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ARTYKUŁ ORYGINALNY / *ORIGINAL ARTICLE*

Heart rate and the use of beta-blockers in stable outpatients with coronary artery disease: Polish baseline results of the CLARIFY registry

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Abstract

Background: Heart rate (HR) is an important risk factor in coronary artery disease (CAD). However, there is little contemporary data on HR and the use of HR-lowering medications, particularly beta-blockers, among patients with stable CAD in routine clinical practice.

Aim: To describe HR in the Polish population of the CLARIFY registry, overall and in relation to beta-blocker use, and to assess the determinants of HR.

Methods and results: CLARIFY is an international, prospective, observational, longitudinal registry of outpatients with stable CAD, defined as either prior myocardial infarction or revascularisation procedure, or evidence of coronary stenosis of at least 50%, or chest pain associated with proven myocardial ischaemia. A total of 33,438 patients from 45 countries in Europe, the Americas, Africa, the Middle East, and Asia/Pacific were enrolled between November 2009 and July 2010. In Poland, 1,004 patients were enrolled between February and June 2010, which was the largest population among countries from Eastern Europe. Most patients were men (72.8%). Mean ± standard deviation age was 62.1 ± 9.1 years. HR determined by pulse was 69.3 ± 9.4 bpm and by electrocardiogram was 68.2 ± 10.6 bpm. Beta-blockers were used in 89.9% of patients. Resting HR ≥ 70 bpm was noted in 49.3% of all patients and in 48.6% of patients on beta-blockers. Resting HR ≥ 70 bpm was significantly more frequent among younger patients, and in those with diabetes, those being treated for arterial hypertension, and who lacked regular physical activity. Patients with HR ≥ 70 bpm at rest had more frequent symptoms of angina and more frequently needed hospitalisation due to heart failure.

Conclusions: Despite a very high rate of beta-blocker use, almost 50% of patients with stable CAD had a resting HR ≥ 70 bpm, which was associated with more frequent angina and ischaemia. Further HR lowering is possible in many patients with CAD. Whether or not this will improve symptoms and outcomes is under investigation.

Key words: heart rate, coronary artery disease, beta-blockers

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INTRODUCTION

Coronary artery disease (CAD) is a leading cause of death in Poland and worldwide [1, 2]. It is estimated that of each 1,000 inhabitants of European countries, 20–40 suffer from stable CAD. We still lack data on clinical characteristics and management of outpatients with stable CAD. Most contemporary data comes from studies evaluating patients from Europe or North America with acute coronary syndromes or who are treated with percutaneous coronary intervention (PCI).

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The prospective observational longitudinal registry of patients with stable coronary artery disease (CLARIFY) study is a registry created to improve our knowledge about patients with stable CAD from a global perspective [3]. The main issue was to define the demographic characteristics, clinical profiles, the implementation of the guidelines, and the long-term prognostic determinants in this group of patients. The very same objectives were pursued in the Polish population.

Heart rate (HR) is one of the determinants of myocardial ischaemia and a well-established prognostic factor in patients with CAD [4–7] or congestive heart failure [8]. HR is also a predictor of the future occurrence of an acute coronary event [4, 9]. The clinical benefits of HR-lowering agents, especially beta-blockers, are well known, particularly in patients with a history of myocardial infarction (MI) [10].

Beta-blockers have an impact on several mechanisms of the heart's work, and they are not only HR lowering agents. However, recent data from the BEAUTIFUL trial indicates that decreasing HR using a pure HR-lowering agent, ivabradine, is associated with the prevention of angina, reduction of myocardial ischaemia, and may prevent acute coronary events [11, 12]. Yet little is known about the HR actually achieved in real clinical practice, including in patients treated with HR-lowering agents.

The main objective of this analysis was to describe the Polish population of the CLARIFY registry, particularly the HR actually achieved, determinants of higher HR, the relationship between HR and the use of beta-blockers, and the incidence of important clinical symptoms like angina or heart failure.

