Original Article

Associated influence of hypertension and heart rate greater than 80 beats per minute on mortality rate in patients with anterior wall STEMI

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Abstract: Acute myocardial infarction as a form of coronary heart disease is characterized by permanent damage/loss of anatomical and functional cardiac tissue. Diagnosis of STEMI includes data on anginal pain and persistent ST-segment elevation. According to the numerous epidemiological studies, arterial blood pressure and heart rate are often increased especially during the first hours of pain due to domination of sympathetic response. We wanted to investigate the associated influence of heart rate greater than 80 beats per minute and hypertension on the mortality in patients with anterior wall STEMI. Research included 140 patients treated in Coronary Unit, Clinical Center Kragujevac form January 2001 to June 2006. 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. Data for history of hypertension were collected and blood pressure levels were measured in a lying position after 5 minutes of rest, and classified according to the VII JNC recommendations as confirmation of hypertension. Collected data were analyzed in SPSS 13.0 for Windows. Heart rate greater than 80 bpm influences the hospital mortality. Systolic blood pressure levels were higher in the survivors, while for the diastolic there was no difference. History of hypertension was singled out as a significant predictor of mortality without difference between the respondents with heart rate greater and lower than 80 bpm in the survivors and fatal. Increased heart rate and hypertension at admission are significant predictors of mortality in patients with anterior wall STEMI.

Keywords: Heart rate greater than 80 bpm, hypertension, STEMI

Introduction

Heart rate as the most important determinant of myocardial oxygen demand and cardiac workload is playing a fundamental role in cardiac metabolic requirements. Increasing heart rate increases myocardial oxygen demand, creating an imbalance in the demand/supply ratio [1]. Until recently, the heart rate level was not considered among the numerous risk factors for cardiovascular disease, particularly for coronary artery disease, including acute myocardial infarction. Nowadays, heart rate is one of the cardiovascular parameters most accessible to the clinician at the bedside. As from a physiological point of view, reasons for the change of attitude on this issue could be found in the fact that heart rate is the main factor influencing cardiac efficacy and performance. That is why lately heart rate has been attracting more interest again [2].

Epidemiological studies have shown that heart rate is a significant risk factor for cardiovascular morbidity and mortality. However, based on previous studies, several questions have been raised concerning the association between high heart rate and cardiovascular disease. The most important question is whether the role of accelerated heart rate in cardiovascular mortality could be related to the fact that people with increased heart rate often present several other risk factors, mainly metabolic disturbances and high blood pressure. Some, but not all, studies have shown that heart rate could be related to cardiovascular diseases even after adjustment for other, more classic, risk factors. The underlying mechanisms associating heart...
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rate to cardiovascular mortality are difficult to establish, but it has been suggested that increased sympathetic activity can be the main factor in this relationship [3].

Increased heart rate tends to intensify the pulsatile nature of the arterial blood flow, thereby favoring the occurrence of injury of the arterial wall. Changes in shear stress direction would expose susceptible regions to a greater number of oscillations in flow direction over time. Moreover, increased heart rate implies an increase in total time spent on systole because of the shortening of diastolic time. The increase in arterial stress caused by increased heart rate can, thus, be also due to the higher mean blood pressure in subjects with increased heart rate [4].

Benetos A. and Bean K. found in their study that the cardiovascular risk related to the level of heart rate was linear. In 1999, they reported that after adjustment for age, systolic blood pressure, total cholesterol, smoking, body mass index, and physical activity, the increase in risk, corresponding to an increment of 20 beats per minute, was 40%, which is about the same as the risk related to an elevation of 15 to 20 mmHg in systolic blood pressure [5].

Increased activity of sympathetic system is considered to be responsible for increasing heart rate and blood pressure levels. The autonomic nervous system controls all organs and organ systems in the body through its antagonistic effects of two components: the sympathetic and parasympathetic nervous system. For most of the organs in the body, including the heart, the sympathetic nervous system acts by stimulating organ function. The increase in sympathetic stimulation leads to an increase in heart rate, cardiac output, and systemic vasoconstriction. Blood pressure and heart rate are regulated by similar mechanisms so the result of the impaired functioning of the autonomic nervous system is an increase of heart rate and the development of clinical hypertension [6, 7].

