JACC: CLINICAL ELECTROPHYSIOLOGY VOL. ■, NO. ■, 2018

Harmful Effects of Exercise Intensity and Exercise Duration in Patients With Arrhythmogenic Cardiomyopathy

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ABSTRACT

OBJECTIVES The goal of this study was to explore the association between exercise duration versus exercise intensity and adverse outcome in patients with arrhythmogenic cardiomyopathy (AC).

BACKGROUND Vigorous exercise aggravates and accelerates AC, but there are no data assessing the harmful effects of exercise intensity and duration in these patients.

METHODS Exercise habits at time of diagnosis were recorded by standardized interviews in consecutive AC patients. Exercise >6 metabolic equivalents was defined as high intensity, and exercise duration was categorized as long if above median. Life-threatening ventricular arrhythmia (VA) was defined as aborted cardiac arrest, documented sustained ventricular tachycardia, ventricular fibrillation, or appropriate implantable cardioverter-defibrillator therapy.

RESULTS We included 173 AC patients (53% probands; 44% female; 41 ± 16 years of age). Median weekly exercise duration was 2.5 h (interquartile range: 2.0 to 5.5 h), and 91 patients (52%) reported high-intensity exercise. VA had occurred in 83 patients (48%) and was more prevalent in patients with high-intensity exercise than low-intensity exercise (74% vs. 20%, $p < 0.001$), and more prevalent in long-duration than short-duration exercise (65% vs. 31%, $p < 0.001$). High-intensity exercise was a strong and independent marker of VA, even when adjusted for the interaction with long-duration exercise (odds ratio: 3.8; 95% confidence interval: 1.3 to 11.0, $p < 0.001$), whereas long-duration exercise was not.

CONCLUSIONS High-intensity exercise was a strong and independent marker of life-threatening VA in AC patients, independent of exercise duration. AC patients could be advised to restrict their exercise intensity. (J Am Coll Cardiol EP 2018;■:■-■) © 2018 The Authors. Published by Elsevier on behalf of the American College of Cardiology Foundation. This is an open access article under the CC BY-NC-ND license (http://creativecommons.org/licenses/by-nc-nd/4.0/).

Arrhythmogenic cardiomyopathy (AC), also known as arrhythmogenic right ventricular cardiomyopathy, is an inheritable heart disease associated with a high risk of life-threatening ventricular arrhythmia (VA) and sudden cardiac death in apparently healthy young individuals. It is a disease of the cardiac desmosomes (1), with an estimated mutation prevalence of up to 1 in 1,000 (2). Dysfunctional desmosomes result in reduced wall-stress tolerance, which leads to cardiac remodeling with an early predilection of the right ventricle (RV), as well as involvement of the left ventricle (LV) (3).

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All authors attest they are in compliance with human studies committees and animal welfare regulations of the authors' institutions and Food and Drug Administration guidelines, including patient consent where appropriate. For more information, visit the *JACC: Clinical Electrophysiology* author instructions page.

Manuscript received December 4, 2017; revised manuscript received January 18, 2018, accepted January 19, 2018.

ABBREVIATIONS AND ACRONYMS

AC = arrhythmogenic cardiomyopathy

CMR = cardiac magnetic resonance imaging

ECG = electrocardiogram

ICD = implantable cardioverter-defibrillator

IQR = interquartile range

LV = left ventricle

MET = metabolic equivalent

RV = right ventricle

VA = ventricular arrhythmia

Regular physical activity is a cornerstone of a healthy lifestyle and is recommended to healthy adults (4). Athletes commonly exercise in vast excess of the recommended minimum doses (5) for healthy individuals. Vigorous exercise aggravates and accelerates AC disease, and athletes are overrepresented in AC patient cohorts (6–8). Athletes are accustomed to an active lifestyle and are often concerned about the inactivity and exercise restrictions recommended in the treatment guidelines during the past decade (9–11). There is no established exercise threshold associated with adverse outcome in AC, and data considering harmful effects of different types of exercise are lacking. Previous studies have reported the total exercise dose or perceived activity level of AC patients (6,12) without separating the impact of exercise intensity and exercise duration. We aimed to explore the impact of exercise intensity, exercise duration, and exercise dose on outcome in AC patients.

METHODS

STUDY POPULATION. We included consecutive patients diagnosed with AC at the Department of Cardiology, Oslo University Hospital, Rikshospitalet, Oslo, Norway, between January 2008 and November 2016 in an observational cohort study. Probands fulfilling AC diagnosis by the current Task Force Criteria (1) underwent genetic testing, and family members of probands with pathogenic mutations were screened and included if mutation positive (1). We defined a proband as the first person in a family to exhibit clinical symptoms or signs that triggered an evaluation of AC. Patients with heart or lung comorbidities were excluded. We performed a clinical examination and recorded any use of AC-related medication. VA, the primary outcome, was defined as a history of 1 or more of the following events: aborted cardiac arrest, documented sustained ventricular tachycardia (>100 beats/min, >30 s) (13) on electrocardiogram or Holter recordings or appropriate implantable cardioverter-defibrillator (ICD) therapy at last clinical follow-up. Appropriate ICD therapy was defined as antitachycardia pacing or shock therapy for documented ventricular tachycardia or ventricular fibrillation. VA and age at the first documented VA were recorded retrospectively by an independent observer blinded to exercise data. Cardiac function and dimensions, the secondary outcomes, were assessed by echocardiography and cardiac magnetic resonance imaging (CMR). Written informed consent was given by all patients, and the study complied with the Declaration of Helsinki and was approved by the Regional Committee for Medical Research Ethics in Norway.

EXERCISE. At time of diagnosis, we advised our AC patients to abstain from competitive sports (11). We interviewed all patients about their exercise habits immediately before their AC diagnosis, either by direct interview during their clinical visit or by telephone calls. Exercise was defined as physical activity performed on a regular basis during the past 3 years (14). Duration of exercise was defined as the actual time in motion and was expressed as average hours per week, which allowed for seasonal variation. Median duration of exercise in our cohort served as the cutoff to categorize exercise duration as short or long. Exercise intensity was assigned from the main reported exercise activity using the 2011 Compendium of Physical Activities (15) and was expressed as metabolic equivalents (METs). Patients were classified as regularly engaging in high-intensity exercise (>6 METs), for example, running, aerobics, fast swimming, or competitive sports (16), or low-intensity exercise (3 to 6 METs), for example, walking, dancing, or weight lifting. Regular physical activity <3 METs was not recorded as exercise. On the basis of exercise intensity and duration, we categorized patients into 4 groups:

1. Low-intensity and short-duration exercise (low/short);
2. Low-intensity and long-duration exercise (low/long);
3. High-intensity and short-duration exercise (high/short);
4. High-intensity and long-duration exercise (high/long)

The exercise dose was calculated by multiplying the exercise intensity in METs by the weekly exercise duration in hours and was expressed as MET-h/week (14).

ELECTROCARDIOGRAM. All patients underwent a 12-lead electrocardiogram (ECG) at the time of diagnosis, and major and minor criteria according to the 2010 AC Task Force Criteria (1) were assessed. A signal-averaged ECG was also obtained at the time of diagnosis (MAC 5000, GE Medical Systems, Milwaukee, Wisconsin) in a subgroup of patients. A pathological signal-averaged ECG was defined according to the 2010 AC Task Force Criteria (1).

CARDIAC MAGNETIC RESONANCE IMAGING. A subgroup of patients without contraindications, including noncompatible ICD leads, underwent CMR