METHODS

CLARIFY is an ongoing, international, prospective, observational, longitudinal cohort study in stable CAD outpatients with a five-year follow-up. Patients were enrolled in 45 countries in Africa, Asia, Australia, Europe, and North and South America. Patients are treated according to usual clinical practice, with no specific tests or therapies defined by the study protocol. In Eastern Europe, 3,009 patients were enrolled in nine countries, at 229 study sites.

Study population

The inclusion criterion was a history of stable CAD, defined as at least one of the following: documented MI or coronary revascularisation (PCI or coronary artery bypass graft surgery [CABG]) > three months earlier, coronary stenosis > 50% in coronary angiography or chest pain with proven myocardial ischaemia in noninvasive stress tests (electrocardiography [ECG], echocardiography, or myocardial imaging). The exclusion criteria were hospitalisation within the last three months for cardiovascular reasons (including revascularisation), planned revascularisation, or conditions that may hamper participation in the five-year follow-up (limited co-operation or legal capacity, serious non-cardiovascular disease, limited life expectancy, severe cardiovascular diseases such as advanced heart failure, valve disease, or a history of valve repair/replacement).

Site selection

The main assumption of the study was that enrolled patients corresponded to a real epidemiological pattern in each participating country. The chosen physicians (cardiologists, internists, and primary care physicians) enrolled, over a short period of time so as to avoid selection bias, 10–15 consecutive patients who met the inclusion criteria and to whom the exclusion criteria were not applicable. The goal was to enroll 25 (12.5–50) patients per 1,000,000 inhabitants to ensure a balanced representation of each country. The assumed number of enrolled patients was exactly achieved in Poland.

Baseline evaluation and data management

Data collected at baseline included demographics, medical history, risk factors, lifestyle, and current symptoms. Patients were examined and HR was determined both by pulse palpation and most recent ECG (performed within the last six months). Blood test results (e.g. haemoglobin, fasting glucose, haemoglobin A1c, creatinine, cholesterol, triglycerides) and current chronic medical treatment (drugs taken regularly more than seven days before entering the study) were also recorded.

A standardised, international, electronic case report form translated into the local language was used for data collection. It was sent electronically to the data management centre where completeness, internal consistency, and accuracy were checked.

Statistical analysis

All data is collected and analysed at the Robertson Centre for Biostatistics, University of Glasgow, UK, which is responsible for managing the database, performing all analyses, and storing the data according to regulations. Baseline variables are summarised as mean and standard deviation (SD), or median, lower and upper quartiles for continuous data depending on the distribution of the data; and as counts and percentages for categorical data. Differences between the groups were tested using one-way analysis of variance (ANOVA), or Kruskal-Wallis test for continuous variables, again depending on the distribution of the data, and Pearson's χ^2 test or Fisher's exact test for categorical variables. A multivariable analysis of independent correlates of HR ≥ 70 bpm was performed using a logistic regression model. The cut-off value of 70 bpm was selected based on the results of several studies showing that this is an important prognostic threshold across a variety of patient populations [11, 13–16]. All clinical baseline variables were considered for entry into the model as predictors of HR ≥ 70 bpm and univariate models for each were produced. The use of HR-lowering medications was considered to be the most important treatment variable, and so this was the only treatment predictor entered in the analyses. The

multivariable model was then built using a stepwise selection method applied to the remaining significant univariate predictors, with the use of HR-lowering medications being forced into the model.

RESULTS

A total of 1,004 patients were screened and then enrolled by 79 investigators in Poland between 25 February and 29 June 2010. This was the largest population of any of the Eastern European countries. All the patients were available for analysis.

Mean ± SD age was 62.1 ± 9.1 years and most of the patients were men (72.8%). The median time since first diagnosis of CAD was six years (IQR 2–10 years). 66.8% of patients had a history of MI, 60.6% had a PCI, and 25.7% a CABG. 30.3% of the patients had angina symptoms. Coronary angiography had been performed in 81% of the patients and 73.8% had undergone noninvasive testing for ischaemia. HR measured by pulse palpation (mean [SD] HR 69.3 [9.4] bpm) was highly correlated with HR measured by ECG (68.2 [10.6] bpm) (Pearson correlation coefficient 0.79, $p < 0.0001$).