Recent analyses in cardiovascular epidemiological studies that attract more attention, are those that showed that the increased heart rate is frequently associated with high blood pressure, obesity, dislipidemia, and elevated hematocrit [8]. This fact could explain why antihypertensive treatment is not sufficiently effective in reducing cardiovascular mortality in patients with hypertension. It has been argued that the association between the above risk factors reflects persistent sympathetic stimulation and the overwhelming evidence in large proportion of hypertensive subjects showed that the majority had sympathetic overactivity, characterized by high heart rate and elevated stroke volume.

Arterial blood pressure is the final result of the multitude of complex factors: those that control the caliber of blood vessels and their response, factors influenced by volume of fluid inside and outside the vascular bed, as well as those affecting the heart minute volume [9]. Body maintains its normal blood pressure by many factors of neurohumoral system that are affecting the minute volume and peripheral vascular resistance. Changes in the function of neurohumoral system and their influence on the increase of the minute volume or peripheral vascular resistance can cause the increase of the blood pressure. The rapid heart rate can be understood as an independent factor and sign of future hypertension. People with higher heart rate have three times higher risk of hypertension compared to people with normal heart rate [10].

Materials and methods

Research 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 partly retrospective, and mostly prospective, population-type study was to determine the predictors of a bad outcome 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 autoimmune diseases; (7) Patients with thrombolytic therapy; (8) EF on admission according to Simpson greater than 35%; (9) KILLIP class I and II.

Acute myocardial infarction was diagnosed according to criteria for diagnosing acute coro-
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Table 1. Distribution of patients with anterior wall acute myocardial infarction with ST-segment elevation according to age and gender

<table>
<thead>
<tr>
<th>Patient characteristics</th>
<th>Fatal outcome</th>
<th>Significance</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>No</td>
<td>Yes</td>
</tr>
<tr>
<td>Number of patients N</td>
<td>100</td>
<td>40</td>
</tr>
<tr>
<td>Age (X±SD (Med, min-max))</td>
<td>63,02±11,34 (65,5; 27-83)</td>
<td>69,60±8,68 (70; 46-83)</td>
</tr>
<tr>
<td>Gender n (%)</td>
<td>Male – 60%</td>
<td>63 (63%)</td>
</tr>
<tr>
<td></td>
<td>Female – 40%</td>
<td>37 (37%)</td>
</tr>
<tr>
<td></td>
<td>21 (52,5%)</td>
<td>19 (47,5%)</td>
</tr>
</tbody>
</table>

*statistically significant difference; *Mann Whitney U test; χ²-test; SD-standard deviation.

ECG was analyzed daily, cardiospecific enzymes were followed (CK, AST, ALT, LDH, troponin TnI); 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.

Body mass index was calculated as the ratio of body weight in kilograms and body height in squared meters, and classified in five categories according to the WHO classification from 1998: underweight-BMI as less than 18.5 kg/m², normal-BMI as 18.5 to 24.9 kg/m², overweight-BMI as 25.0 to 29.9 kg/m², and obese-BMI greater than or equal to 30 kg/m². After classification of patients according to these guidelines we divided them in only two categories: those with normal weight (<25 kg/m²) and those with higher body weight (>25 kg/m²) [11].

Lipoprotein profile components (total cholesterol, HDL-cholesterol, LDL-cholesterol, triglycerides, atherogenic indices calculated form this parameters) were followed and classified according to the National Cholesterol Educational Program guidelines. Total cholesterol was defined as desirable (<5.2 mmol/L); borderline-high (5.2-6.2 mmol/L); and high (≥6.2 mmol/L). HDL-cholesterol as low (<1.03 mmol/L-man and <1.29 mmol/L-woman), normal (1.03/1.29-1.55 mmol/L), and high (≥1.55 mmol/L). Triglycerides as normal (<1.7 mmol/L); borderline-high (1.7-1.9 mmol/L); high (1.9-5.6 mmol/L) and very high (≥5.6 mmol/L). According to a consensus recomendations of AHA, NIH and NCEP from 2004, LDL-cholesterol levels were classified as: desirable (<2.6 mmol/L), normal (2.6-3.3 mmol/L), borderline-high (3.3-
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4.1 mmol/L, high (4.1-4.9 mmol/L) and very high (>4.9 mmol/L) [12].

