ARTYKUŁ ORYGINALNY / ORIGINAL ARTICLE

The relationship between admission heart rate and early prognosis in patients with ST-elevation myocardial infarction

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Abstract

Background: Heart rate (HR) is a basic cardiovascular parameter. The relationship between HR and cardiovascular mortality and morbidity has been indicated in clinical trials and epidemiological studies.

Aim: The evaluation of the relationship between HR upon hospital admission and the in-hospital prognosis in a group of patients with ST-elevation myocardial infarction (STEMI).

Methods: The medical records of 927 patients were subject to retrospective analysis. The patients were classified on the basis of HR upon hospital admission: < 60 bpm (n = 75), 60–69 bpm (n = 169), 70–79 bpm (n = 245), 80–89 bpm (n = 172), 90–99 bpm (n = 134), and ≥ 100 bpm (n = 132). A group of patients with HR of 60–69 bpm on hospital admission (n = 169) constituted a reference group. Patients with atrioventricular blocks and arrhythmias were excluded from the analysis. Early mortality and co-existing diseases were evaluated in the study population.

Results: Patients with HR ≥ 90 bpm demonstrated heart failure symptoms considerably more often than patients with HR of 60–69 bpm (p = 0.0010). In-hospital mortality was significantly higher in patients with a HR of more than 90 bpm and bradycardia. The relationship between HR and cardiovascular mortality is shown with a J-shaped curve.

Conclusions: HR is strictly correlated with early cardiovascular mortality in a population of patients with STEMI. The relationship between HR and early mortality is demonstrated by a J-shaped curve.

Key words: heart rate, ST-elevation myocardial infarction, early mortality, J-curve

Kardiol Pol 2015; 73, 3: 177–182

INTRODUCTION

Resting heart rate (HR) is one of the basic cardiovascular (CV) parameters that can be easily measured. A normal HR ranges from 60 to 100 bpm. It is regulated by the activity of the autonomic nervous system with the involvement of nitric dioxide as one of the transmitters [1]. Some available data provides evidence that resting HR can also be influenced by genetic factors [2]. Previous studies have revealed that increased HR, even within the normal range, is related to increased CV risk. The impact of HR on CV outcome was evaluated both in a healthy population and in a group of patients with stable coronary artery disease (CAD), acute coronary syndrome (ACS), and heart failure (HF) [3–5]. Therefore, reduction of HR is one of the therapeutic goals in patients with CAD or HF. Owing to the fact that a cutoff value for HR, above which CV risk is significantly increased, has not yet been established due to insufficient evidence, a clearly defined therapeutic goal has also not been determined. The objective of the present study was to evaluate the impact of HR upon the admission to hospital on the early prognosis among patients with ST elevation myocardial infarction (STEMI).

METHODS

A retrospective analysis of the medical records of 927 consecutive STEMI patients hospitalised in the Clinical Department of Cardiology in the years 2008–2009 was carried out.

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Received: 28.08.2014   Accepted: 12.06.2014   Available as AoP: 21.08.2014

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The patients were classified on the basis of HR upon hospital admission: < 60 bpm (75 patients), 60–69 bpm (169 patients), 70–79 bpm (245 patients), 80–89 bpm (172 patients), 90–99 bpm (134 patients), and ≥ 100 bpm (132 patients). A group of patients with HR of 60–69 bpm upon hospital admission (n = 169) constituted a reference group. This particular range was determined on the basis of the standard definition of a normal HR (lower limit) as well as clinical studies that revealed the increase of CV risk at HR value above 70 bpm (upper limit). Patients with second- or third-degree atrioventricular block and those with supraventricular or ventricular arrhythmias were excluded from the analysis. The occurrence of dyslipidaemias, excessive body weight, nicotine abuse, and diabetes were evaluated in the study population. The diagnosis and treatment of STEMI were determined according to European Society of Cardiology STEMI Guidelines [6]. Hypertension was diagnosed on the basis of two blood pressure measurements taken during the two days following therapy for hypertension in anamnesis. Excessive body weight was defined as follows: overweight — body mass index (BMI) 25.0–29.99 kg/m² and obesity — BMI > 30 kg/m². Glomerular filtration rate (GFR) was estimated with the Modification of Diet in Renal Disease (MDRD) formula. A cutoff value for impaired filtration was set on the clinical symptoms with the presence of abnormalities without any known reason. The definition of HF was based on the clinical symptoms with the presence of abnormalities in clinical examination and echocardiography. For the purpose of the study, HR values were obtained in 12-lead electrocardiography performed upon hospital admission.