Patients were divided into three categories according to baseline pulse palpation HR at rest: ≤ 60 bpm (218, 21.7%), 61–69 bpm (291, 29.0%), and ≥ 70 bpm (495, 49.3%). Resting HR ≥ 70 bpm was significantly more frequent among younger patients, in those with a history of diabetes, treated arterial hypertension, no or light regular physical activity, and higher body mass index. Patients with a higher HR had more frequent angina symptoms, lower left ventricular ejection fraction, and more often were admitted to hospital due to heart failure. Additionally, they less frequently had stenosis > 50% of the right coronary artery, or a sinus rhythm identified in ECG, and less frequently underwent noninvasive testing for myocardial ischaemia. They also had higher blood pressure (both systolic and diastolic). Patients with low HR (≤ 60 bpm) had lower fasting triglycerides and higher high-density lipoprotein. There was no significant association between HR and gender, history of MI, invasive treatment (CABG or PCI), or time since the first CAD diagnosis. The most important characteristics of clinical and laboratory parameters according to HR are shown in Table 1.

Overall, 89.9% of patients were treated with beta-blockers (any one at any dose), 95.1% with acetylsalicylic acid, 12.7% with thienopyridines, and 95.8% with lipid-lowering agents. Other HR-lowering agents like ivabradine (4.5%), diltiazem or verapamil (4.9%), amiodarone/dronedarone (0.9%), and digoxin or derivatives (0.9%) were used less often. Patients treated with ivabradine had higher HR, but there were no significant differences in the proportions of higher HR in subgroups treated with other HR-lowering agents (including beta-blockers). Additionally, patients with higher HR were treated more often with oral anticoagulants, antidiabetic agents, and proton pump inhibitors. The median number of HR-lowering agents was one in the whole population and in each HR subgroup. The most important medications according to HR are shown in Table 2.

The entire population was also divided into two groups according to treatment with beta-blockers. Men, patients with a history of treated hypertension, prior MI, or CABG were significantly more frequently treated with beta-blockers, in contrast to patients with peripheral artery disease, carotid disease, and asthma/chronic obstructive pulmonary disease, where beta-blockers were used significantly less often.

Patients treated with beta-blockers had higher body mass index, greater waist circumference, and lower left ventricular ejection fraction. Mean (SD) HR assessed by palpation or ECG was lower in the beta-blocker group (69.1 [9.1] vs. 71.4 [11.5] and 67.9 [10.3] vs. 70.7 [12.6], respectively), but there was no significant difference in the proportion of patients with HR ≥ 70 bpm (48.6% vs. 55.4%, $p = 0.19$) despite the use of these agents. Also there were no differences in the usage of beta-blocker according to age or history of PCI (Table 3).

Patients treated with beta-blockers more frequently received acetylsalicylic acid and angiotensin-converting enzyme inhibitors, in contrast to ivabradine and verapamil or diltiazem, which were used less often (Table 3).

Multivariable logistic regression analysis indicated that elevated systolic blood pressure, full reimbursement of cardiovascular agents and diabetes were significantly associated with higher HR, in contrast to increasing physical activity, noninvasive testing for myocardial ischaemia, or stenosis > 50% of the right coronary artery, which had a protective effect. Social factors were independent correlates of HR as well. Patients unable to work had a higher HR than those who were employed full time (Table 4). Also it turns out that not taking HR-lowering agents is not significantly associated with a higher HR after adjustment for these other variables.

DISCUSSION

The CLARIFY registry offers a unique opportunity for very detailed information on the determinants of higher HR in stable CAD patients in Poland and also all over the world. Despite the proven prognostic importance of HR and the threshold ≥ 70 bpm in patients with CAD or heart failure [4–9], these determinants are still poorly defined.

Overall, almost half of patients with stable CAD had resting HR ≥ 70 bpm and only about 20% had HR ≤ 60 bpm, which is the guidelines-recommended target for HR in patients with angina on beta-blockers [17]. Due to the very high beta-blocker use (about 90%), similar to that seen in a previous Polish RECENT study [18], the proportions of beta-blocker-treated patients in various HR categories were nearly the same. These findings are also consistent with results from the EuroHeart Survey on angina in which 19% of patients had HR ≤ 62 bpm [19] and with the overall results of the CLARIFY registry where half of the population had an HR ≥ 70 bpm and only 28% of patients had HR ≤ 60 bpm [20].