Results

Mean age of patients with anterior wall STEMI in a total sample showed significant difference between survivors and respondents with the fatal outcome (Mann Whitney U test; p=0.002). Those patients who survived were significantly younger. There was no significant gender-related difference ($\chi^2$-test; p=0.252) in these two groups, although in both groups there was a slightly higher distribution of male patients (Table 1).

Heart rate on admission in patients with anterior wall STEMI was significantly different between survivors and patients with fatal outcome (Mann Whitney U test; p=0.000), with higher levels in patients with fatal outcome. Mean heart rate in these patients was 102.05±23.16 (95.5; 50-182) bpm, while 87.97±16.70 (86; 46-132) were the mean values of heart rate on admission in the survivors. According to the outcome, in the total sample, there was significant difference in the incidence of heart rate lower / greater or equal to 80 beats per minute ($\chi^2$-test; p=0.008), with 72% of respondents having the heart rate greater than 80 bpm in survivors, and 92.5% of respondents with these heart rate levels in the group of patients who died (Table 2).

Hypertension had the significant influence on mortality ($\chi^2$-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 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 (t-test; p=0.043). Mean systolic blood pressure in patients who died was 130.9±22.4 (130.0; 90-200), comparing to 139.6±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 (t-test; p=0.292). In both groups, mean diastolic blood pressure was about 85 mmHg - 87.19±1.99 (89.0; 60-130) for the subjects who survived, and 84.25±14.53 (90; 50-110) for those with fatal outcome (Table 2).

After analyzing the total number of subjects, we divided them into groups according to the heart rate levels to those with heart rate lower and those with greater than 80 beats per minute. The aim was to investigate whether we can find a difference in the association between high heart rate and high blood pressure levels.

Hypertension in patients with anterior wall STEMI and heart rate greater than 80 beats per

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**Table 2. Haemodynamic characteristics of patients with anterior wall acute myocardial infarction with ST-segment elevation who survived and those who died**

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Fatal outcome</th>
<th>Significance</th>
</tr>
</thead>
<tbody>
<tr>
<td>Heart rate on admission (X±SD (Med, min-max))</td>
<td>No</td>
<td>Yes</td>
</tr>
<tr>
<td>Heart rate ≥80 / &lt;80 bpm n (%)</td>
<td>Yes</td>
<td>72 (72.0%)</td>
</tr>
<tr>
<td>History of hypertension</td>
<td>Yes</td>
<td>68 (68.0%)</td>
</tr>
<tr>
<td>Systolic blood pressure (X±SD (Med, min-max))</td>
<td>139.6±22.64 (140.0; 90-200)</td>
<td>130.9±22.4 (130.0; 80-200)</td>
</tr>
<tr>
<td>Diastolic blood pressure (X±SD (Med, min-max))</td>
<td>87.19±1.99 (89.0; 60-130)</td>
<td>84.25±14.53 (90; 50-110)</td>
</tr>
</tbody>
</table>

*statistically significant difference; \(^* \) t-test; \(^* \) \( \chi^2 \)-test; \(^* \) Mann Whitney U test; bpm - beats per minute; SD - standard deviation.
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Univariate model singled out history of hypertension and heart rate on admission greater than 80 beats per minute as statistically significant risk factors for mortality, among other risk factors. When they were included in multivariate model, high heart rate on admission (>80 bpm) remained significant and was singled out as strong and independent risk factor with a high influence on mortality in patients with anterior wall STEMI. Hypertension lost the significance that had in the univariate model, so it can be considered as one of the most important risk factors influencing the mortality, but not the independent one as well (Table 4).

Discussion

It is familiar that the individuals with elevated heart rate are more likely to develop accelerated atherosclerosis and acute coronary syndromes, and to have higher cardiovascular mortality risk. There is a lot of evidence showing that high heart rate is very important factor influencing bad outcomes in these patients [13].

