Current outpatient therapy of stable coronary artery disease in Switzerland

A countrywide investigation with focus on resting heart rate

Stéphane Cook, Jean-Christophe Stauffer, Otto M. Hess, Paul Erne

Summary

Principle: Stable coronary artery disease (CAD) is frequent in Switzerland. Heart rate plays a key role in the ischaemic cascade and its control remains a milestone in treatment of patients with symptomatic angina pectoris. The aim of the present study was to take a snapshot of the current cardiovascular risk profile and drug therapy of patients suffering from stable CAD in outpatient clinics in Switzerland, with special emphasis on resting heart rate (RHR) and its association with therapy, symptoms and quality of life.

Methods: Prospective cross-sectional survey at 28 cardiologist care practices in Switzerland. Diagnoses, cardiovascular risk factors, CAD history and baseline clinical examination were systematically registered. General wellbeing and incidence of angina pectoris on daily activities were estimated using a modified Seattle quality of life (QoL) questionnaire.

Results: Between February 2007 and July 2008, 283 patients (202 men and 81 women) with stable CAD were included. 126 patients (44%) presented an RHR of 70 bpm or more and composed the high RHR group, whereas 156 patients (56%) had an RHR <70 bpm. Frequency and severity of angina pectoris rise proportionally to RHR. Moreover, patients in the higher RHR group restrict their daily activities due to fear of angina pectoris occurrence.

Conclusions: Patients with stable CAD suffer from angina pectoris despite revascularisation procedures and intensive medical therapy. RHR correlates with the frequency and severity of angina pectoris and restricts both QoL and physical activity.

Introduction

Coronary artery disease (CAD) is the most frequent cause of hospitalisation and death in Switzerland [1]. CAD prevention and treatment is therefore of the utmost clinical significance. CAD is a multifactor disease process whose evolution is determined by the presence or absence of different factors. Factors associated with an increased risk of CAD are termed CAD risk factors. Factors associated with a decreased risk of developing CAD are considered "protective". Since the first Framingham study launched in 1948 [2, 3] several modifiable risk factors have been recognised such as diabetes mellitus, hypertension, dyslipidaemia, smoking, sedentary lifestyle or a diet rich in saturated fats. Controlling these risk factors separately will slow down the progression and extension of atherosclerotic disease. In parallel, epidemiological studies also demonstrated that a high resting heart rate was associated with an increase in cardiovascular mortality in the general population and in CAD-prone subjects [2–5]. Recently, a decrease in high resting heart rate in patients suffering from CAD has been found to lower cardiovascular mortality rates [6]. Consequently, high resting heart rate is a cardiovascular risk factor.

The aim of the present cross-sectional survey was to take a snapshot of the current cardiovascular risk profile and drug therapy of patients suffering from stable CAD in outpatient clinics in Switzerland, with special emphasis on resting heart rate and its association with therapy, symptoms and quality of life.

Material and methods

Enrolment criteria

The REALITY study (The cuRrent statE of Angina treatment in outpatient popuLation and heart rate monIToring surveY) was performed prospectively between February 2007 and July 2008. All Swiss cardiologists working in outpatient clinics were invited to participate in data collection and asked to recruit 10 random patients with stable CAD. From these, 28 Swiss cardiologists finally participated in the trial. All patients with known stable CAD were considered. Patients with unstable angina pectoris, overt heart failure or arrhythmia were excluded. All patients included provided written informed consent. The study fulfilled local ethics requisites and complied with the Declaration of Helsinki regarding investigations in humans.

Correspondence:
Prof. Stéphane COOK
Head of Cardiology
University of Fribourg
CH-1700 Fribourg
Switzerland
E-mail: stephanecook@mac.com

Data acquisition

Participants were assessed at baseline during a visit to their outpatient clinic. Resting heart rate was determined by digital palpation of the radial or carotid artery during 30 seconds according to European guidelines [7]. The physician in charge was then asked to fill in a standardised Case Report Form (CRF), which was then collected and analysed by an independent clinical research unit (Five Office Ltd, Clinical Research, Wetzikon, Switzerland) and reported to the investigators. The questionnaire contained 76 different items.

