Letter to the Editor

Does endurance exercise cause atrial fibrillation in women?

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Prolonged endurance sport practice might increase the risk of atrial fibrillation (AF), possibly caused by myocardial and autonomic adaption to exercise [1]. As recently addressed by Turagam et al., questions regarding the duration, intensity and type of exercise that increase the risk of AF, and the natural history of the arrhythmia in athletes, still remain unanswered [2]. In addition, there is a lack of data on gender differences in the association between endurance exercise and AF.

We are aware of two studies that have investigated the risk of AF by physical activity (PA) in women exclusively. Everett et al., demonstrated a modestly reduced risk of AF in physically active women [3]. The effect was attenuated by body mass index (BMI), suggesting that the association might be explained by weight reduction related to PA. In the Women’s Health Initiative Observational Study, PA reduced the risk of AF and modified the association between obesity and AF [4]. Also in the Cardiovascular Health Study, that included >3000 women, PA was associated with a reduced risk of AF [5]. Physiological adaptations to PA and exercise are, however, likely to differ between individuals engaging in leisure-time activities and athletes exposed to prolonged endurance exercise, and few women have been included in exercise studies. In a Swedish study, repeated participation in the 90-kilometer cross-country ski race Vasaloppet was associated with increased risk of AF in men, but not in women [6].

We recently demonstrated a gradually increased risk of AF by cumulative years of regular endurance exercise in Norwegian men aged ≥53 years [7]. Of 2501 female invitees to this cohort study, 371 participated in a 54-kilometer cross-country ski race in 1999. The remaining 2130 had participated in a population-based health study and were invited in order to cover the range of exposure from physical inactivity to prolonged endurance sport practice. During 2012, 286 female veteran skiers and 1393 women from the general population filled out an identical questionnaire. Informed consents were obtained. The study was approved by the Regional Committee for Medical and Health Research Ethics and complied with the Declaration of Helsinki. The methods of the study have been described in detail previously [7]. AF, exercise, comorbidity and other possible confounding factors were self-reported. Regular endurance exercise was defined as bouts of ≥30 min ≥three times per week with the purpose of increasing endurance capacity. Odds ratios (ORs) with 95% confidence intervals for self-reported AF were calculated by using weighted multivariable logistic regression analysis. Women aged >75 years were excluded in order to reduce recall bias.

In total, 110 out of 1449 women included in this analysis had AF. The prevalence of self-reported AF among female veteran skiers (n = 278, mean age 62 (53–75) years) was 8%. While 815 had never exercised regularly, 634 had exercised at some point of life, 89 of them regularly for ≥40 years. Table 1 shows characteristics of the study participants by category of endurance exercise. Women who had never exercised regularly were older compared to women who had exercised at some point of life. Women who had exercised ≥20 years had lower BMI, less hypertension and less lipid-lowering treatment than women who had exercised <20 years. Table 2 shows the number of AF cases and crude and adjusted ORs for AF by category of regular endurance exercise. Although not statistically significant, the crude analysis suggests a U-shaped association, with the lowest estimate in women who had exercised regularly for 20–39 years. After multivariable adjustment, women who had exercised regularly for ≥40 years had an increased risk of self-reported AF (n = 9) of borderline significance, compared to women who had never exercised. The other categories of exercise were not associated with AF.

At present, no conclusions can be drawn regarding the association between endurance exercise and risk of AF in women. Some physiological and culturally determined gender differences, however, might influence this association: the age-adjusted prevalence of AF is lower in women compared to men [8], and AF prevalence depends largely on the prevalence of established risk factors in studied populations. In our study, women were younger and had lower prevalence of concomitant heart diseases, hypertension and diabetes mellitus compared to men.
Furthermore, gender differences in the exposure to exercise are likely to play a role. A few decades ago, women were not allowed to participate in many endurance sports events. As AF is most likely to occur after prolonged exercise and years after the exposure, insufficient follow-up time and a low number of endpoints are possible explanations for the lack of an association between exercise and AF in women. In the study of participants in Vasaloppet, only 12 women developed AF during the follow-up time of >50,000 person-years [6]. Women might also be less attracted to exhausting endurance sport practice, have a more balanced relation between exercise and other activities, and be less prone to passionate exercise behavior and exercise addiction.

Although not fully understood, atrial remodeling and autonomic imbalance are among the suggested underlying mechanisms for AF in athletes. Atrial morphological and functional changes have been demonstrated in female athletes [9], but in a recent study, female veteran athletes had less pronounced atrial remodeling, lower sympathetic tone and lower blood pressure than their male counterparts [10]. Women have physiologically lower heart rates, but low heart rates seem to predict AF only in men [11,12]. Finally, the interplay between endurance exercise, sex hormone release and electrophysiological gender differences remains an unexplored field.

The result of our analysis indicates that prolonged endurance exercise might cause AF also among athletic women. Our study demonstrates that women still represent a minority of participants in endurance sport events. However, the number of female endurance athletes has increased, and we believe that a sample size sufficient to study the association between endurance sport practice and risk of AF in women could be reached through international collaboration. Future studies should include female athletes and investigate gender differences in the association between endurance exercise and risk of AF.

### Conflict of interest

Marius Myrstad has received a speaker fee from MSD. The other authors report no relationships that could be construed as a conflict of interest.

### References