

## CURRENT STATE OF ANGINA TREATMENT IN THE OUTPATIENT POPULATION AND HEART RATE MONITORING SURVEY IN LATVIA (REALITY LATVIA)

Inga Balode\*, Sanda Jēgere\*\*, Iveta Mintāle\*\*, Inga Narbute\*\*, Ilja Zakke\*\*,  
Gustavs Latkovskis\*\*,\*\*\*, and Andrejs Ērglis\*\*,\*\*\*

\* Rīga Stradiņš University, Dzirciema iela 16, Rīga, LV-1017, LATVIA  
E-mail: inga.balode@lv.netgrs.com

\*\* Pauls Stradiņš Clinical University Hospital, Pilsoņu iela 13, Rīga, LV-1002, LATVIA

\*\*\* Faculty of Medicine, University of Latvia, Raina bulv. 19, Rīga, LV-1586, LATVIA

Contributed by Andrejs Ērglis

*The aim of the REALITY Latvia survey was to accumulate information about treated stable angina outpatients regarding their characteristics, heart rate (HR), treatment, and quality of life. Thirty cardiologists were involved with 1–15 patients each. In total, data about 300 patients were obtained. Patients were examined and questioned during one visit. A high HR was defined above 70 beats per minute (bpm), in accordance to recent evidence. Mean HR was  $70.3 \pm 11.3$  bpm and 45% of patients had HR above 70 bpm. The opinion of practitioners regarding HR differed. For example, a HR level within the range 70–80 bpm was perceived by cardiologists as “normal”, “borderline high” and “high”. The mean target HR that physicians wanted to achieve was  $60.1 \pm 4.7$  bpm. Beta blockers were used in 91% of cases. The more widely used beta blockers were metoprolol (47%) and bisoprolol (35%) in mean daily doses  $69.7 \pm 30.1$  mg and  $5.3 \pm 2.0$  mg, respectively. REALITY Latvia data suggest that, despite wide use of beta blockers, HR control in stable angina patients is insufficient. This is caused by insufficient understanding of HR as a treatment target by physicians and use of beta blockers in suboptimal dosages.*

**Key words:** angina, heart rate, antianginal treatment, outpatient.

### INTRODUCTION

Coronary artery disease (CAD) is still highly prevalent; it is the main cause of mortality worldwide and a major burden on public health (Leal *et al.*, 2006). According to global and regional projections of mortality, CAD will remain the leading cause of death for the next 20 years (Mathers and Loncar, 2006). Latvian statistical data (Anonīms, 2008) indicate that mortality from cardiovascular diseases in Latvia is higher than the average in the European Union. Due to high prevalence of CAD, Latvia belongs to ill-disposed regions (Anonyous, 2004). Stable angina pectoris is one of the most common presentations of CAD. In spite of recent advances, mainly in terms of secondary prevention, chronic stable angina remains a major public health concern and its management continues to be a challenge.

Heart rate (HR) plays a major role in pathophysiology of CAD. An increase of HR negatively affects both components of the myocardial oxygen balance: increases oxygen consumption and decreases oxygen supply. In patients with stable CAD most episodes of myocardial ischemia are associated with an increase in HR (Deedwania and Carbajal,

1992; Hinderliter *et al.*, 1991; Panza *et al.*, 1992). The possibility of developing ischemia is proportional to the value and duration of the HR increase (Andrews *et al.*, 1993). Several epidemiological studies suggest that high HR is associated with increased total as well as cardiovascular (CV) mortality. This association has been proved not only in patients with CAD (Diaz *et al.*, 2005; Palatini, 2005) but also in the general population (Benetos *et al.*, 1999; Menotti *et al.*, 2001) and various patient populations (Fox *et al.*, 2007), such as patients after myocardial infarction (Disegni *et al.*, 1995; Aronow *et al.*, 1996; Futterman and Lemberg, 1999) and arterial hypertension (Gillman *et al.*, 1993; Palatini *et al.*, 1999; King *et al.*, 2006; Palatini *et al.*, 2006). The prognostic value of increased resting HR in stable CAD patients with left ventricular dysfunction has been confirmed in a prospective way by analysis of a large cohort from the placebo arm of the BEAUTIFUL trial. The BEAUTIFUL study proved that  $HR \geq 70$  beats per minute (bpm) significantly increases cardiovascular (CV) risk in CAD patients (Fox *et al.*, 2008).

Based on a large body of evidence, high HR as an independent CV risk factor has been included in the latest Euro-

pean and Latvian guidelines on CV disease prevention (Ērglis u.c., 2007; Graham *et al.*, 2007)

Consistent with understanding of the importance of HR in the pathophysiology of CAD, HR reduction should be an important therapeutic target for angina management. However, despite the fact that HR is one of the most frequently assessed clinical parameters, there is lack of information about the HR level in clinical practice, particularly in outpatients. It is also not known what proportion of treated outpatients have increased HR, how practitioners evaluate HR, when do they plan to decrease HR and what is the preferable (target) HR they want to achieve.

The aim of the REALITY Latvia survey was to characterise outpatients with stable angina, to clarify the level of heart rate in this population, to describe current treatment and to evaluate the influence of angina symptoms on everyday activities and quality of life.

## MATERIALS AND METHODS

300 outpatients with treated stable angina were included in this observational survey during the period from March until May 2006. Thirty cardiologists working in Latvia participated in the survey and included 1–15 patients each. There were no exclusion criteria.

Data were collected during one visit and a case report form for each included patient was filled.

The case report form contained six parts:

### 1. Demographic data.

2. Physical examination (including measurement of HR). After ten minutes of rest, HR was measured in sitting position by pulse palpation for 1 minute. Additionally, there were three questions for practitioners: how the physician evaluates the level of measured HR (as “normal”, “borderline high” or “high”); does the practitioner plan to decrease HR, and which target HR he/she is planning to achieve?