Definitions

Angina pectoris was defined as chest pain or discomfort due to coronary heart disease and scored in accordance with the Canadian Cardiovascular Society four-level system. Dyspnoea was defined as shortness of breath and graded according to the four-level classification of the New York Heart Association. Obesity was defined as BMI >27kg/m² according to the National Health and Nutrition Examination Survey (NHANES II).

Quality-of-life (QoL) assessments

Disease-specific quality of life was assessed by a simplified version of the Seattle angina questionnaire [8]. From the 76 items in the questionnaire 5 domains assessed physical limitation, anginal stability, anginal frequency, treatment satisfaction and disease perception.

Statistical analysis

Normally distributed variables were analysed by parametric tests and non-normally distributed data using non-parametric tests. Based on resting heart rate, the patients were divided into two groups: one group with resting heart rate lower than 70 bpm, one with resting heart rate similar or higher than 70 bpm. Continuous variables are expressed as mean ± standard deviation and differences were compared using Student's t test or Mann-Whitney test. Categorical variables are expressed as counts and percentages and differences were assessed by Fisher exact test or chi-square test, as appropriate. Analyses were performed using SAS/STAT® statistical software (2003, SAS Institute Inc., SAS Campus Drive, Cary, North Carolina 27513, USA). P-values are two-sided.

Results

During the study period 283 patients (202 men and 81 women) with stable CAD were included.

Table 1
Baseline patient characteristics.

Patients, n	All mean (%)	RHR <70 bpm	RHR ≥70 bpm	p-value (two-sided)
Cardiovascular risk factors	283	157	126	
Age, yrs [IQR]	69 [62, 78]	69 [62, 78]	69 [62, 78]	0.95
Males, n (%)	202 (71%)	112 (71%)	90 (71%)	0.99
Current smoking, n (%)	45 (16%)	20 (13%)	25 (20%)	0.10
Arterial hypertension, n (%)	191 (67%)	98 (62%)	93 (74%)	0.04
Dyslipidaemia, n (%)	222 (78%)	120 (92%)	102 (96%)	0.20
Obesity, n (%)	124 (44%)	58 (37%)	66 (52%)	0.01
Diabetes mellitus, n (%)	74 (26%)	33 (21%)	41 (33%)	0.03
History of coronary artery disease				
Previous MI, n (%)	84 (30%)	45 (29%)	39 (31)	0.68
Previous coronary revascularisation, n (%)	200 (71%)	117 (75%)	83 (66%)	0.11
- CABG, n (%)	35 (12%)	19 (12%)	16 (13%)	0.88
- PCI, n (%)	142 (50%)	85 (54%)	57 (45%)	0.14
- PCI + CABG, n (%)	23 (8%)	13 (8%)	10 (8%)	0.92
Duration of stable angina, yrs [IQR]	4.21 [0.51, 6.15]	4.15 [0.67,5.98]	4.28 [0.34, 6.20]	0.84
Frequency of angina pectoris, nb of events/week [IQR]	3.1 [1,4]	2.7 [1,3]	3.6 [1,5]	0.03
CCS Functional Classification of Angina, class [IQR]	1.95 [2, 2]	1.88 [1, 2]	2.03 [2, 2]	0.05
Physical examination				
Resting heart rate ≥70 bpm, n (%)	126 (45%)	–	–	–
Systolic blood pressure, mm Hg [IQR]	140.0 [128, 150]	137 [125, 145]	143.8 [130, 159]	0.003
Diastolic blood pressure, mm Hg [IQR]	80.8 [75, 88]	79.5 [75, 85]	82.5 [77, 90]	0.006
BMI, kg/m² [IQR]	26.8 [24.1, 29.0]	26.5 [24, 28.4]	27.2 [24.2, 29.6]	0.11

IQR denotes 25%–75% interquartile range; MI is for myocardial infarction; CABG for coronary artery bypass graft surgery; PCI, percutaneous coronary intervention; CCS, Canadian Cardiovascular Society Angina Classification.

Baseline patient and treatment characteristics

Baseline patient characteristics are summarised in table 1. Patients suffered from stable angina pectoris for a mean duration of 4.3 ± 5.7 years. One third had had myocardial infarction in the past; 70% underwent coronary revascularisation (50% percutaneous coronary intervention, 12% coronary artery bypass graft surgery, and 8% both). The average age was 69 ± 11 years. Active smoking was found in 16%, obesity in 44%, dyslipidaemia in 78%, hypertension in 67% and diabetes mellitus in 26%. Physical examination revealed an average blood pressure of $140 \pm 19 / 81 \pm 9$ mmHg. Body Mass Index was 26.8 ± 3.8 kg/m². The average resting heart rate was 69 ± 13 bpm.