**Statistical analysis**
Continuous data is presented as a mean ± standard deviation, whereas categorical data is demonstrated in the form of percentages and frequencies. Differences in baseline characteristics between subgroups were evaluated with the χ² test where applicable. Multivariate analysis was performed to evaluate the relationship between HR upon hospital admission and in-hospital mortality. The parameters used in the multivariate analysis were established taking into account their univariate statistical significance and clinical judgement. Age, impaired GFR, and hypertension were taken into account in the multivariate analysis. Receiver operating characteristic (ROC) analysis was performed to indicate HR values which constitute curve inflection points for increased CV mortality. All statistical tests were two-sided. P < 0.05 was considered to be statistically significant. Statistical analyses were performed with MedCalc software (ver.12.4.0.0 MedCalc Software, Ostend, Belgium).

**RESULTS**
The study group consisted of 927 patients (624 men; 67%). The mean age was 65.1 ± 12.1 years. No statistically significant differences have been reported in relation to the patients’ age or gender between the subgroups. The mean time of hospitalisation was 8.4 ± 5 days. The basic characteristics of the study group are presented in Table 1. The left ventricular ejection fraction (LVEF) was significantly lower only in the group of patients with HR ≥ 100 bpm (p = 0.0012). Cardiogenic shock occurred more frequently in the group of patients with tachycardia (HR ≥ 100 bpm); p = 0.021. Bradycardia (HR < 60 bpm) occurred in 75 (8.1%) patients and tachycardia (HR ≥ 100 bpm) in 132 (14.2%) patients. Heart failure symptoms occurred least often in the group of patients with HR 60–69 bpm. The occurrence of these symptoms significantly increased when the HR rose to the value of 90 bpm or above (p = 0.001) (Fig. 1). Nonetheless, the occurrence of HF did not correlate with increased CV death frequency (p = 0.72) in the multivariate analysis. The occurrence of hypertension in the study population was at the level of 68% and was similar across the examined subgroups: < 60 bpm (45 patients, 60%), 60–69 bpm (111 patients, 66%); 70–79 bpm (178 patients, 72.7%); 80–89 bpm (109 patients, 63.3%); 90–99 bpm (93 patients, 69%); and ≥ 100 bpm (95 patients, 72%), p = NS. In the multivariate analysis the occurrence of hypertension was related to the lower CV mortality in the course of STEMI (odds ratio [OR] 0.42, 95% confidence interval [CI] 0.24–0.73). The number of occurrences of past MI or stroke in the examined subgroups was similar. No differences were observed in terms of the frequency of dyslipidaemias, diabetes, smoking, abnormal body weight, or impaired renal function. In-hospital mortality was significantly higher in the group of patients with bradycardia and in those with HR over 90 bpm. In-hospital mortality in the study subpopulations was as follows: < 60 bpm (8 patients, 10.6%), p = 0.0397; 60–69 bpm (6 patients, 3.6%); 70–79 bpm (10 patients, 4.1%), p = 0.79; 80–89 bpm (15 patients, 8.7%), p = 0.062; 90–99 bpm (21 patients, 15.7%), p = 0.0008; and ≥ 100 bpm (31 patients, 23.5%), p < 0.0001 (Fig. 2). The multivariate analysis after taking into consideration factors such as age, hypertension, and impaired renal function, showed that HR constituted an independent risk factor for in-hospital CV death (OR 1.51, 95% CI 1.25–1.82). Cardiovascular mortality in the study population was shown with a J-curve with the lowest mortality in the reference group (HR 60–69 bpm), and showed a tendency to rise towards both the lower and higher values of HR. ROC analysis was performed to determine the HR values that indicate the inflection points on that curve. In the group with higher HR, a significant increase in CV death was observed at HR > 88 bpm, while in the group of patients with bradycardia the same phenomenon was noticed at HR values below 41 bpm. In-hospital mortality was the lowest in patients with HR 60–69 bpm and with nadir 61 bpm.
The relationship between admission heart rate and early prognosis in patients with STEMI