3. Symptoms of angina (mean number of attacks and consumption of short-acting nitrates, grade of angina pain according to Canadian Cardiovascular Society classification).

4. Medical history (life style, history of CAD, previous drug treatment, information regarding invasive treatment of CAD, concomitant diseases).

5. Drug treatment of stable angina (including current treatment (antitrombotic agents, antianginal agents, lipid-lowering drugs, angiotensin-converting enzyme inhibitors (ACEI) etc. together with generic names of agents, dosages and duration of treatment).

6. Influence of angina symptoms on everyday activity and quality of life. This part included four questions about the influence of angina symptoms on everyday activity, emo-

tional comfort of patient and level of satisfaction with current treatment.

High HR was defined as above 70 (bpm), in accordance to recent evidence (Fox *et al.*, 2008).

Data were processed using methods of descriptive statistics and analysed differences by using the Statistical Package for the Social Sciences (SPSS), version 15.0.

## RESULTS

**Characteristics of patients.** Mean age of patients ( $n = 300$ ) was  $65 \pm 9$  years and 191 (63.7%) were men. Mean body weight in men was  $86.4 \pm 13.4$  kg, in women:  $77.5 \pm 13.3$  kg. Mean height in men was  $183.1 \pm 7.9$  cm, in women:  $163.5 \pm 8.0$  cm. Mean body mass index was  $28 \pm 4$  kg/m<sup>2</sup>. Forty seven (16%) patients were smokers (mean number of cigarettes per day:  $15.0 \pm 9.4$ , mean duration of smoking:  $27.8 \pm 11.6$  years). Forty eight (16%) of the patients were previous smokers (mean number of previously smoked cigarettes per day:  $16.6 \pm 8.4$ , mean duration of previous smoking:  $23.3 \pm 10.0$  years, mean period after stopping smoking:  $8.4 \pm 7.5$  years).

The most frequent concomitant diseases were hypertension and heart failure: 67% and 54%, respectively (Table 1).

Table 1

THE PREVALENCE OF CONCOMITANT DISEASE

| Disease  | Prevalence n (%) |
|--|------------------|
| Hypertension: (systolic pressure > 140 mm Hg, or diastolic > 90 mm Hg, or on treatment for hypertension) | 201 (67)         |
| Diabetes mellitus  | 20 (7)           |
| Peripheral vascular disease  | 5 (2)            |
| Cerebrovascular disease  | 10 (3)           |
| Asthma   | 2 (1)            |
| Chronic obstructive pulmonary disease  | 3 (1)            |
| Depression   | 4 (1)            |
| Erectile dysfunction (if men)  | 4 (1)            |
| Heart failure  | 54 (18)          |
| Renal insufficiency (eg creatinine > 2 mgdL-1 or > 180 µmol/L)   | 5 (2)            |

The mean level of total cholesterol was  $5.4 \pm 1.3$  mmol/l, low density lipoprotein cholesterol:  $3.2 \pm 1.1$  mmol/l, high density lipoprotein cholesterol:  $1.3 \pm 0.4$  mmol/l, and triglycerides:  $1.8 \pm 1.0$  mmol/l. Prevalence of different grades of angina pain, according to the Canadian Cardiovascular Society classification, was as follows: class I — 18%, class II — 47%, class III — 31%, class IV — 3% of patients. History of myocardial infarction, previous percutaneous coronary intervention and previous coronary artery bypass graft surgery was positive in 144 (48%), 119 (40%) and 36 (12%) patients, respectively.

**Heart rate.** Mean HR was  $70.3 \pm 11.3$  (bpm). In men HR was  $70.0 \pm 11.8$ , in women:  $70.8 \pm 10.2$  bpm ( $P > 0.05$ ). The distribution of HR in the study population is shown in Figure 1.

Table 2

HEART RATE BREAKDOWN IN TOTAL POPULATION, PROPORTION OF PATIENTS WITH PLANNED DECREASE OF HEART RATE AND CORRESPONDING TARGET HEART RATE

|   | ≤ 62 bpm   |           | 63–70 bpm  |           | 71–76 bpm  |           | 77–82 bpm  |           | 82 bpm     |            |
|---|------------|-----------|------------|-----------|------------|-----------|------------|-----------|------------|------------|
|   | n          | %         | n          | %         | n          | %         | n          | %         | n          | %          |
| Total population, % (n = 300)                       | 89         | <b>30</b> | 76         | <b>25</b> | 51         | <b>17</b> | 48         | <b>16</b> | 36         | <b>12</b>  |
| Planned to decrease HR (% from respective subgroup) | 2          | <b>2</b>  | 29         | <b>38</b> | 33         | <b>65</b> | 45         | <b>94</b> | 36         | <b>100</b> |
| Target HR, mean ±SD (if planned to decrease)        | 60.0 ± 0.0 |           | 57.9 ± 3.9 |           | 59.9 ± 4.6 |           | 60.4 ± 4.1 |           | 61.5 ± 5.8 |            |

SD, standard deviation; bpm, beats per minute

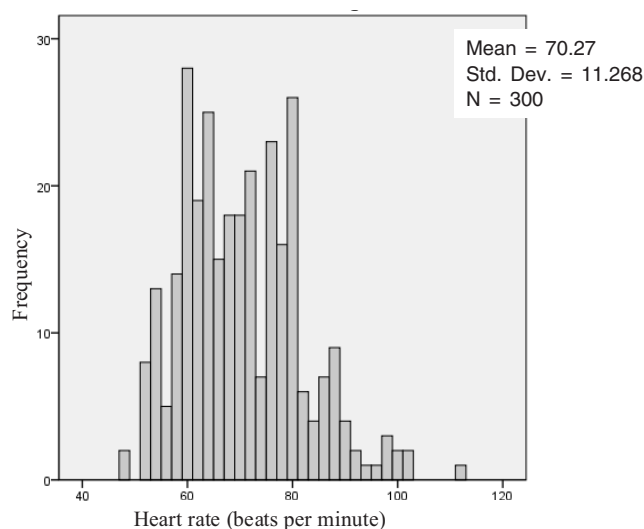


Fig. 1. Distribution of heart rate in the study population.