Table 1. The most significant characteristics of the Polish population classified according to resting heart rate

Parameter	No. of patients	Population	Total (n = 1,004)	HR ≤ 60 bpm (n = 218)	HR 61–69 bpm (n = 291)	HR ≥ 70 bpm (n = 495)	P
Age	1,004	Mean (SD)	62.1 (9.1)	63.5 (9.7)	61.9 (8.9)	61.63 (8.9)	0.0368
Gender	1,004	Male	731 (72.8)	157 (72.0)	216 (74.2)	358 (72.3)	0.8092
Body mass index	1,004	Median [Q1, Q3]	28.4 [25.9, 30.9]	27.9 [25.7, 30.4]	28.0 [25.9, 30.7]	28.7 [26.1, 31.4]	0.0283
Time since first CAD diagnosis [years]	1,004	Median [Q1, Q3]	6 [2, 10]	5 [2, 11]	6 [2, 12]	5 [2, 10]	0.3399
Myocardial infarction	1,004	N (%)	671 (66.8)	133 (61.0)	200 (68.7)	338 (68.3)	0.1179
PCI	1,004	N (%)	608 (60. 6)	134 (61.5)	179 (61.5)	295 (59.6)	0.8277
CABG	1,004	N (%)	258 (25.7)	68 (31.2)	68 (23.4)	122 (24.6)	0.1022
Hospitalisation for CHF	1,004	N (%)	44 (4.4)	4 (1.8)	11 (3.8)	29 (5.9)	0.0450
Treated hypertension	1,004	N (%)	789 (78.6)	158 (72.5)	226 (77.7)	405 (81.8)	0.0178
Diabetes	1,004	N (%)	279 (27.8)	49 (22.5)	70 (24.1)	160 (32.3)	0.0062
Physical activity	1,004	No physical activity weekly	106 (10. 6)	21 (9.6)	24 (8.2)	61 (12.3)	0.0011
		Light physical activity	489 (48.7)	87 (39.9)	140 (48.1)	262 (52.9)	
		At least 20 min of physical activity once or twice a week	207 (20.6)	48 (22.0)	70 (24.1)	89 (18.0)	
		At least 20 min of physical activity at least 3 times a week	202 (20.1)	62 (28.4)	57 (19.6)	83 (16.8)	
Any angina	1,004	N (%)	304 (30.3)	63 (28.9)	68 (23.4)	173 (34.9)	0.0026
Angina and CCS class	1,004	No angina	700 (69.7)	155 (71.1)	223 (76.6)	322 (65.1)	0.0453
		Angina CCS class I	99 (9.9)	19 (8.7)	24 (8.2)	56 (11.3)	
		Angina CCS class II	170 (16.9)	35 (16.1)	38 (13.1)	97 (19.6)	
		Angina CCS class III	35 (3.5)	9 (4.1)	6 (2.1)	20 (4.0)	
HDL [mmol/L]	692	Median [Q1, Q3]	1.2 [1.0, 1.4]	1.3 [1.1, 1.5]	1.2 [1.0, 1.4]	1.2 [1.0, 1.4]	0.0411
Fasting TG [mmol/L]	733	Median [Q1, Q3]	1.4 [1.1, 1.9]	1.2 [0.9, 1.6]	1.5 [1.0, 1.9]	1.5 [1.1, 2.0]	< 0.0001
Heart rate (palpation)	1004	Mean (SD)	69.3 (9.4)	57.9 (3.3)	65.3 (2.1)	76.7 (7.1)	
Heart rate (ECG) [bpm]	775	Mean (SD)	68.2 (10.6)	58.7 (6.3)	64.6 (6.4)	75.1 (9.6)	
SBP [mm Hg]	1,004	Mean (SD)	132.6 (15.7)	130.2 (14.9)	130.9 (15.5)	134.7 (15.9)	0.0002
DBP [mm Hg]	1,004	Mean (SD)	79.6 (9.5)	77.2 (9.6)	79.3 (8.6)	80.8 (9.7)	< 0.0001
LVEF [%]	713	Mean (SD)	52.9 (9.6)	53.5 (8.7)	54.2 (9.2)	51.8 (10.1)	0.0104
RCA stenosis > 50%	1,004	N (%)	438 (43.6)	111 (50.9)	135 (46.4)	192 (38.8)	0.0057
Non invasive test for myocardial ischaemia	1,004	N (%)	741 (73.8)	163 (74.8)	233 (80.1)	345 (69.7)	0.0057
ECG rhythm	775	Sinus rhythm	740 (95.5)	179 (96.8)	218 (98.2)	343 (93.2)	0.0124
		AF/atrial flutter	9 (1.2)	0 (0)	0 (0)	9 (2.4)	
		Paced rhythm	26 (3.4)	6 (3.2)	4 (1.8)	16 (4.3)	