One of the most interesting aspects of recent analyses in cardiovascular epidemiological studies is the realization that the increased heart rate is frequently associated with high blood pressure, obesity, dyslipidemia, and ele-

<table>
<thead>
<tr>
<th>Table 3. Haemodynamic characteristics of patients with anterior wall acute myocardial infarction with ST-segment elevation who survived and those who died - subgroup of patients with heart rate greater than 80 beats per minute</th>
</tr>
</thead>
<tbody>
<tr>
<td>Parameters in subgroup with HR &gt; 80 bpm</td>
</tr>
<tr>
<td>No</td>
</tr>
<tr>
<td>History of hypertension on admission</td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td>Systolic blood pressure (X±SD (Med, min-max))</td>
</tr>
<tr>
<td>Diastolic blood pressure (X±SD (Med, min-max))</td>
</tr>
</tbody>
</table>

Table 4. Univariate and multivariate analysis of risk factors influencing the mortality of patients with anterior wall acute myocardial infarction with ST-segment elevation

<table>
<thead>
<tr>
<th>Risk factors</th>
<th>Univariate</th>
<th>Multivariate</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>expB (95% CI)</td>
<td>Significance</td>
</tr>
<tr>
<td>Heart rate ≥ 80 bpm</td>
<td>1.040 (1.017-1.063)</td>
<td>p=0.000*</td>
</tr>
<tr>
<td>Systolic blood pressure</td>
<td>0.994 (0.986-1.003)</td>
<td>p=0.170 / /</td>
</tr>
<tr>
<td>Diastolic blood pressure</td>
<td>0.987 (0.962-1.012)</td>
<td>p=0.291 / /</td>
</tr>
<tr>
<td>History of hypertension</td>
<td>0.304 (0.109-0.848)</td>
<td>p=0.023*</td>
</tr>
</tbody>
</table>

*statistically significant difference; χ²-test; t-test; HR–heart rate; bpm—beats per minute; SD—standard deviation.
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was more pronounced for systolic than for diastolic hypertension, and was proved in different age and gender groups [16].

This research confirmed the bigger significance of systolic than diastolic blood pressure levels. Systolic blood pressure levels on admission had statistically significant difference in the total sample of patients (t-test; p=0.043), as well as in the subgroup of patients with heart rate greater than 80 beats per minute (t-test; p=0.049). Mean systolic blood pressure in patients who died, in total group was 130.95±22.44 (130.0; 80-180), comparing to 139.60±22.64 (140.0; 90-200) in those who survived. In the subgroup with heart rate greater than 80 beats per minute higher values recorded in those who survived 139.64±22.32 (140.0; 90-190); mean systolic blood pressure in those who died was 130.54±22.99 (130.0; 80-180). In both groups we confirmed the connection between high heart rate and hypertension.

A group of researchers found that heart rate is a better indicator of coronary heart disease mortality in hypertensive than in normotensive patients. The results show that hypertensive patients with heart rate greater than 80 beats per minute are in the greater risk compared to hypertensive patients whose heart rate values were less than 60 beats per minute [17].

Clinical studies have shown that regardless of gender, age and ethnicity, there is an increased risk of overall and cardiovascular mortality with increasing resting heart rate or when heart rate exceeds 84, 90 or 100 beats per minute [18]. In this research the average heart rate in patients with anterior wall STEMI, in survivors was 87.97±16.70 beats per minute, and 102.05±23.16 beats per minute in the group of patients who died, which confirms the results in the mentioned studies. According to the data of the Institute of Public Health Kragujevac, acute anterior wall myocardial infarction with ST-segment elevation is the leading cause of hospital mortality during the five-year follow-up at the Center for Cardiology, Clinical Center Kragujevac.

Heart rate greater than 80 beats per minute was singled out as an independent predictor of hospital mortality. In patients with a fatal outcome average heart rate was 102.05±23.16
Coronary heart disease is more often in a population after the age of 60 years [20]. Results of this research confirm these evidence because the mean age of patients with anterior wall STEMI in survivors was 63.02±11.34, and 69.60±8.68 years in the group of patients with the fatal outcome. According to the Framingham study risk for the development of the coronary heart disease in man older than 40 is 48%, while for the woman of the same age risk is 31% [21]. In this study there was no statistically significant gender-related difference between the patients who survived and those who died during the research ($\chi^2$-test; $p=0.252$), but results somewhat concur with the Framingham study because in both groups there was a slightly higher distribution of males.