DISCUSSION

The impact of increased HR on the pathophysiology of CAD is related to the basic metabolism of cardiomyocytes. Myocardium is provided with oxygen mainly during the diastole phase (up to 80%). The increase of HR leads both to augmented oxygen demand and the reduction of its supply caused by the reduction of diastole duration. Moreover, the increased HR in CAD patients may also result in coronary vasoconstriction, leading to the impairment of additional oxygen supply [7]. Consequently, CAD patients may develop angina symptoms. It is also possible that the mechanism of exacerbated ischaemia is responsible for the extension of infarction. Previous observations demonstrated that the incidence of ischaemic episodes in a group of patients with HR > 80 bpm was twice as high as that among patients with HR values below 70 bpm [8]. The increased HR is also related to atherosclerosis progression and may cause rupture of unstable atherosclerotic plaque, which can lead to MI [9]. Davidovic et al. [9] performed a follow-up

Table 1. Basic characteristics of the study population

<table>
<thead>
<tr>
<th>HR (bpm)</th>
<th>n</th>
<th>Age Mean ± SD</th>
<th>Male gender</th>
<th>Diabetic</th>
<th>GFR ≤ 60 ml/min</th>
<th>Hypertension</th>
<th>Smokers</th>
<th>BMI &gt; 25 kg/m²</th>
<th>Dyslipidaemia</th>
<th>Heart failure</th>
<th>Ejection fraction</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt; 60</td>
<td>75</td>
<td>65.12 ± 10.52</td>
<td>57 (76%)</td>
<td>51 (68%)</td>
<td>15 (20%)</td>
<td>45 (60%)</td>
<td>39 (52%)</td>
<td>24 (32%)</td>
<td>41 (55%)</td>
<td>24 (32%)</td>
<td>46.86 ± 10.51</td>
</tr>
<tr>
<td>60–69</td>
<td>169</td>
<td>63.73 ± 11.99</td>
<td>123 (71%)</td>
<td>97 (58%)</td>
<td>26 (15%)</td>
<td>61 (35%)</td>
<td>50 (29%)</td>
<td>27 (16%)</td>
<td>35 (21%)</td>
<td>27 (16%)</td>
<td>42.53 ± 11.50</td>
</tr>
<tr>
<td>70–79</td>
<td>245</td>
<td>65.23 ± 12.40</td>
<td>173 (73%)</td>
<td>131 (53%)</td>
<td>34 (14%)</td>
<td>84 (34%)</td>
<td>52 (21%)</td>
<td>37 (15%)</td>
<td>41 (17%)</td>
<td>37 (15%)</td>
<td>40.35 ± 11.60</td>
</tr>
<tr>
<td>80–89</td>
<td>172</td>
<td>66.85 ± 13.39</td>
<td>110 (64%)</td>
<td>108 (62%)</td>
<td>30 (22%)</td>
<td>74 (43%)</td>
<td>50 (29%)</td>
<td>25 (14%)</td>
<td>47 (27%)</td>
<td>25 (14%)</td>
<td>39.45 ± 11.70</td>
</tr>
<tr>
<td>≥ 90</td>
<td>132</td>
<td>65.44 ± 12.02</td>
<td>86 (65%)</td>
<td>78 (60%)</td>
<td>35 (26.3%)</td>
<td>68 (51%)</td>
<td>52 (39%)</td>
<td>25 (19%)</td>
<td>45 (34%)</td>
<td>25 (19%)</td>
<td>34.26 ± 11.85</td>
</tr>
</tbody>
</table>

