International Journal of Cardiology 257 (2018) 16–23

Contents lists available at ScienceDirect

International Journal of Cardiology

journal homepage: www.elsevier.com/locate/ijcard

Exercise electrocardiogram in middle-aged and older leisure time sportsmen: 100 exercise tests would be enough to identify one silent myocardial ischemia at risk for cardiac event

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ARTICLE INFO

Article history:
Received 12 July 2017
Received in revised form 5 October 2017
Accepted 19 October 2017

Keywords:
Exercise test
Prevention, sports, leisure time
Silent myocardial ischemia
Coronary artery disease

ABSTRACT

Background: The importance of exercise electrocardiogram (ECG) has been controversial in the prevention of cardiac events among sportsmen. The aim of this study was to determine the frequency of silent myocardial ischemia (SMI) from an exercise ECG and its relationship with induced coronary angiographic assessment and potentially preventable cardiac events.
Methods: This prospective cohort study included leisure time asymptomatic sportsmen over 35 years old, referred from 2011 to 2014 in the Sports Medicine Unit of the University Hospital of Saint-Etienne.
Results: Of the cohort of 1500 sportsmen (1205 men; mean age 50.7 ± 9.4 years; physical activity level 32.8 ± 26.8 MET-h/week), 951 (63%) had at least one cardiovascular disease (CVD) risk factor. Family history, medical examination and standard resting 12-lead were collected. A total of 163 exercise ECGs (10.9%) were defined as positive, most of them due to SMI (n = 129, 8.6%). SMI was an indication for coronary angiography in 23 cases, leading to 17 documented SMIs (1.1%), including 11 significant stenoses requiring revascularization. In multivariate logistic regression analysis, a high risk of CVD (OR = 2.65 [CI 95%: 1.33–5.27], $p = 0.005$) and an age >50 years (OR = 2.71 [CI 95%: 1.65–4.44], $p < 0.0001$) were independently associated with confirmed SMI.
Conclusions: The association of positive exercise ECG with significant coronary stenosis was stronger among sportsmen with CVD risk factors and older than 50 years. Screening by exercise ECG can lower the risk of cardiac events in middle-aged and older sportsmen. One hundred tests would be enough to detect one silent myocardial ischemia at risk for cardiac event.

Abbreviations: ACC, American College of Cardiology; ACSM, American College of Sports Medicine; AF, atrial fibrillation; AHA, American Heart Association; BMI, body mass index; CAC, coronary artery calcium; CAD, coronary artery disease; CI, confidence interval; CMR, adenosine cardiovascular magnetic resonance imaging; CHD, coronary heart disease; CVD, cardiovascular disease; CTA, coronary computed tomography angiography; EAPC, European Association for Preventive Cardiology; ECG, electrocardiogram; ENS, exercise nuclear stress testing; ESC, European society of cardiology; HCM, hypertrophic cardiomyopathy; HR, heart rate; iRBBB, incomplete right bundle branch block; LAD, left anterior descending; LBBB, left bundle branch block; LVH, left ventricular hypertrophy; MAP, maximal aerobic power; MET, metabolic equivalent of task; NST, nuclear stress test; OR, odds ratio; OSA, obstructive sleep apnea; PA, physical activity; PSB, premature supra-ventricular beat; PVB, premature ventricular beat; RCA, right coronary artery; SCD, sudden cardiac death; SD, standard deviation; SMI, silent myocardial ischemia; TTE, transthoracic echocardiography; USPSTF, US Preventive Service Task Force; WPW, Wolff-Parkinson-White.

