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# Myocardial Fibrosis in Competitive Triathletes Detected by Contrast-Enhanced CMR Correlates With Exercise-Induced Hypertension and Competition History

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## ABSTRACT

**OBJECTIVES** This study analyzed the presence of myocardial fibrosis detected by late gadolinium-enhancement (LGE) cardiac magnetic resonance (CMR) in correlation with the performance of competitive triathletes objectified by an exercise test and individual competition history.

**BACKGROUND** Myocardial fibrosis detected by LGE CMR has been reported to occur in 0% to 50% of asymptomatic athletes. However, the cause and mechanisms of myocardial fibrosis are unclear.

**METHODS** Eighty-three asymptomatic triathletes undergoing >10 training h per week (43 ± 10 years of age; 65% male) and 36 sedentary controls were studied by using LGE and extracellular volume (ECV) CMR. Parameters of physical fitness were measured by spiroergometry. Triathletes reported their lifetime competition results.

**RESULTS** LGE CMR revealed focal nonischemic myocardial fibrosis in 9 of 54 (17%) male triathletes ($LGE^+$) but in none of the female triathletes ($p < 0.05$). $LGE^+$ triathletes had higher peak exercise systolic blood pressure (213 ± 24 mm Hg) than $LGE^-$ triathletes (194 ± 26 mm Hg; $p < 0.05$). Furthermore, left ventricular mass index was higher in $LGE^+$ triathletes (93 ± 7 g/m$^2$) than in $LGE^-$ triathletes (84 ± 11 g/m$^2$; $p < 0.05$). ECV in $LGE^-$ myocardium was higher in $LGE^+$ triathletes (26.3 ± 1.8%) than in $LGE^-$ triathletes (24.4 ± 2.2%; $p < 0.05$). $LGE^+$ triathletes completed longer cumulative distances in swimming and cycling races and participated more often in middle and Iron Man distances than $LGE^-$ triathletes. A cycling race distance of >1,880 km completed during competition had the highest accuracy to predict LGE, with an area under the curve value of 0.876 ($p < 0.0001$), resulting in high sensitivity (89%) and specificity (79%). Multivariate analysis identified peak exercise systolic blood pressure ($p < 0.05$) and the swimming race distance ($p < 0.01$) as independent predictors of LGE presence.

**CONCLUSIONS** Myocardial fibrosis in asymptomatic triathletes seems to be associated with exercise-induced hypertension and the race distances. There appears to be a safe upper limit, beyond which exercise may result in myocardial fibrosis. (J Am Coll Cardiol Img 2017;■:■–■) © 2017 by the American College of Cardiology Foundation.

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**ABBREVIATIONS AND ACRONYMS**

**CMR** = cardiac magnetic resonance

**ECV** = extracellular volume

**LGE** = late gadolinium enhancement

**LV** = left ventricle

**MOLLI** = modified look locker inversion recovery

**NT-proBNP** = N-terminal pro-B-type natriuretic peptide

**ROC** = receiver operating characteristic

**RV** = right ventricle

**$VO_{2max}$** = maximal oxygen uptake

Moderate regular exercise has beneficial effects on the cardiovascular system, and regular activity is recommended for primary and secondary prevention of cardiovascular diseases (1,2). On the other hand, exercise is also associated with sudden cardiac death during or immediately after physical exertion in a minority of athletes (3,4). Currently, it is unclear whether there is a safe upper limit beyond which the potential negative effects of exercise may outweigh its benefits (5).

Cardiac magnetic resonance (CMR) imaging is well suited to study the adaptive changes of athletes' heart, including alterations of left and right ventricular volumes and mass and function related to training (6,7). Late gadolinium enhancement (LGE) detects areas of focal myocardial fibrosis, which has been reported to occur in 0% to 50% of asymptomatic athletes (8–14). Extracellular volume (ECV) imaging by T1 mapping CMR assesses diffuse myocardial fibrosis, which is missed by LGE (15,16). Recent validation studies showed good agreement between ECV and myocardial fibrosis quantified by histology (17,18), and an increased ECV was found to be an independent predictor of death and cardiac events (19). The cause of myocardial fibrosis in athletes remains speculative. Objective information about the athlete's actual physical fitness by exercise test and long-term competition history could give insight into the mechanisms of myocardial scarring, but that information is scarce (8–10). Furthermore, most previous LGE CMR studies examined only male athletes, neglecting the growing proportion of female competitive athletes (8,9,11,12).

The purpose of this study was to analyze presence, localization, and extent of focal and diffuse myocardial fibrosis obtained by LGE and ECV CMR in competitive male and female triathletes. We hypothesized that the presence of myocardial fibrosis is correlated with the performance of triathletes objectified by an exercise test and individual competition history.

## METHODS

**TRIATHLETES AND CONTROLS.** The institutional ethics committee approved this study, and all subjects gave written informed consent. Triathletes were contacted through advertisement at local triathlon clubs, and the athletes were included if they trained for a minimum of 10 h per week and if they had regularly participated in triathlons at various distances in the previous 3 years. Triathletes were asked to report their lifetime competition history, including distances completed during swimming, cycling, and running and the finishing time of each competition by using a standardized questionnaire. Control subjects were eligible if they exercised less than 3 h per week. Study exclusion criteria were contraindications for CMR or any systemic diseases. Two triathletes with known arterial hypertension were excluded from the study. All triathletes and controls did not have any cardiovascular diseases and reported no intake of any cardiac or illicit medication. All subjects underwent the CMR study before the exercise test, which was performed on the same day. All subjects were instructed to arrive rested, having not exercised, and having not consumed alcohol in the preceding 72 h. Any food and caffeine intake was restricted to 3 h preceding the CMR. The exercise test was performed 3 h after CMR. Blood samples were drawn immediately before the CMR from an antecubital vein, with the subject in the supine position for 5 min, to obtain concentrations of hematocrit, creatine kinase, high-sensitivity troponin T, and N-terminal pro-B-type natriuretic peptide (NT-proBNP).

**CMR PROTOCOL.** CMR was performed using a 1.5-T Achieva scanner (Philips Healthcare, Best, the Netherlands). The CMR protocol included standard steady-state free-precession cine CMR in the short axis for left ventricle (LV) and right ventricle (RV) volumetry and LV mass. T1 mapping was performed using a Modified Look Locker Inversion Recovery (MOLLI) sequence with a 5s(3s)3s scheme on 3 short-axes slices (apical, mid, and basal) before and 15 min after administration of contrast medium (20). At 10 min after a bolus injection of 0.2 mmol/kg gadoterate meglumine (Dotarem, Guerbet, Sulzbach, Germany) at a rate of 2.5 ml/s, end-diastolic LGE images were acquired using phase-sensitive inversion recovery (PSIR) sequences in short-axis orientation covering the entire heart and in 2-, 3-, and 4-chamber views.

**CMR DATA ANALYSIS.** Two investigators independently and blindly analyzed each CMR using cvi42 software (Circle Cardiovascular Imaging Inc., Calgary, Alberta, Canada). CMR parameters were indexed to the subject's calculated body surface area and are given as the mean of the 2 investigators' measurements. Evaluation of LV and RV volumes and LV mass was performed in standard fashion using short-axis cine images (21). Focal myocardial fibrosis was quantified by short-axis LGE images using a threshold method with a cutoff of >5 standard deviations (SD)