All p values refer to heart rate (HR) 60–69 bpm group; p-value for HR > 90 bpm group; BMI — body mass index; GFR — glomerular filtration rate.
of 140 patients with anterior wall STEMI. The multivariate analysis showed that only HR > 80 bpm and decreased level of HDL cholesterol counted as independent factors related to fatal outcome. A similar relationship was also observed among the participants of the PAMISCA study [10]. A group of 1,054 patients with ACS was subject to analysis (43.5% with ST segment elevation and 56.5% without it). The authors of the study provided evidence that a group of patients with HR ≥ 70 bpm after ACS had higher CV and non-CV mortality rates. These patients were hospitalised due to HF more often than patients with HR < 70 bpm. The benefits of decreased HR were also demonstrated in a population with stable CAD and impaired LV systolic function who received ivabradine, a HR lowering agent, in the BEAUTIFUL study [11]. The results showed that patients with HR ≥ 70 bpm had a higher risk of CV death hospitalisation due to congestive HF than patients with HR < 70 bpm. The advantages of HR decrease caused by beta-blockers and calcium channel blockers were presented in a meta-regression of 14 randomised clinical trials performed by Cucherat [12]. In these studies a correlation between the use of HR lowering agents and the reduction of all-cause and CV mortality as well as the recurrence of non-fatal MI were observed. The meta-regression performed by the author implies that the main advantages in these trials resulted from the lowering of HR.

The above-mentioned studies describe a linear correlation between HR and increased CV risk. Contrary to that pattern, a non-linear model of the relationship between resting HR and CV risk was observed in the INVEST study [13]. The presented results show that the correlation between resting HR is a J-shaped relationship with nadir at 59 bpm for the entire study population. The results obtained for the last subgroup of the INVEST trial are similar to those obtained in the present study, i.e. the increased HR and bradycardia were related to the increased early CV mortality, which was demonstrated with a J-curve with nadir at 61 bpm. Parodi et al. [14] performed a six-month follow-up on a group of 2,477 STEMI patients. Cox analysis revealed that age, peak creatine-kinase, the occurrence of cardiogenic shock, a suboptimal percutaneous coronary intervention (PCI) result, previous MI, and HR > 80 bpm were predictors for six-month death in the study population. Higher mortality in a group with HR < 60 bpm was also observed. It should be noted that the number of patients with low HR during our follow-up was relatively small, which means that the correlation of bradycardia and CV mortality requires further studies with the participation of a larger population of patients. Higher mortality in the group with low HR can also be attributed to a pre-agonal state manifested through decreased HR. Antoni et al. [15] analysed the relationship between discharge HR and mortality among 1,453 patients with STEMI undergoing primary PCI. In the study group HR at discharge was a predictor for all-cause and CV mortality after four-year follow-up. The authors noticed that the difference between admission and HR on discharge was not related to all-cause or CV mortality.

A J-curve relationship between HR and the CV outcome was also described by Bangalore et al. [16] in an analysis of the association of HR on admission to hospital and in-hospital CV events among participants of the CRUSADE initiative. The authors analysed 135,164 medical records of patients with non-ST elevation ACS. Bradycardia and elevated HR were associated with an increase in all-cause mortality and a higher incidence of stroke.

HR on hospital admission is a factor that is also used in risk stratification in the course of ACS on the GRACE scale [17]. This model assumes a risk increase of 30% for every HR increase of 30 bpm (adjusted hazard ratio 1.30, 95% CI 1.23–1.47). The above-mentioned J-shaped relationship between HR and the outcome of ACS may lead to the conclusion that the use of GRACE score for risk evaluation may not be adequate in a population of patients with ACS and bradycardia. In contrast, the occurrence of both tachycardia and decreased HR was identified as a predictor for increased early CV mortality in the ACC/AHA guidelines for the management of patients with unstable angina/non-ST-elevation myocardial infarction [18].

In the present study the occurrence of HF symptoms was observed significantly more often among patients with elevated resting HR. Similar outcomes were presented by Mulder et al. [19], who used a murine model of HF to demonstrate that decreased resting HR results in improved LV systolic function and increased stroke volume. In the SHIFT trial a better outcome in a population of patients with HF was observed among patients whose HR decreased to a value below 70 bpm after the administration of ivabradine, a selective HR reducing agent [20]. In this group CV death or rehospitalisation due to the exacerbation of HF occurred less frequently than in patients with a higher HR value. The pathophysiology of a worse outcome in the population with HF and tachycardia is related to the limited oxygen consumption due to the shortened diastole, which leads to impaired coronary blood flow. The elevated HR is also linked to the decrease of myocardial contractile function in the course of HF. Such a relationship was also demonstrated in experimental studies [21].