HR — heart rate; CAD — coronary artery disease; PCI — percutaneous coronary intervention; CABG — coronary artery bypass grafting; CHF — congestive heart failure; CCS — Canadian Cardiovascular Society; HDL — high density lipoprotein; TG — triglycerides; ECG — electrocardiogram; SBP — systolic blood pressure; DBP — diastolic blood pressure; LVEF — left ventricular ejection fraction; RCA — right coronary artery; AF — atrial fibrillation

Table 2. Pharmacotherapy of the Polish population classified according to resting heart rate

Parameter	No. of patients	Population	Total (n = 1,004)	HR ≤ 60 bpm (n = 218)	HR 61–69 bpm (n = 291)	HR ≥ 70 bpm (n = 495)	P
Aspirin	1,004	N (%)	955 (95.1)	208 (95.4)	279 (95.9)	468 (94.5)	0.6870
Thienopyridine	1,004	N (%)	128 (12.7)	23 (10.6)	42 (14.4)	63 (12.7)	0.4297
Oral anticoagulants	1,004	N (%)	64 (6.4)	11 (5.0)	9 (3.1)	44 (8.9)	0.0038
Beta-blockers	1,004	N (%)	903 (89.9)	200 (91.7)	264 (90.7)	439 (88.7)	0.3987
Ivabradine	1,004	N (%)	45 (4.5)	3 (1.4)	12 (4.1)	30 (6.1)	0.0194
Calcium antagonists	1,004	N (%)	268 (26.7)	49 (22.5)	71 (24.4)	148 (29.9)	0.0685
Verapamil or diltiazem	1,004	N (%)	49 (4.9)	5 (2.3)	15 (5.2)	29 (5.9)	0.1219
Angiotensin-converting enzyme inhibitors	1,004	N (%)	753 (75.0)	161 (73.9)	225 (77.3)	367 (74.1)	0.5536
Angiotensin II receptor blockers	1,004	N (%)	175 (17.4)	37 (17.0)	48 (16.5)	90 (18.2)	0.8175
Lipid-lowering drugs	1,004	N (%)	962 (95.8)	208 (95.4)	283 (97.3)	471 (95.2)	0.3450
Long-acting nitrates	1,004	N (%)	139 (13.8)	29 (13.3)	36 (12.4)	74 (14.9)	0.5799
Diuretics	1,004	N (%)	388 (38.6)	78 (35.8)	103 (35.4)	207 (41.8)	0.1254
Digoxin and derivatives	1,004	N (%)	9 (0.9)	1 (0.5)	2 (0.7)	6 (1.2)	0.7478
Amiodarone/dronedarone	1,004	N (%)	9 (0.9)	3 (1.4)	3 (1.0)	3 (0.6)	0.5600
Antidiabetic agents	1,004	N (%)	238 (23.7)	40 (18.3)	60 (20.6)	138 (27.9)	0.0076
Proton pump inhibitors	1,004	N (%)	280 (27.9)	59 (27.1)	67 (23.0)	154 (31.1)	0.0485
Number of heart rate lowering agents	1,004	Median [Q1, Q3]	1 [1, 1]	1 [1, 1]	1 [1, 1]	1 [1, 1]	0.2360