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https://doi.org/10.1016/j.ijcard.2017.10.081
0167-5273/

1. Introduction

Regular aerobic exercise at moderate intensity leads to many health benefits [1,2], although vigorous exercise may be associated with a transiently increased risk of sudden cardiac death (SCD), revealing unsuspected cardiovascular disease (CVD) [3–5]. While the rate of sports-related SCD in young adults has been reported to be 1/100 000 subjects [6], this figure can increase up to 1/10 000 in those over the age of 35 who performed vigorous intensity physical activity (PA) [4,5]. Although the risk-benefit ratio advocates strongly in favour of regular PA, prevention of SCD may require a specific screening program among leisure time and competitive sportsmen. The present guidelines mainly concern athletes between 12 and 35 years and include medical history, physical examination with a debate about 12-lead resting electrocardiogram (ECG) [4–8]. For middle-aged sportsmen, the current recommendations vary widely, particularly for exercise ECG [9]. In the USA, the American Heart Association (AHA) [3,8,10], the American College of Cardiology (ACC) [10], the US Preventive Service Task Force (USPSTF) [11] and the American College of Sports Medicine (ACSM) [12,13] do not recommend routine exercise ECG in preparticipation screening. In Europe, however, the European Association for Preventive Cardiology (EAPC, formerly EACPR) recommends its use in specific groups [7].

In this context, this study assesses the relevance of screening asymptomatic leisure time sportsmen older than 35 years with exercise ECG, a population poorly investigated with regard to the risk of SCD [7], by including coronary angiography when needed to determine the frequency of exercise-induced silent myocardial ischemia (SMI).

2. Methods

2.1. Study population

The prospective cohort study included leisure time sportsmen over 35 years old who performed exercise ECG screening in the Sports Medicine Unit of the University Hospital of Saint-Etienne from September 2011 to August 2014. Inclusion criteria were to be referred as asymptomatic by their general practitioner for an exercise ECG screening test performed as a standard procedure to resume PA and/or as a systematic preparticipation' screening to be declared as sportsmen. Exclusion criteria were established CAD and uninterpretable ST segment because of a bundle branch block.

We systematically recorded personal and familial history recorded, physical examination, resting 12-lead ECG (Cardiosoft, GE Healthcare, CT, USA) and a maximal exercise ECG. The ethics committee (*IRBN372016/CHUSTE*) and the national commission for informatics and liberties (*CNIL165853*) approved the study.

2.2. Preparticipation screening

2.2.1. Cardiovascular risk factors

Cardiovascular risk factors were obtained through a modified and French translated version of the AHA Preparticipation Questionnaire [4,7]. Family history focused on premature SCD in first-degree relatives. Personal history evaluated risk factors for CVD [14] using SCORE index (European Systematic Coronary Risk Estimation), based on age, sex, total cholesterol, systolic blood pressure and smoking status [7,14].

2.2.2. Symptoms

Subjects with symptoms related to exercise (chest pain, palpitations, fainting, shortness of breath or abnormal dyspnoea, fatigue) were excluded [15].

2.2.3. Current level of physical activity

PA was quantified in weekly metabolic equivalent of task as (MET) and expressed in h/week (i.e., intensity in MET × duration × frequency), using the Compendium of Physical Activities, ranged from 0.9 (sleeping) to 18 MET (running at 17 km/h) [1,7]. The threshold values chosen to classify subjects into four groups were the following: (1) 7.5–14.9, (2) 15–29.9, (3) 30–59.9, and (4) ≥ 60 MET-h/week [1].

2.3. Resting 12-lead ECG

Resting 12-lead ECG performed in a supine position was analyzed by two independent readers using standardized criteria for athletes [2,6,15,16] and searching for variants such as: incomplete right bundle branch block, ST-T segment alteration or premature ventricular or supraventricular beats, atrial fibrillation of flutter. Disagreements were reviewed by a third reader.

2.4. Exercise ECG

2.4.1. Exercise ECG procedure

Cycle ergometer tests (Ergomedic, Monark, Sweden) were performed in the upright position using a progressive loading with steps ranging from 20 to 40 W every 2 min until exhaustion. Increment was adapted by gender, age and usual PA to achieve predicted maximal heart rate in 10–12 min under continuous monitoring [17].