After comparison of HR levels in different age groups (30–39, 40–49, 50–59, 60–69, 70–79, above 80 years), no significant differences were found. In patients with current angina symptoms (n = 267) HR level was higher than in patients without angina symptoms (n = 25):  $70.6 \pm 11.2$  bpm vs  $67.9 \pm 11.2$  bpm, but the difference was not significant ( $P > 0.05$ ). Patients with angina symptoms at rest (n = 50) had significantly higher HR than those who did not have angina at rest (n = 222):  $73.6 \pm 13.9$  bpm vs  $69.2 \pm 10.6$  bpm ( $P = 0.01$ ).

In 135 (45%) of patients the HR level was above 70 bpm and in 36 (12%) above 82 bpm. The HR level was significantly higher in patients for whom it was planned to decrease in comparison with those for whom a HR decrease was not planned ( $78.5 \pm 9.2$  bpm vs  $62.6 \pm 6.7$  bpm ( $P = 0.001$ )). Practitioners had planned to decrease the HR level in 114 patients with HR above 70 bpm (84.4% of all patients with HR above 70 bpm). However, physicians were not planning to decrease HR in 35% of patients with HR within the range 71–76 bpm and in 6% of patients with HR within the range 77–82 bpm. The target HR (in cases where cardiologists were planning to decrease HR) was  $60.1 \pm 4.7$  bpm, with a slight variation between groups of different HR levels (Table 2).

The HR breakdown in three subjective levels: “high”, “borderline high” and “normal” (interpretation of physicians)

Table 3

HEART RATE BREAKDOWN IN 3 SUBJECTIVE LEVELS (PRACTITIONER EVALUATION)

| HR subjective level | Number of patients, n | ≤ 62 bpm |           | 63–70 bpm |           | 71–76 bpm |           | 77–82 bpm |           | ≥ 83 bpm |           |
|---------------------|-----------------------|----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|----------|-----------|
|                     |                       | n        | %         | n         | %         | n         | %         | n         | %         | n        | %         |
| High                | 57                    | 0        | <b>0</b>  | 1         | <b>2</b>  | 9         | <b>16</b> | 18        | <b>32</b> | 29       | <b>51</b> |
| Borderline high     | 79                    | 3        | <b>4</b>  | 22        | <b>28</b> | 22        | <b>28</b> | 25        | <b>32</b> | 7        | <b>9</b>  |
| Normal              | 164                   | 86       | <b>52</b> | 53        | <b>32</b> | 20        | <b>12</b> | 5         | <b>3</b>  | 0        | <b>0</b>  |

bpm, beats per minute

showed that HR as “normal” was assessed in a total of 164 cases and in 25 cases when HR was above 70 bpm: in 20 (12%) cases when HR was within the range 71–76 bpm and in five (3%) cases when HR was within the range 77–82 bpm (Table 3). Mean HR in the subjective levels “normal”, “borderline high”, and “high” was  $63 \pm 7$  bpm,  $74 \pm 7$  bpm and  $85 \pm 9$  bpm, respectively.

An HR within the range 70–80 bpm was in many cases assessed by cardiologists as “normal”, “borderline high” and also as “high” (Fig. 2).

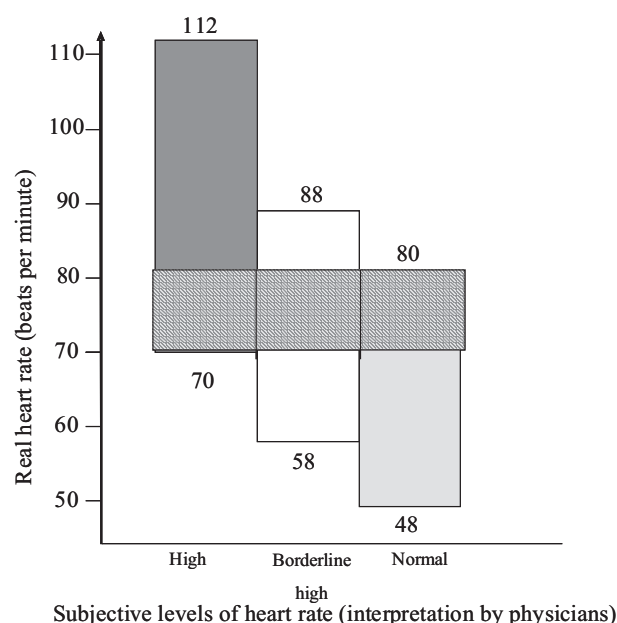


Fig. 2. Subjective interpretation of heart rate by cardiologists.

Of all patients with an HR evaluation as „normal”, in 11% of cases a further decrease of HR was planned. When assessment of HR was „borderline high” or „high”, an HR decrease was planned in 89% and 100% of patients, respectively.

**Treatment.** Treatment of patients with different classes of drugs is reflected in Figure 3. Regarding antitrombotics, 91% of all patients were treated with aspirin, 16%, with clopidogrel, and 4%, with oral anticoagulants. 54% of patients were using isosorbide mononitrate and 12% isosorbide dinitrate. 47% of patients were receiving beta blocker metoprolol, 35% bisoprolol, 4% carvedilol, 1% atenolol and 4% — other beta blocker. Of the calcium channel blockers the most frequently used was amlodipin (48% of all patients) and only 9% from patients were using other calcium channel blockers. Non dihydropyridine calcium channel blockers were used only by five patients (1%). Of statins the most frequently used was atorvastatin (72%) and of ACEI — perindopril (51%). Metabolic agent trimetazidin was used in 26% of cases.