In our study, multivariable analysis revealed some independent predictors of higher HR. Diabetes, higher systolic blood pressure and social factors such as inability to work were correlated with a higher risk of HR ≥ 70 bpm. On the other hand, performing noninvasive testing and increased physical activity had a protective influence. The relationship between stenosis > 50% of the right coronary artery, reimbursement of cardiovascular agents and higher HR seems to be rather accidental. Not taking HR-lowering agents appeared not to be significantly associated with risk of higher HR after adjustment for these other variables.

These findings have very important clinical implications. Despite treatment with HR-lowering agents, especially beta-blockers, the proportion of patients with elevated HR remains high. According to European and American guidelines for the management of stable angina, beta-blockers are the first-line anti-anginal therapy [21, 22]. One of the factors that may limit the use of beta-blockers is low blood pressure, but the data shows that patients with HR ≥ 70 bpm had generally higher blood pressure. It seems that there is a potential for increasing and adjusting the dose of beta-blockers or adding the second agent (ivabradine) to achieve better HR control.

There are other potential limitations of proper treatment with beta-blockers: inadequate knowledge of evidence or treatment targets by clinicians [23], comorbidities that could be a contraindication or decreased tolerance to beta-blockers, side effects of beta-blockers, or access to medical care and reimbursement.

However, there is a discussion as to whether other HR-lowering agents could provide benefits similar to those of beta-blockers. In stable CAD there is no difference between beta-blockers and calcium antagonists in reducing the rate of cardiac death or MI [24]. Ivabradine, the pure HR-lowering drug, did not improve overall clinical outcome [11], but subgroup analysis of patients with HR ≥ 70 bpm showed that ivabradine reduced the incidence of coronary events [7, 12]. The ongoing SIGNIFY trial may answer the question as to whether ivabradine, a pure HR-lowering agent, can improve clinical outcomes in patients with CAD but without heart failure [25].

Higher HR was also correlated with lack of, or low, physical activity. Thus efforts to encourage lifestyle changes seem to be another safe and effective way of reducing HR.

CONCLUSIONS

It is worth reiterating that, despite a very high rate of treatment with beta-blockers, about half of the stable CAD patients in Poland still have HR ≥ 70 bpm. Patients with higher HR more often have symptoms of angina and more frequently need hospitalisation due to heart failure. It seems that there

Table 3. The most important characteristics and medications of the Polish population classified according to beta-blocker usage

