard deviation (minimal-maximal) for the continuous variables (a median and mode were also calculated for some of them). The methods for verification of hypotheses included: $\chi 2$-test, t-test, Shapiro-Wilk test and Fisher's exact test. Univariant logistic regression analysis was used for evaluation of the independent influence of various variables on the outcome and odds ratio (OR) for the strength of each variable. The results were considered to be statistically significant for p-value <0.05.

Results

Acute myocardial infarction with persistent ST-elevation (STEMI) was diagnosed in 344 (50.4%) - of them 231 (68.5%) were males, p<0.05 versus females. Acute myocardial infarction without ST-elevation (NSTEMI) was also more prevalent among males - 180 (59.8%) compared to females - 121 (40.2%), p<0.05. The mean age of the patients with STEMI and NSTEMI was 64.5 ± 13.7 and 69.4 ± 11.4 years respectively, p<0.0001.

Regarding the presence of the major cardiovascular RF, analyzed in our study, the results were as follows:

• Arterial hypertension - n = 589 (86.4%), of them 537 (91.2%) on regular antihypertensive treatment (combination therapy with at least 2 antihypertensive drugs from different classes – n = 486, 90.1%). Blood pressure <140/90 mm Hg was measured in 502 (85.2%) of the hypertensive patients at admittance;

• Dyslipidemia - n = 347 (50.9%), of them 107 (30.1%) being treated with lipid-lowering therapy;

• Type 2 DM - n = 171 (25.1%). Oral medication was used for glycemic control in 91 (53.2%) of the patients and 67 (39.2%) were on insulin therapy.

• Active smoking - n = 178 (26.1%), of them males - n=142 (79.8%), females - n = 36 (20.2%), p<0.05. The average number of cigarettes, smoked per day was 22.5 ± 11.5 (1-60), mean period of

smoking - 17.2 ± 7.4 (2-40) years (p = N.S. for males versus females for the daily number of cigarettes and duration of smoking).

Most of the patients - 479 (70.2%) had a combination of 2 RF. The most frequent combination was HTN plus dyslipidemia (n = 307, 64.1%).

The outcome of the patients with AMI was favourable for 567 (86.4%). In-hospital mortality was 13.6% (n=89) for the entire group: 14.1% (n=46) for STEMI and 12.7% (n = 38) for NSTEMI, p = N.S. Gender difference in mortality was present only for NSTEMI (6.8% for males versus 19.8 for females, p<0.05). The mean hospital stay of the patients who survived the acute phase of the myocardial infarction was 6.2 ± 8.8 (1-16) days, median and mode - 5.1 days. The mean period of hospital stay for STEMI was 5.9 ± 5.2 days versus 6.5 ± 11.8 days for NSTEMI, p=0.004.

The impact of the analyzed RF on the outcome after AMI is shown in table 1.

Variable	OR	95% confidence interval for OR		p
		Lower limit	Upper limit	
Arterial hypertension	3.19	1.89	5.39	<0.0001
Type 2 diabetes mellitus	2.2	1.3	3.72	0.003
Dyslipidemia	1.8	1.06	3.06	0.03
Smoking	0.35	0.17	0.73	0.005

Table 1: Impact of the analyzed risk factors on the short-term clinical outcome after acute myocardial infarction.
Univariant logistic regression analysis was used for assessment of the independent influence of the analyzed risk factors on the clinical outcome.
OR - odds ratio for unfavourable outcome (in-hospital death); p - level of significance

Discussion

In this study we found that HTN was the most common cardiovascular RF among patients with AMI, followed by dyslipidemia, active smoking and type 2 DM. The prevalence of these RF among our patients was comparable to the published data from similar studies in Europe and the Unites States[1-5, 8]. Most of our patients had at least 2 cardiovascular RF in their profile and HTN plus dyslipidemia were present in as many as 64.1% of them. This finding was important because according to our results HTN had the strongest impact for unfavourable outcome (OR = 3.2) in patients with AMI followed by type 2 DM and dyslipidemia.

Large international studies also showed that HTN, dyslipidemias, smoking (active and passive) and type 2 DM had strong influence on cardiovascular health, increasing significantly and independently the risk for major cardiovascular events such as acute coronary syndromes, stroke, etc.[1, 5, 8-15]. However, there are some controversies about the level of significance of each of these RF for the prognosis (early and late) after an overt cardiovascular event[11, 12, 16-18]. One of the possible reasons for this issue not to be fully specified so far is that these RF are often present (clustered) together in the same patients and the information from the medical history about their duration and out-hospital control - not always reliable[5, 8, 10].

Surprisingly, our results set an unexpected point of view about the influence of active smoking on the early prognosis of patients with AMI. The anticipated negative impact of this RF on the clinical outcome was not confirmed. Our analysis showed that active smoking reduced substantively pre- and in-hospital mortality of patients with AMI. According to various studies smoking was associated mostly with negative effect on cardiovascular health[13, 18-21]. Smoking - active or passive had been considered to be a very strong RF for coronary artery disease and other vascular complications[15, 18, 21]. REGICOR National survey in Spain analyzed the effect of restricting smoking in public places. The results of this study showed significant reduction in morbidity, mortality and hospitalizations for an acute myocardial infarction for a period of 3 years (2006-2008) compared to the earlier period (2002-2005) before restriction[20].

Despite the data tipping the scales toward negative impact of smoking we were not the first to describe the paradoxical lower mortality rate among smokers with acute myocardial infarction compared to non-smokers. In 2013 the results of a major survey conducted in South Korea, including >29 000 patients with AMI (42.3% of them smokers) revealed that smoking was associated with 48% reduction of mortality in the first year after a heart attack after statistical adjustment for the influence of other factors[16].

One of the possible explanations for this phenomenon according to us was the so called "ischemic preconditioning". It had been well established that carbon monoxide in tobacco smoke bound irreversibly to hemoglobin, displacing O_2[15, 18, 21]. It would lead to varying degree and duration of hypoxemia and hypoxia of tissues, including the

myocardium, particularly in the presence of haemodynamically significant coronary stenoses. The ischemic preconditioning of the myocardium in smokers could be associated with lower mortality in AMI due to a better-developed collateral coronary network (repeated myocardial ischemia was proven to be the most powerful stimulus for the development of coronary collaterals) (6, 15, 16). In addition, we found that the time interval "Onset of angina symptoms - search for medical help" in smokers, included in our study was much shorter compared to non-smokers (mean time interval 533.6 ± 110.1 min. versus 1426.6 ± 354.5 min. respectively, p = 0.004). This could additionally contribute to a lower mortality rate among smokers with AMI.

Study limitations: The number of patients, included in our study does not allow the conclusions of the results to be extrapolated over the entire population of patients with AMI. Besides, we investigated the influence of only 4 modifiable RF, but it is possible that some other common modifiable RF such as obesity, sedentary lifestyle, diet, etc. could also interfere and influence the early prognosis after AMI.

In conclusion, prevalence of HTN, dyslipidemia, type 2 DM and active smoking in patients with AMI in our study was high with HTN being the most influential RF in regard to the early post-infarction prognosis. While the first three RF were associated with increased early mortality, surprisingly active smoking reduced the risk for unfavourable outcome. The observed paradoxical "beneficial" effect of smoking on mortality reduction in the acute phase of myocardial infarction was probably due to ischemic preconditioning of the myocardium, but further clarification would be necessary by larger studies, focused on this topic.

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