Apparent sex differences in risk of life-threatening events in arrhythmogenic cardiomyopathy are related to exercise habits

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On behalf: Center for Cardiological Innovation

Topic(s):
Myocardial Disease – Clinical: Arrhythmogenic Right Ventricular Cardiomyopathy

Funding Acknowledgements:
This study was supported by Center for Cardiological Innovation funded by the Norwegian Research Council

Background: Arrhythmogenic cardiomyopathy (AC) is an inheritable heart disease characterized by high risk of ventricular arrhythmias and exercise intolerance. Male sex is associated with higher risk of life-threatening events. However, this may be challenged by the fact that men exercise more than women.

Purpose: To assess whether the sex differences in arrhythmic outcome in AC-patients are driven by sex differences in exercise exposure.

Methods: We included AC-patients diagnosed between 1997 and 2017 in a longitudinal cohort study. We assessed exercise habits during the preceding 3 years before inclusion, and exercise dose was expressed as metabolic equivalent hours per week (MET-hours/week). Life-threatening events were defined as sustained ventricular tachycardia, aborted cardiac arrest or appropriate therapy from an implantable cardioverter-defibrillator at the time of diagnosis and prospectively during follow-up.

Results: We included 170 AC-patients (52% probands, 44% female, age 41±16 years). Males had higher exercise doses than female patients (36 [IQR, 14 to 54] vs. 12 [IQR, 8 to 22] MET-hours/week; P<0.001). Fifty-seven patients (34%) had previous life-threatening events, and 45 (26%) had life-threatening events during 5.7 (IQR, 2.8 to 9.4) years of follow-up. Male sex seemed to be a marker of previous life-threatening events (OR 2.0 [95% CI, 1.0 to 3.8]; P<0.05), but not when adjusted for exercise dose (Adjusted OR 1.3 [95% CI, 0.6 to 2.7]; P=0.44). Male sex also seemed to be a predictor of life-threatening events during follow-up (HR 2.0 [95% CI 1.0 to 3.9]; P=0.04) (Figure, left panel), but not when adjusted for exercise dose (Adjusted HR 1.5 [95% CI 0.8 to 3.0]; P=0.26) (Figure, right panel).

Conclusions: Sex differences in arrhythmic risk in AC were attributable to higher exercise doses in male AC-patients. This highlights the importance of exercise assessment in these patients, and challenges the current opinion of male sex as a risk factor in itself. Risk stratification based on sex may underestimate the risk of physically active female AC-patients.
Abstract: P3681

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