Long-acting nitrates were less used in younger patients < 50 years old than in elderly patients ≥ 70 years old (21% and 79%, respectively). The same tendency was observed with beta blockers: 84% in group of patients younger than 50 years and 79% in patients who were ≥ 70 years old (Table 4).

Analysis of treatment according to angina status (Canadian Cardiovascular Society classification — class I to IV) showed increased usage of long acting nitrates (24%, 68%, 83%, 100% in class I, II, III, IV, respectively), calcium antagonists (52%, 56%, 60%, 44% in class I, II, III, IV respectively) and metabolic agent trimetazidin (22%, 27%, 25%, 44% in class I, II, III, IV, respectively) with severity of angina symptoms.

Analysis of treatment according to HR level showed, that usage of beta blockers in groups of patients with different HR level was from 89% of cases in group with HR < 63 bpm to 94% of cases in patients with HR ≥ 82 (see Fig. 4), but the differences between groups were not significant ( $P > 0.05$ ).

Mean HR did not differ significantly in patients with or without prescribed beta blockers, and target HR ( $60.1 \pm 4.7$  bpm) was not achieved in either group. There were slightly more patients with a planned decrease of HR in the group using beta blockers (49%) in comparison with patients not using beta blockers (42%), but the difference was not significant ( $P > 0.05$ ). The average time of using beta blockers was 28 months for metoprolol, 20 months for bisoprolol and 19 months for other beta blockers. HR did not differ statistically significantly according to usage of different beta blockers.

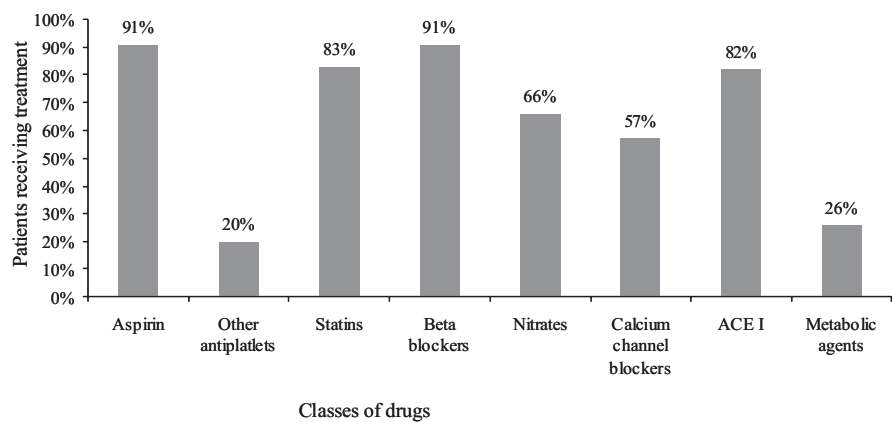


Fig. 3. Treatment of patients with different classes of drugs. ACEI, angiotensin-converting enzyme inhibitors

Table 4

TREATMENT ACCORDING TO AGE

| Treatment                | Total population<br>n = 300 |    | < 50 years<br>n = 19 |    | 50–59 years<br>n = 62 |    | 60–69 years<br>n = 106 |    | ≥ 70 years<br>n = 109 |    |
|--------------------------|-----------------------------|----|----------------------|----|-----------------------|----|------------------------|----|-----------------------|----|
|                          | n                           | %  | n                    | %  | n                     | %  | n                      | %  | n                     | %  |
| Antitrombotic agents     | 289                         | 96 | 18                   | 95 | 59                    | 95 | 103                    | 97 | 105                   | 96 |
| Long-acting nitrates     | 197                         | 66 | 4                    | 21 | 41                    | 66 | 64                     | 60 | 86                    | 79 |
| Beta blockers            | 274                         | 91 | 16                   | 84 | 60                    | 97 | 95                     | 90 | 99                    | 91 |
| Calcium channel blockers | 170                         | 57 | 9                    | 47 | 39                    | 63 | 65                     | 61 | 55                    | 50 |
| Lipid-lowering drugs     | 250                         | 83 | 16                   | 84 | 55                    | 89 | 89                     | 84 | 87                    | 80 |
| ACEI                     | 246                         | 82 | 15                   | 79 | 52                    | 84 | 83                     | 78 | 94                    | 86 |
| ARB                      | 9                           | 3  | 0                    | 0  | 2                     | 3  | 2                      | 2  | 4                     | 4  |
| Trimetazidin             | 77                          | 26 | 7                    | 37 | 14                    | 23 | 30                     | 28 | 25                    | 23 |

ACEI, angiotensin-converting enzyme inhibitors; ARB, angiotensin-receptor blockers

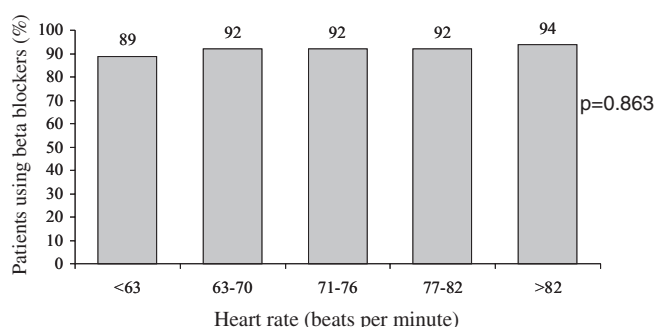


Fig. 4. Treatment with beta blockers according to heart rate.

Average daily doses of different beta blockers in the total population and according to concomitant diseases are summarized in Table 5. There is a tendency that co-morbidities considered as contraindications for usage of beta blockers or symptoms of intolerance are not associated with smaller doses in comparison with those used in the total population.