Exercise ECG was considered maximal level if subjects (i) achieved 90% of their maximal predicted heart rate (220-age or 210-age for men and women, respectively), and (ii) reached a blood lactate level (YSI 2300 Stat plus, Xylem Inc., White Plains, NY, USA) ≥8 mmol/l as measured between 2 and 5 min of recovery.

2.4.2. Positive exercise ECG criteria

The criteria for a positive exercise ECG were defined as a 1.5-mm ascendant or as a 1-mm horizontal or downsloping ST segment depression occurring 80 ms after the J point, using PQ interval as the isoelectric line. It had to be noted in at least 3 consecutive beats and in at least 2 contiguous leads [18,19]. Exercise ECG was still defined as positive regardless of the amount of time the ST segment remains depressed during recovery.

Exercise-induced threatening arrhythmia was defined at the ventricular level as frequent (>10% of total QRS complexes), or polymorphic (>3 morphological features) and/or repetitive (ventricular triplets or bursts) ectopic ventricular activity. An intraventricular conduction abnormality was defined by the appearance of a complete left bundle branch block (LBBB) during exercise [8].

An abnormal blood pressure profile was defined as a lack of increase in systolic blood pressure from baseline during exercise, despite an increase in workload and a lack of decrease in systolic blood pressure from maximal exercise, despite the end of the exercise [20].

2.4.3. SMI assessment procedure after positive exercise ECG

After a positive exercise ECG, second line tests performed were nuclear stress testing (ENS) or coronary computed tomography angiography (CTA). Coronary angiography was performed in second line test only if SMI pre-test probability was high. Transthoracic echocardiography (TTE) was systematic. After a positive second line test, third line tests were performed as adenosine cardiovascular magnetic resonance imaging (CMR) if SMI probability was low or coronary angiography if SMI probability was high. SMI was defined as an obstructive coronary artery disease (CAD) with a diameter stenosis ≥50% by coronary angiography [4,5] (intermediate 50–70% and major >70%). Fractional flow reserve was not a routine measurement during coronary angiography in our settings.

2.5. Statistical analysis

The subjects' characteristics were analyzed using descriptive statistics and were reported as mean (± standard deviation, SD) and frequencies (%). Univariate analyses were conducted using chi-squared (or Fisher exact tests if statistical conditions were not satisfied) for categorical variables and Student's *t*-test (or Wilcoxon rank-sum tests if statistical conditions were not satisfied) for quantitative variables. Odds ratios (OR; confidence interval, CI 95%) were used to reflect odds of each studied variable in both steps (suspected and confirmed SMI) relative to baseline. Relationship between level of PA and ST segment depression in subjects who had positive exercise ECG was analyzed using chi-squared and linear regression. Multivariate logistic regression analysis was performed using suspected (Model A), then confirmed (Model B) SMI as a dependant variable. The explanatory variables were gender, age, PA levels, CVD risk factors, body mass index (BMI), SCORE, symptoms, resting ECG, maximal heart rate, maximal aerobic power (MAP), and test indication according to EAPC (Appendix A) [7]. All explanatory variables with $p < 0.2$ were included into the multivariate models, which were calculated using backward by elimination of nonsignificant variables.

All analyses were performed using SAS 9.3 (SAS Institute, Cary NC) where $p < 0.05$ was considered statistically significant. All tests were two-sided.

3. Results

3.1. Baseline characteristics

The study population included 1500 middle-aged sportsmen (Fig. 1), of which 1205 were men (80%). Mean age was 50.7 ± 9.4 years, ranging 35–80 years (Table 1).

3.1.1. Cardiovascular risk characteristics and symptomatology

Overweight (BMI > 25 kg/m^2) was one of the most common risk factors, concerning 40% of the subjects and 951 (63%) had at least one CVD risk factor (Table 1). There were 32 suspected valvular heart diseases, 13 uncontrolled resting hypertension and 16 other cardiac diseases.

3.1.2. Quantification of physical activity

Mean PA level was 32.8 ± 26.8 MET-h/week, which corresponds to an average of 5 h/week of vigorous sports activities. Most subjects