126 patients (44%) presented a resting heart rate of 70 bpm or more and composed the high resting heart rate group, whereas 156 (56%) had a resting heart rate <70 bpm. Table 1 compares the baseline characteristics of the two groups. A finding of note was heart failure in 8.5% of the patients which was more frequent in patients with a higher resting heart rate (15 out of 126, 11.8%) than in patients with lower resting heart rate (8 of 157, 5.1%, p = 0.06). Table 2 summarises ongoing drug therapy. It was noteworthy, and although the total number of drugs was similar between the groups (4.26 ± 1.28 vs 4.51 ± 1.46, p = 0.13), patients in the higher resting heart rate group more frequently received calcium antagonist (45/157 or 30% vs 49 /126 or 40%, p = 0.07) and less probably a beta-blocker (127/157 or 81% vs 85/126 or 67%, p = 0.007) than patients in the other group. Moreover, 13% of the patients (7% vs 18%, p = 0.01) were not given beta-blockers due to contraindication.

Resting heart rate and angina pectoris

Frequency and severity of angina pectoris are summarised in figure 1. Number of angina pectoris events rises proportionally to resting heart rate. Particularly, patients with resting heart rate <70 bpm suffered from 2.7 ± 3.0 angina pectoris episodes/week, while patients in the higher resting heart rate group had 3.6 ± 3.4 episodes/week (p = 0.03). Interestingly, the mean heart rate increased in both groups (all: +9%; low RHR: +3% vs high RHR: +17%, p< 0.001) during follow-up.

Resting heart rate and quality of life (QoL)

Restriction of daily activities was found in 38% vs 26% (p = 0.02) of the patients in the higher vs lower resting heart rate group. This restriction was explained by fear of angina pectoris occurrence (table 3).

Discussion

Stable coronary artery disease is found in 3–5% of the general population in Europe and accounts for up to 6% of the consultations in primary care practices [9, 10]. The aims of treatment are to improve the quality of life and reduce both CAD-mediated morbidity (prevention of myocardial infarction and heart failure) and mortality. In this representative population of Swiss primary cardiologist care patients, we found the following: a) patients with stable CAD frequently suffer from angina pectoris episodes despite regular follow-up and expanded medical therapy; b) these episodes are associated with a decrease in quality of life and restriction in physical exercise due to fear of angina pectoris, c) half of the patients have an RHR higher than

Table 2
Drug treatment in stable CAD.

	All	RHR <70 bpm	RHR ≥70 bpm	p-value (two-sided)
Patients, n	283	157	126	
Nitrates, n (%)	143 (51%)	80 (51%)	63 (51%)	0.94
Calcium antagonists, n (%)	94 (34%)	45 (30%)	49 (40%)	0.07
Beta-blockers, n (%)	212 (75%)	127 (81%)	85 (67%)	0.007
Statin, n (%)	236 (84%)	126 (81%)	110 (88%)	0.13
Antiplatelet therapy, n (%)	279 (98.6%)	154 (98%)	125 (99%)	0.43

Table 3
Resting heart rate and quality of life.

	All	RHR <70 bpm	RHR >70 bpm	p-value (two-sided)
Patients, n	283	157	126	
Fear of angina pectoris events leads to limitation of physical activity, n (%)	87 (31%)	40 (26%)	47 (38%)	0.02
Regular physical activity, n (%)	152 (54%)	93 (60%)	59 (47%)	0.03
Angina pectoris at rest, n (%)	48 (18%)	25 (17%)	23 (19%)	0.72