Table 5

#### AVERAGE DOSE OF BETA BLOCKERS ACCORDING TO CO-MORBIDITY

|                             | Atenolol<br>(n = 2),<br>mean dose<br>±SD | Bisoprolol<br>(n = 106),<br>mean dose<br>±SD | Carvedilol<br>(n = 12),<br>mean dose<br>±SD | Metoprolol<br>(n = 141),<br>mean dose<br>±SD |
|-----------------------------|--|--|---|--|
| Total population            | 25.0 ± 0.0                               | 5.3 ± 2.0                                    | 17.2 ± 13.5                                 | 69.7 ± 30.1                                  |
| Diabetes mellitus           | -  | 6.0 ± 2.2                                    | 25.0 ± 21.7                                 | 73.4 ± 37.4                                  |
| Peripheral arterial disease | -  | 4.5 ± 3.3                                    | 6.25  | 78.6 ± 26.7                                  |
| Bronchial asthma            | -  | 10.0   | -   | 50.0   |
| COPD                        | -  | 3.8 ± 1.4                                    | 25.0  | 66.7 ± 28.9                                  |
| Depression                  | -  | 5.0 ± 3.5                                    | -   | 75.0 ± 28.9                                  |
| Erectile dysfunction        | -  | 6.3 ± 5.3                                    | -   | 80.0 ± 44.7                                  |

SD, standard deviation

The dose of metoprolol was significantly ( $P < 0.05$ ) higher in groups of patients with higher HR. The same tendency was not observed for bisoprolol. Irrespectively of how physicians assessed HR (“normal”, “borderline high” or “high”) the frequency of usage of beta blockers did not differ significantly. However, doses of beta blockers — higher subjective levels of HR were associated with significantly ( $P < 0.01$ ) higher dose of metoprolol ( $63 \pm 28$  mg if level was “normal”,  $70 \pm 29$  mg if level was “borderline high” and  $84 \pm 32$  mg if the level was considered as “high”). Doses of bisoprolol did not change according to the subjective level of HR.

The beta blocking agent used was switched within the last 12 months in 33 (12%) patients of all 274 patients using beta blockers. In eight patients the change was made due to intolerance: bradycardia (3), exacerbation of bronchial asthma or chronic obstructive pulmonary disease (2), dizziness and fatigue (2), prolonged QT (1) and in 19 patients due to other reasons: insufficient efficiency (13), decision of

doctor (5), desire of patient (2). Nine (35%) patients from all 26 not using beta blockers were using them previously, but stopped later. Of them, four cases were due to side effects: erectile dysfunction (1), bradycardia (2), exacerbation of bronchial asthma (1), and five — due to other reasons: decision of doctor (3), desire of patient (2).

155 (52%) of REALITY Latvia patients were post revascularization cases. Of these, 82 cases (65% of all revascularised patients) symptoms of angina were persisting and in 125 cases (81% of all revascularised patients) treatment with antianginal agents was needed.

**Influence of angina on quality of life.** The most frequent answers of patients to the question about influence of angina symptoms on everyday activities were: “somewhat limited” — 28% and “a little limited” — 29%. On the question about influence of angina on enjoyment of life during the last month, 27% of patients answered “somewhat limited” and 32% “a little limited”. Asked how often they worry that he/she may have a heart attack, 36% of patients answered “sometimes” and in 35% cases the answer was “rarely”. On the question about satisfaction with current antianginal treatment 26% of patients answered “rather satisfied” and in 39% of cases the answer was “almost satisfied” (Fig. 5).

We observed a relationship between HR and the level of worry about heart attacks. Patients who were more often worried that he/she may have a heart attack had a higher heart rate than those who were not worried about attacks ( $P < 0.01$ ) (Table 6).

Answers on questions about the influence of angina on quality of life did not significantly differ in patients not using beta blockers in comparison with those on beta blockers. There were also no significant differences in answers on quality of life questions between groups of patients with different HR level.

## DISCUSSION

Characteristics of patients in the REALITY Latvia survey were typical for CAD in general as the proportion of males and females, mean age, body mass index, percentage of smokers and hypertension as the most frequent co-morbid-

Table 6

#### HEART RATE ACCORDING TO LEVEL OF WORRY ABOUT HEART ATTACKS

| How often does the patient worry that he/she may have heart attack? | n   | HR (bpm)<br>Mean ± SD |
|---|-----|-----------------------|
| All the time  | 4   | 65.5 ± 10.0           |
| Often   | 59  | 74.6 ± 12.4           |
| Sometimes   | 107 | 70.5 ± 11.0           |
| Rarely  | 104 | 68.2 ± 11.1           |
| Never   | 22  | 68.3 ± 11.3           |

SD, standard deviation; bpm, beats per minute





Fig. 5. Answers of patients on questions about influence of angina on quality of life.

ity follow the same trends as in trials with participation of CAD patients (Anonymous, 2008). The data are also comparable to the population in the Euro Heart Survey (EHS), where 156 cardiology clinics participated from 34 countries with 3031 patients, included on the basis of a new clinical diagnosis of stable angina by a cardiologist (Daly *et al.*, 2006).