In population-type studies investigating the other risk factors, woman always had higher resting heart rate comparing to man of the same age and presence of the same risk factors. This gender-related difference, in range from 3 to 7 beats per minute, is present in both developed and developing countries, all ages and according to some, but not all studies, it increases with aging [6]. In this research the gender-related difference in heart rate levels was lost in both, survivors and patients with the fatal outcome as a result of higher mean age of patients with anterior wall STEMI, and a higher prevalence of male patients in the research.

Systolic Hypertension in Europe (Syst-Eur) followed over 4500 elderly hypertensive patients with no treatment. Systolic blood pressure on admission was 160-219 mmHg and diastolic <95 mmHg. Analyse of the group with placebo revealed that people with heart rate on admission greater than 79 bpm have twofold higher risk for total, cardiovascular and non-cardiovascular mortality comparing to those with the lower levels [23].

People with high heart rate develop hypertension more often. Italian TensioPulse Study investigated association between heart rate and other cardiovascular risk factors in 38000 hypertensive patients, and found the significant link between high heart rate and higher systolic and diastolic blood pressure in both, male and female. Large French study analysed data bases and found that patients with higher
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Heart rate (>85 bpm) have higher systolic blood pressure for 12 mmHg, and diastolic for 7 mmHg, comparing to those with lowest heart rate (<65 bpm) [24]. This research confirmed the higher significance of elevated systolic than diastolic blood pressure, and the connection of this parameter with high heart rate.

Diastolic blood pressure levels in this study wasn’t significantly different according to mortality in the subgroup (t-test; p=0,322). Both groups had mean values of diastolic blood pressure of about 85 mmHg (87,15±14,81 (90,0; 60-120) – survivors; 84,19±14,51 (90; 50-110) – fatals). According to the results of the Framingham study in elderly patients (>65 years) the most important predictor of risk for coronary heart disease was pulse pressure, than systolic blood pressure, and diastolic blood pressure was not proportional to the risk for coronary heart disease [25]. This was also confirmed in this study where the mean age of patients was 69,6 years, and they also had bigger significance of systolic than diastolic blood pressure levels. Systolic blood pressure levels on admission were higher in those who survived 139,64±22,32 (140,0; 90-190). Mean systolic blood pressure in those who died was 130,54±22,99 (130,0; 80-180).

In one study with the elderly patients treated from isolated systolic hypertension, heart rate greater than 79 beats per minute was significant, independent predictor for total and cardiovascular mortality with 1.89 higher mortality risk which was also confirmed in this research [24].

Some epidemiologic studies found that the borderline or persistent hypertension is always associated with significant elevation of heart rate, and this remained significant after the adjustment of several other risk factors like body mass index, age and metabolic parameters. The link was found in different age groups and in both genders [3].

Great French study confirmed the significant association between high heart rate and high blood pressure. Non-treated hypertensive patients had in average 6 beats per minute higher heart rate comparing to normotensive patients. Association between these parameters was independent of age showing that the link doesn’t just exist in younger patients with hyperdynamic circulation, as it was thought, it exists in elderly also, which was also confirmed with this research where the heart rate on admission greater than 80 bpm was associated with higher incidence of hypertension in the elderly patients [15].

During the 1945, in American soldiers, team of researchers found that the transient tachycardia was a predictor of future hypertension. Several other studies confirmed these findings. Younger individuals with normal blood pressure levels, but with positive family history for hypertension have higher heart rate and the greater risk for developing hypertension themselves later comparing to individuals with no family history for hypertension [26].

History of prior hypertension in patients with anterior wall STEMI and heart rate greater than 80 beats per minute was more often present in those who died comparing to survivors, but without significant statistical difference (χ²-test; p=0,069). In this subgroup of patients hypertension was present on admission, according to anamnestic data, in 70,8% of patients who survived, and in 86,5% of those who died during the research.

Conclusions

Hypertension and high heart rate are both major risk factors for acute myocardial infarction. Heart rate greater than 80 beats per minute has a significant influence on mortality in patients with anterior wall STEMI. Patients with anterior wall STEMI elevation and heart rate greater than 80 beats per minute have higher levels of systolic blood pressure in the group of survivors with no difference between the groups in levels of diastolic blood pressure. History of hypertension had no statistically significant difference between patients with anterior wall STEMI who survived and those who died in the subgroup with heart rate greater than 80 beats per minute like in the total number of respondents, but still represents one of the major and important risk factors.

Conflict of interest

None.

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References