Figure 1

Frequency and severity of angina pectoris. A) Comparison of frequency of angina pectoris events per week stratified by quartile of resting heart rate (p = 0.12). B) Comparison of severity of angina pectoris events in accordance with the Canadian Cardiovascular Society (CCS) four-level system stratified by quartile of resting heart rate. CCS 1: angina only during strenuous or prolonged physical activity. CCS 2: Slight limitation, with angina only during vigorous physical activity. CCS 3: Symptoms with everyday living activities. CCS 4: Inability to perform any activity without angina or angina at rest (p = 0.30).
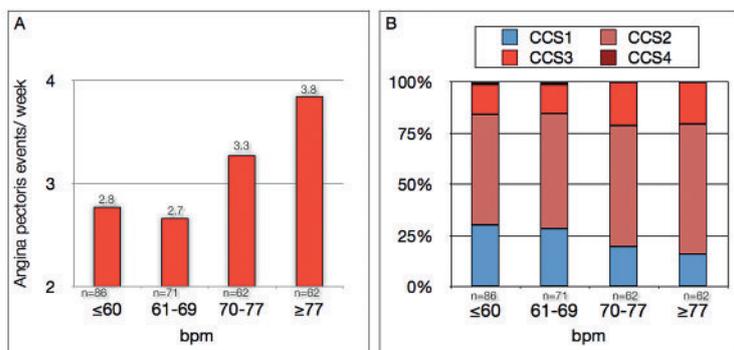
70 bpm; d) when comparing patients with RHR >70 bpm to patients with RHR <70 bpm, patients in the higher RHR group had more risk factors, suffer more frequently from angina pectoris, had a more reduced quality of life and exercise capacity than those in the lower RHR group.

Under low-dose beta-blocker therapy (average metoprolol dose: 68mg/d versus 150–200mg/d full dose; atenolol: 57mg/d versus full dose 100mg/d), the mean RHR of patients included in the present study was almost 70 bpm. This certainly reflects the reality in our country but is significantly higher than the RHR in patients with stable CAD recommended by current European [11] and American [12] guidelines (55–60 bpm in patients with stable CAD). In line with this finding, angina pectoris was more frequent and more severe in patients with higher RHR than patients with lower RHR. This is expected since heart rate regulates both myocardial oxygen demand and coronary perfusion: a high resting heart rate will shift the metabolic threshold towards ischaemia. Accordingly, several studies demonstrated that lowering heart rate also decreases the frequency and severity of angina pectoris in patients with stable CAD.

Moreover, angina pectoris appears to impact on quality of life and physical exercise; the worse the anginal symptoms, the more limited the physical function. This corroborates previous studies demonstrating that poor angina control decreases quality of life and increases cardiovascular events. In comparison to patients without repeated revascularisations after coronary angioplasty, Wever and collegues demonstrated that patients needing repeated revascularisations suffered more frequently from angina pectoris, had a lower quality of life and more limited physical exercise capacity [13]. Of the 934 patients included in the *Study of Economics and*

Quality of Life, Hlatky et al. found that patients with higher CCS scores had lower quality of life estimated by the Duke activity status index [14]. In addition, dimensions assessing physical wellbeing were more impaired in the higher RHR group compared with the lower RHR group, indicating that the severity of angina symptoms may affect these dimensions as well. Risk factor reduction and physical activity enhancement are effective means of mitigating CAD and disability. The present study reiterates the concept already found in the *Coronary Artery Surgery Study* registry by Diaz and colleagues [15], viz. patients with higher RHR are at higher risk of having more concomitant cardiovascular risk factors. As already discussed in one of our previous papers, high RHR probably belongs to the same spectrum of disease, with enhanced sympathetic stimulation and increased oxygen demands [5].

Finally, our study underlines a key concept: on the one hand, high RHR usually reflects limited physical capacity. On the other hand, because of fear of angina, patients with higher RHR are more prone to avoid physical activity. Therefore, high RHR perpetuates a vicious circle.

Study limitations

The study has major limitations which need to be considered when interpreting the data. The most important is the number of patients included in the study, which may not allow generalisation to all patients in our country. Secondly, paired nonparametric tests were used for comparisons of the higher and lower RHR groups, since the groups were considered to be dependent (matched for gender and age). Thirdly, beta-blockers were more frequently used in the group with lower RHR, and thus could have influenced the results of this study. Finally, the questionnaires were filled by the attending physician and this might introduce reporting biases such as overestimating quality of life.

Conclusions

Patients with stable CAD often suffer from angina pectoris despite revascularisation procedures and intensive medical therapy. This fact, well documented in the literature, has also been addressed in the Swiss population. Resting heart rate correlates with numbers of cardiovascular risk factors, frequency and severity of angina pectoris, and restricts both the quality of life and physical activity. Lowering elevated heart rate could therefore represent a valuable treatment and prevention strategy for these patients.

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