Our data indicate that stable angina outpatients in Latvia have a relatively high HR despite widely used treatment with beta blockers. Almost half of patients (45%) have HR at rest above 70 bpm, which is the level, which is associated with significantly higher CV risk (Fox *et al.*, 2008). These data are in line with the global situation in Europe. Investigators of the EHS survey showed, that despite treatment, 53% of angina patients had a HR higher than 70 bpm (Daly *et al.*, 2008). Even if mean HR in REALITY Latvia was lower than in EHS (70 bpm vs 73 bpm) and the proportion of patients with high HR (above 70 bpm) was slightly lower than in EHS, the situation with perception of HR as a major treatment target in management of stable angina by cardiologists in Latvia does not seem very optimistic. Our data show a big gap (10 bpm) between the mean actual HR of the patients and mean target HR that cardiologists want to achieve when planning to decrease it. Taking into account that patients in the REALITY Latvia population are already treated by cardiologists, this difference is very worrying. In real life angina patients are frequently treated by general practitioners. Understanding the role of HR in pathophysiology and prognosis of CAD can be significantly weaker among general practitioners than among cardiologists,

and therefore, HR control in patients treated by general practitioners can be even worse.

According to our data, physicians do not have a clear view, which exactly level of HR should be considered as high for CAD patients and should be treated specifically to decrease it. An HR between 70 and 80 can be evaluated by cardiologists as “normal”, “borderline high” or “high”. However, perception of a certain level of HR as high seems crucial to induce specific treatment for reduction of HR. Cardiologists did not plan to reduce HR in 41% of cases when HR was above 70 bpm and in 6% of cases when HR was already above 77 bpm. However, when evaluation of the HR was regarded as “high”, decision of reduction of HR is taken in 100% of cases.

These findings strongly demonstrate that not HR *per se* (being high or not) determines decision of practitioners to reduce it, but perception of HR as high does. Hence, in order to have better HR control in CAD patients, certain changes in the perception of physicians should take place. Taking into account evidence regarding increased cardiovascular risk in CAD patients with HR  $\geq 70$  bpm (Fox, 2008), patients could significantly benefit if practitioners consider HR above 70 bpm as high.

In general, patients in the REALITY Latvia survey were better treated in comparison with the population in EHS. In REALITY, a larger proportion of patients were using aspirin (91% vs 78%), other antiplatelets (20% vs 9%), statins (83% vs 48%), beta blockers (91% vs 67%), ACEI (82% vs 40%) than in EHS (Daly, 2005). Wider use of beta blockers

in REALITY Latvia was associated with lower mean HR and lower proportion of patients with HR above 70 bpm than in EHS. The usage of preventive treatment in REALITY Latvia was high and comparable with that in large CAD trials where patients used optimal basic therapy — BEAUTIFUL, EUROPA, COURAGE (Anonymous, 2003; 2008; Boden, 2007; Anonymous, 2008). This indicates a favourable trend in following guidelines and considering cardiovascular prevention by treating angina patients.

Despite very wide usage of beta blockers in the REALITY Latvia population (91%), doses of beta blockers were relatively low in comparison with those suggested by clinical trials. This is not unique to Latvia as meta-analysis from 55 315 patients after myocardial infarction (Gislason, 2006) showed, that under-dosing of beta blockers is typical in the community (patients were using 50% or less of the dosages used in clinical trials) and associated with poor long-term compliance.

Of note, 52% of REALITY patients were previously revascularised and most of them were also using antianginal agents. This observation underlines the necessity for pharmacological treatment (preventive, less antianginal) after revascularisation.

We found that patients with current symptoms of angina at rest had significantly higher HR than those without, but the difference between higher HR in patients with current angina symptoms in comparison with those without symptoms did not reach statistical significance. This could be explained by a very small number of patients without current symptoms ( $n = 25$ ) in the survey.

Quality of life analysis showed that stable angina patients in Latvia are relatively satisfied with their quality of life and treatment. The majority of patients pointed out that their daily life and enjoyment of life was slightly limited due to angina symptoms and agreed that they are almost satisfied with their current treatment. The significant relationship between higher HR in patients who were worried about heart attacks, in comparison with HR in less worried patients, proves potential of high HR to influence quality of life negatively.

In our survey data were collected only at one visit. Together with a relatively small number of patients this limitation for interpretation of the results should be acknowledged. To understand how HR evaluation by practitioners and how the decisions made regarding HR reduction influence further treatment, symptoms of angina and quality of life, longer studies with follow-up period are needed.

In conclusion, the results of the REALITY Latvia survey suggest that stable angina outpatients managed by cardiologists in Latvia are relatively well treated. Despite a high proportion of patients using beta blockers, HR control is insufficient. There is big gap (10 bpm) between mean actual HR of the patients and mean target HR that doctors want to achieve when planning to decrease it. HR above 70 bpm,

which is the level with proved increase of CV risk in CAD patients, was observed in a substantial proportion of treated angina patients. It was mainly due to suboptimal use of medication to achieve the target HR. Perception of a certain level of HR as high is crucial for making decision about a further HR decrease, but practitioners do not have a common view about the exact level of HR, which should be considered as high. Therefore, much remains to be done in order to establish HR as a treatment target, to increase awareness of benefits from HR reduction, and options to achieve target HR with pharmacological treatment.

## ACNOWLEDGMENTS

*This survey was supported by Servier. REALITY Latvia National Coordinator Andrejs Ērglis, investigators Gustavs Latkovskis, Iveta Mintāle and authors are grateful to all REALITY investigators: Vēsma Ārgale, Anīta Baika, Ludmila Basina, Solveiga Budrēviča, Gaļina Dormidontova, Veronika Ečina, Arčils Gersamija, Silvija Hansone, Inga Jasinkeviča, Maija Keiša, Māra Klovāne, Ausma Kondratoviča, Liga, Liepa, Ilga Lūse, Lija Mora, Natalja Pontaga, Ilze Sarmīte Rozentāle, Nadežda Rožkova, Irēna Aija Rubīne, Mārīte Skulte, Alla Soboļeva, Māra Stabulniece, Iveta Strižko, Larisa Timošina, Gunta Vēvere, Santa Viltēre, Māra Vītola, Ausma Vīva.*