Parameter	Total available	Population	Any BB (n = 903)	No BB (n = 101)	P
Age	1,004	Mean (SD)	62.2 (9.0)	61.7 (9.4)	0.6022
Gender	1,004	Male	668 (74.0)	63 (62.4)	0.0130
Body mass index	1,004	Median [Q1, Q3]	28.4 [26.0, 31.1]	27.1 [24.7, 30.0]	0.0012
Waist circumference [cm]	1,004	Median [Q1, Q3]	97 [90, 104]	94 [84, 102]	0.0369
Heart rate (palpation)	1,004	Mean (SD)	69.1 (9.1)	71.4 (11.5)	0.0218
Heart rate (ECG)	775	Mean (SD)	67.9 (10.3)	70.7 (12.6)	0.0260
Heart rate [bpm]	1,004	Hart rate (palpation) ≥ 70 bpm	439 (48.6)	56 (55.4)	0.1929
Left ventricular ejection fraction [%]	713	Mean (SD)	52.68 (9.6)	55.33 (8.5)	0.0358
Treated hypertension	1,004	N (%)	720 (79.7)	69 (68.3)	0.0080
Peripheral arterial disease	1,004	N (%)	91 (10.1)	20 (19.8)	0.0031
Myocardial infarction	1,004	N (%)	615 (68.1)	56 (55.4)	0.0104
Percutaneous coronary intervention	1,004	N (%)	549 (60.8)	59 (58.4)	0.6423
Coronary artery bypass grafting	1,004	N (%)	243 (26.9)	15 (14.9)	0.0085
Carotid disease	1,004	N (%)	33 (3.7)	9 (8.9)	0.0299
Asthma/COPD	1,004	N (%)	47 (5.2)	11 (10.9)	0.0202
Haemoglobin A1c [%]	74	Mean (SD)	6.83 (1.1)	8.23 (1.4)	0.0034
Creatinine [μmol/L]	587	Median [Q1, Q3]	87 [76, 97]	80 [68, 93]	0.0499
High density lipoprotein [mmol/L]	692	Median [Q1, Q3]	1.2 [1.0, 1.4]	1.3 [1.1, 1.6]	0.0036
Low density lipoprotein [mmol/L]	689	Median [Q1, Q3]	2.6 [2.0, 3.2]	2.8 [2.2, 3.8]	0.0264
Coronary territories with stenosis > 50%: LAD	1,004	N (%)	505 (55.9)	37 (36.6)	0.0002
Coronary angiography not done	1,004	N (%)	162 (17.9)	29 (28.7)	0.0089
Aspirin	1,004	N (%)	865 (95.8)	90 (89.1)	0.0069
Symptoms indicative of intolerance or contraindication to BB	1,004	N (%)	74 (8.2)	58 (57.4)	< 0.0001
Ivabradine	1,004	N (%)	28 (3.1)	17 (16.8)	< 0.0001
Verapamil or diltiazem	1,004	N (%)	25 (2.8)	24 (23.8)	< 0.0001
ACE inhibitors	1,004	N (%)	687 (76.1)	66 (65.3)	0.0182

BB — beta-blockers; ECG — electrocardiography; COPD — chronic obstructive pulmonary disease; LAD — left anterior descending artery; ACE — angiotensin-converting enzyme

is a possibility of further lowering the HR in many patients with stable CAD. Whether or not this will improve symptoms and outcomes is under investigation.

CLARIFY REGISTRY INVESTIGATORS IN POLAND

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Table 4. Multivariable logistic regression results from stepwise model using the patients in Poland. All significant variables associated with an elevated heart rate (≥ 70 bpm) and forcing heart rate reducing drugs into the model

Variable	Level	Odds ratio (95% confidence interval)	Pr > Chi-square
Systolic blood pressure [per 10 mm Hg]		1.2 (1.1, 1.3)	0.0004
Employment	Employed part-time	0.8 (0.4, 1.3)	0.0007
Employment	Unable to work	1.7 (1.0, 2.6)	
Employment	Unemployed	3.1 (0.9, 10.9)	
Employment	Retired	0.9 (0.6, 1.2)	
Employment	Other	2.4 (1.1, 5.3)	
Diabetes	Yes	1.5 (1.1, 2.0)	0.0057
Physical activity	No physical activity weekly	1.0 (0.6, 1.5)	0.0272
Physical activity	At least 20 min vigorous physical activity once or twice a week	0.7 (0.5, 1.0)	
Physical activity	At least 20 min vigorous activity at least 3 times a week	0.6 (0.4, 0.9)	
Right coronary artery stenosis > 50%	Yes	0.7 (0.5, 0.9)	0.0030
Non invasive test performed	Yes	0.6 (0.5, 0.9)	0.0032
Reimbursement of cardiovascular agents	Fully reimbursed	2.8 (1.8, 4.2)	< 0.0001
Taking hart rate-lowering medications	No	0.8 (0.5, 1.4)	0.4221