In the present study the elevated blood pressure in the acute phase of MI was related to lower CV mortality (OR 0.42, 95% CI 0.24–0.73). A similar result was obtained in the Registry of Information and Knowledge About Swedish Heart Intensive Care Admissions (RIKS-HIA) — the elevated blood pressure in patients with ACS was related to better outcome [22]. Abridgnani et al. [23] showed that complications of MI, such as intraventricular conduction disturbances, cardiogenic shock, ventricular fibrillation, and rupture of free myocardium wall, were significantly more frequent in a population of patients with normal blood pressure than in...
those with elevated blood pressure in the course of MI. Also, higher in-hospital mortality was reported in the first group.

The above presented circumstances led to the conclusion that the key value for preserved myocardium function is a proper oxygen supply maintained through optimal HR or higher blood pressure compensating for impaired perfusion.

**Limitations of the study**

All participants of the present study received proper pharmacotherapy in accordance with actual guidelines (including beta-blockers). Nonetheless, the administration of beta-blockers prior to admission to hospital (which could affect HR upon admission) was not taken into account due to the retrospective character of the analysis. The HR values during hospitalisation were not analysed for the same reason.

**CONCLUSIONS**

1. Admission HR is correlated with in-hospital CV mortality in STEMI patients.
2. The relationship between HR and early mortality is demonstrated by the J-shaped curve.

**Conflict of interest:** none declared

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Wpływ częstotliwości rytmu serca przy przyjęciu do szpitala na rokowanie wczesne u chorych z zawałem serca z uniesieniem odcinka ST

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Streszczenie

Wstęp: Częstotliwość rytmu to łatwy w ocenie parametr o potwierdzonym w wielu badaniach wpływie na śmiertelność i chorobowość z przyczyn sercowo-naczyniowych.

Cel: Celem badania była ocena wpływu częstotliwości rytmu serca przy przyjęciu do szpitala na rokowanie wczesne u pacjentów z zawałem serca z uniesieniem odcinka ST (STEMI) z uwzględnieniem czynników ryzyka sercowo-naczyniowego oraz chorób współistniejących.

Metody: Analizą objęto 927 (67% stanowili mężczyźni) osób hospitalizowanych z powodu STEMI. Chorych podzielono ze względu na częstotliwość rytmu serca przy przyjęciu na grupy: < 60/min (n = 75), 60–69/min (n = 169), 70–79/min (n = 245), 80–89/min (n = 172), 90–99/min (n = 134) i ≥ 100/min (n = 132). Odniesienie stanowiła grupa o częstotliwości rytmu 60–69/min przy przyjęciu. Z analizy zostali wyłączeni chorzy z zaawansowanymi zaburzeniami rytmu i przewodzenia.

Wyniki: Pacjenci z częstotliwością rytmu serca ≥ 90/min istotnie częściej prezentowali objawy niewydolności serca w porównaniu z osobami z częstotliwością rytmu 60–69/min (p = 0,0010). Śmiertelność wewnątrzszpitalna była istotnie statystycznie wyższa w grupach: z częstotliwością rytmu > 90/min i u chorych z bradykardią. Związek między częstotliwością rytmu przy przyjęciu a wcześną śmiertelnością z przyczyn sercowo-naczyniowych przyjmuje kształt krzywej J.

Wnioski: Tachykardia wiąże się z częstszym występowaniem objawów niewydolności serca. Przyspieszona czynność serca przy przyjęciu pogarsza rokowanie wczesne u chorych ze STEMI. Zależność ta przyjmuje kształt krzywej J.

Słowa kluczowe: częstotliwość rytmu, zawał serca z uniesieniem odcinka ST, rokowanie wczesne, śmiertelność

Kardiol Pol 2015; 73, 3: 177–182