## REFERENCES

- Anonīms (2008). Latvijas veselības statistikas gadagrāmata par 2007. gadu [Annual book of Latvian health statistics about 2007]. Veselības statistikas un medicīnas terminoloģiju aģentūra, 2008 (in Latvian).
- Anonymous (2003). The European trial on reduction of cardiac events with perindopril in patients with stable coronary artery disease investigators. Efficacy of perindopril in reduction of cardiovascular events in stable coronary artery disease: Randomised, double-blind, placebo controlled, multicentre trial (the EUROPA study). *Lancet*, **362**, 782–788.
- Anonymous (2004). World Health Organization. <https://apps.who.int/infobase/Comparisons.aspx>
- Anonymous (2008). The BEAUTIFUL Study Group. The BEAUTIFUL study: Randomized trial of ivabradine in patients with stable coronary artery disease and left ventricular systolic dysfunction — baseline characteristics of the study population. *Cardiology*, **110**, 271–282.
- Andrews, T.C., Fenton, T., Toyosaki, N., Glasser, S.P., Young, P.M., MacCallum, G., Gibson, R.S., Shook, T.L., Stone, P.H. (1993). The Angina and Silent Ischemia Study Group (ASIS). Subsets of ambulatory myocardial ischemia based on heart rate activity. Circadian distribution and response to anti-ischemic medication. *Circulation*, **88**, 92–100.
- Aronow, W.S., Ahn, C., Mercando, A.D., Epstein, S. (1996). Association of average heart rate on 24-hour ambulatory electrocardiograms with incidence of new coronary events at 48-month follow-up in 1,311 patients (mean age 81 years) with heart disease and sinus rhythm. *Amer. J. Cardiol.*, **78**(10), 1175–1176.
- Benetos, A., Rudnicki, A., Thomas, F., Safar, M., Guize, L. (1999). Influence of heart rate on mortality in a French population: Role of age, gender and blood pressure. *Hypertension*, **33**, 44–52.
- Boden, W.E., O'Rourke, R., Teo, K.T., Hartigan, P.M., Maron, D.J., Kostuk, W.I., Knudston, M., Dada, M., Casperson, P., Harris, C.L., Chaitman, B.R., Shaw, L., Gosselin, G., Navaz, S., Title, L.M. Gau, G., Blaustein A.S., Booth, D.C., Bates, E.R., Spertus, J.A., Berman, D.S., Mancini, J., Weintraub, W.S. for the COURAGE Trial Research Group. (2007). Optimal Medical Therapy with or without PCI for Stable Coronary Disease.

*New Engl. J. Med.*, **356**. This article (10.1056/NEJMoa070829) was published at www.nejm.org on 27 March 2007.