Nowowiejska-Wiewióra (Zabrze); Artur Olszewski (Bartoszyce); Krzysztof Orzechowski (Świdnik); Tomasz Pitsch (Knurów); Beata Poprawa (Tarnowskie Góry); Andrzej Prokop (Sosnowiec); Aldona Regulska (Krosno); Roman Sadłowski (Bytów); Marek Sidor (Lubartów); Benwenuta Sikorska-Buczkowska (Gniezno); Ilona Skoczylas (Pyskowice); Joanna Słaboszewska (Wejherowo); Dorota Sobczyk (Kraków); Marek Sołtysiak (Lubin); Tomasz Stasiuk (Kwidzyń); Witold Streb (Rybnik); Jerzy Sudnik (Sokółka); Piotr Szałkowski (Gdańsk); Aleksander Szpak (Brzeg); Marek Szulc (Morąg); Paweł Turek (Kraków); Grzegorz Walawski (Leżajsk); Jolanta Walczewska (Kraków); Magdalena Węglarz (Bydgoszcz); Małgorzata Winter (Wrocław); Mariola Wrębiak-Trznadel (Dąbrowa Górnicza); Ryszard Wysocki (Ostrów Wielkopolski); Dorota Zalewska (Skała); Joanna Zdrojewska (Szczecin); Rafał Zimoląg (Nowa Sól)

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Częstotliwość rytmu serca i farmakoterapia beta-adrenolitykami u pacjentów ambulatoryjnych ze stabilną chorobą wieńcową: charakterystyka wyjściowa polskiej populacji rejestru CLARIFY

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Streszczenie

Wstęp: Częstotliwość rytmu serca (HR) jest ważnym czynnikiem ryzyka u pacjentów ze stabilną chorobą wieńcową (CAD). Wciąż mało jest aktualnych danych na temat HR i farmakoterapii za pomocą leków obniżających HR (w tym beta-adrenolityków) w codziennej praktyce klinicznej u pacjentów ze stabilną CAD.

Cel: Celem niniejszego artykułu jest omówienie wyjściowej charakterystyki polskiej populacji rejestru CLARIFY, również w odniesieniu do leczenia beta-adrenolitykami oraz ocena czynników wpływających na HR.

Metody i wyniki: CLARIFY to międzynarodowe, prospektywne badanie obserwacyjne dotyczące ambulatoryjnych pacjentów ze stabilną CAD. Kryteriami włączenia były: wywiad zawału serca, przebyte leczenie rewaskularyzacyjne, stwierdzenie w koronarografii co najmniej 50% zwężeń w tętnicach wieńcowych lub występowanie dolegliwości stenokardialnych z udowodnionym niedokrwieniem w testach prowokacyjnych. Pomiędzy listopadem 2009 r. a lipcem 2010 r. do badania włączono 33 438 pacjentów z 45 krajów Europy, Ameryki Północnej i Południowej, Afryki, Azji, Australii i Oceanii. W Polsce między lutym a czerwcem włączono 1004 osób, co stanowi największą grupę chorych wśród krajów tzw. Europy Wschodniej. W większości byli to mężczyźni (72,8%). Średni (± SD) wiek wynosił 62,1 ± 9,1 roku, średnia HR oceniana za pomocą fali tętna wynosiła 69,3 ± 9,4, a za pomocą elektrokardiogramu 68,2 ± 10,6 uderzeń na minutę. Beta-adrenolityki były stosowane u 89,9% pacjentów. Spoczynkową HR ≥ 70/min stwierdzono u 49,3% wszystkich chorych i u 48,6% pacjentów leczonych beta-adrenolitykami. Spoczynkowa HR ≥ 70/min istotnie częściej występowała u młodszych pacjentów, z cukrzycą, leczonym nadciśnieniem tętniczym i niestosujących regularnie wysiłku fizycznego. U chorych ze spoczynkową HR ≥ 70/min częściej występowały objawy dławicowe i częściej wymagali hospitalizacji z powodu niewydolności serca.

Wnioski: Pomimo bardzo wysokiego odsetka pacjentów ze stabilną CAD leczonych beta-adrenolitykami nadal u niemal 50% osób spoczynkowa HR wynosi ≥ 70/min, co wiąże się z częstszym występowaniem objawów dławicowych i niedokrwieniem mięśnia sercowego. U wielu z tych chorych można w istotny sposób zwolnić spoczynkową HR. Odpowiedź na pytanie, czy takie postępowanie będzie się wiązało z poprawą rokowania i zmniejszeniem dolegliwości, wymaga przeprowadzenia dalszych badań.

Słowa kluczowe: częstotliwość rytmu serca, stabilna choroba wieńcowa, beta-adrenolityki

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