- Daly, C.A., Clemens, F., Lopez Sendon, J.L., Tavazzi, L., Boersma, E., Danchin, N., Delahaye, F., Gitt, A., Julian, D., Mulcahy, D., Ruzyllo, W., Thygesen, K., Verheugt, F., Fox, K.M. (2005). The initial management of stable angina in Europe, from the Euro Heart Survey: A description of pharmacological management and revascularization strategies initiated with the first month of presentation to a cardiologist in the Euro Heart Survey of Stable Angina. *Eur. Heart J.*, **26**, 1011–1022.
- Daly, C.A., De Stavola, B., Lopez-Sendon, J.L., Tavazzi, L., Boersma, E., Clemens, F., Danchin, N., Delahaye, F., Gitt, A., Julian, D., Mulcahy, D., Ruzyllo, W., Thygesen, K., Verheugt, F., Fox, K.M. (2006). Predicting prognosis in stable angina — results from the Euro Heart Survey of stable angina: Prospective observational study. *BMJ*, **332**, 262–267.
- Daly, C., Tavazzi, L., Fox, K., Euro Heart Survey of Angina Investigators (2008). Inadequate control of heart rate in patients with stable angina: Results from the European Heart Survey. *Eur. Heart J.*, **29** (Abstract Supplement), 204.
- Deedwania, P.C., Carbajal, E.V. (1992). Role of myocardial oxygen demand in the pathogenesis of silent ischemia during daily life. *Amer. J. Cardiol.*, **70**, 19F–24F.
- Diaz, A., Bourassa, M.G., Guertin, M.C., Tardif, J.C. (2005). Long term prognostic value of resting heart rate in patients with suspected or proven coronary artery disease. *Eur. Heart J.*, **26**(10), 967–974.
- Disegni, E., Goldbourt, U., Reicher-Reiss, H., Kaplinsky, E., Zion, M., Boyko, V., Behar, S. and the SPRINT study group (1995). The predictive value of admission heart rate on mortality in patients with acute myocardial infarction. *J. Clin. Epidemiol.*, **48**, 1197–1205.
- Ērglis, A., Kalvelis, A., Lejnicks, A., Dzērve, V., Latkovskis, G., Mintāle, I., Zakke, I., Rasa, I. (2007). *Kardiovaskulāro slimību (KVS) profilakses vadlīnijas* [Guidelines on cardiovascular disease prevention]. Rīga. 45. lpp. (in Latvian).
- Fox, K., Borer, J.S., Camm, A.J., Danchin, N., Ferrari, R., Sendon, J.L.L., Steg, P.G., Tardif, J.C., Tavazzi, L., Tendera, M., for a Heart Rate working Group (2007). Resting heart rate in cardiovascular disease. *J. Amer. Coll. Cardiol.*, **50**, 823–830.
- Fox, K., Ford, I., Steg, P.G., Tendera, M., Robertson, M., Ferrari R. (2008). Heart rate as a prognostic risk factor in patients with coronary artery disease and left-ventricular systolic dysfunction (BEAUTIFUL): A subgroup analysis of a randomised controlled trial. *Lancet*, **372**(9641), 817–821.
- Futterman, L.G., Lemberg, L. (1999). Heart rate is a simplistic marker of mortality in acute myocardial infarction. *Amer. J. Crit. Care*, **8**(3), 197–199.
- Gillman, M.W., Kannel, W.B., Belanger, A., D'Agostino, R.B. (1993). Influence of heart rate on mortality among persons with hypertension: The Framingham study. *Amer. Heart J.*, **125**(4), 1148–1154.
- Gislason, G.H., Rasmussen, J.N., Abildstrom, S.Z., Gadsboll, N., Buch, P., Friberg, J., Rasmussen, S., Kober, L., Stender, S., Madsen, M., Torp-Pederden, C. (2006). Long term compliance with beta-blockers, angiotensin-converting inhibitors, and statins after acute myocardial infarction. *Eur. Heart J.*, **27**, 1153–1158.
- Graham, I., Atar, D., Borch-Johnsen, K., Boysen, G., Burell, G., Cifkova, R., Dallongeville, J., De Backer, G., Ebrahim, S., Gjelsvik, B., Herrmann-Lingen, C., Hoes, A., Humphries, S., Knapton, M., Perk, J., Priori, S.G., Pyörälä, K., Reiner, Z., Ruilope, L., Sans-Menendez, S., Reimer, V.S.O., Weissberg, P., Wood, D., Yarnell, Y., Zamorano, J.L. (2007). European guidelines on cardiovascular disease prevention in clinical practice: Executive summary. *Eur. Heart J.*, **28**, 2375–2414.
- Hinderliter, A., Miller, P., Bragdon, E., Ballenger, M., Sheps, D. (1991). Myocardial ischemia during daily activities: The importance of increased oxygen demand. *J. Amer. Coll. Cardiol.*, **18**, 405–412.
- King, D.E., Everett, C.J., Mainous, A.G., Liszka, H.A. (2006). Long-term prognostic value of resting heart rate in subjects with prehypertension. *Amer. J. Hypertens.*, **19**(8), 796–800.
- Leal, J., Luengo-Fernandez, R., Gray, A., Petersen, S., Rayner, M. (2006). Economic burden of cardiovascular diseases in the enlarged European Union. *Eur. Heart J.*, **27**(13), 1610–1619.
- Mathers, C.D., Loncar, D. (2006). Projections of global mortality and burden of disease from 2002 to 2030. *PLoS Med.*, **Nov**, 3, e442.
- Menotti, A., Mulder, I., Nissinen, A., Giampaoli, S., Feskens, E.J., Kromhout, D. (2001) Prevalence of morbidity and multimorbidity in elderly male populations and their impact on 10-year all-cause mortality: The FINE study (Finland, Italy, Netherlands, Elderly). *J. Clin. Epidemiol.*, **54**, 680–686.
- Palatini, P., Benetos, A., Julius, S. (2006). Impact of increased heart rate on clinical outcomes in hypertension. Implications for antihypertensive drug therapy. *Drugs*, **66**, 133–144.
- Palatini, P., Casiglia, E., Julius, S., Pessina, A.C. (1999). High heart rate: A risk factor for cardiovascular death in elderly men. *Arch. Intern. Med.*, **159**, 585–592.
- Palatini, P. (2005). Heart rate: A strong predictor of mortality in subjects with coronary artery disease. *Eur. Heart J.*, **26**(10), 943–945.
- Panza, J.A., Diodati, J.G., Callahan, T.S., Epstein, S.E., Quyyumi, A.A. (1992). Role of increases in heart rate in determining the occurrence and frequency of myocardial ischemia during daily life in patients with stable coronary artery disease. *J. Amer. Coll. Cardiol.*, **20**, 1092–1098.

Received 19 July 2010

## AMBULATORO STENOKARDIJAS PACIENTU ĀRSTĒŠANAS UN SIRDS RITMA NOVĒROJUMS LATVIJĀ (*REALITY LATVIA*)

Novērojuma mērķis bija iegūt informāciju par ambulatori ārstētu stenokardijas pacientu populāciju Latvijā, noskaidrot pacientu profilu, sirds ritmu, stabilas stenokardijas ārstēšanas paradumus un pacientu dzīves kvalitāti. Vienas vizītes ietvaros tika apkasoti un iztaujāti 300 ārstēti stabilas slodzes stenokardijas pacienti. 30 kardiologi katrs ievāca datus par 1–15 pacientiem un aizpildīja gadījuma ziņojuma veidlapas. Datu analīzes laikā, atbilstoši jaunākajiem zinātniskajiem atzinumiem par palielinātu sirdsdarbības frekvenci, tika definēts līmenis virs 70 x/min. Vidējā sirdsdarbības frekvence bija 70,3 ± 11,3 x/min un 45% pacientu tā bija virs 70 x/min. Ārstu viedoklis par sirdsdarbības frekvenci atšķīrās, piemēram, frekvence starp 70 un 80 tika atzīta gan kā „normāla”, gan „uz robežas ar augstu”, gan „augsta”. Vidējā sirdsdarbības frekvence, ko ārsti plānoja sasniegt, bija 60,1 ± 4,7 x/min. Beta blokatori tika lietoti 91% gadījumos. Biežāk lietotie beta blokatori bija metoprolols (47% gadījumu) un bisoprolols (35% gadījumu). Vidējā dienas deva metoprololam bija 69,7 ± 30,1 mg dienā, bisoprololam — 5,3 ± 2,0 mg. Novērojuma rezultāti ļauj secināt, ka, neraugoties uz plašu beta blokatoru lietošanu, sirdsdarbības frekvences kontroles līmenis ir nepietiekams. Tas skaidrojams ar ārstu nepietiekamo izpratni par sirdsdarbības frekvences samazināšanu kā līdzekli stenokardijas ārstēšanas mērķu sasniegšanai un beta blokatoru lietošanu salīdzinoši mazās devās.