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INVITED EDITORIAL

Cardiovascular screening of master athletes: insights from the Master Athletes Screening Study

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This editorial refers to 'Masters athlete screening study (MASS): incidence of cardiovascular disease and major adverse cardiac events and efficacy of screening over five years', by B.N. Morrison *et al.* https://doi.org/10.1093/eurjpc/zwad090.

The master athlete (MA) is generally an individual ≥35 years old who trains and participates in specifically designed competitions. Master athletes are former professional athletes who wish to continue competition, usually in a different sport, or individuals who return to competitive sports after a period of inactivity or who decide to start training systematically in adult life to improve their fitness. While the systematic practice of physical activity matches with the holistic concept of active ageing, the ever-increased participation of MAs in competitions requires tailoring an appropriate pre-participation screening (PPS) that addresses the increased cardiovascular (CV) risk of this population.[1] Cardiovascular prevention is a lifelong process from the cradle to the grave and beyond,[2] but if paediatric athletes are predominantly affected by congenital and genetic diseases,[3] MAs are mainly affected by coronary artery disease (CAD); ischaemic and non-ischaemic myocardial fibrosis; supraventricular tachyarrhythmias, in particular atrial fibrillation; and aortic dilatation.[1]

In this issue, Morrison *et al.*[4] present the results of the Master Athletes Screening Study (MASS), a 5-year prospective study, which represents an important step forward in the definition of an appropriate PPS protocol in MAs, a growing athletic population. The inclusion criteria were not very strict, as eligible participants had to engage in moderate to vigorous intensity physical activity at least 3 days per week during the preceding 3 months.[4] The authors included 798 MAs who underwent CV screening on a yearly basis including personal and family history, sport practice and the use of drugs,[5] 12-lead electrocardiogram (ECG), resting blood pressure, anthropometrics, and Framingham Risk Score (FRS). Those presenting abnormal findings underwent stress ECG (Stage 2) and/or a consultation with a sports cardiologist or other evaluations (Stage 3). The participants were then followed up for 4 years to record major adverse cardiac events (MACE) (sudden cardiac arrest/death, myocardial infarction, stroke), and additional CV diagnoses, as arrhythmias (37%), which were the most common finding during follow-up. Major adverse cardiac events occurred despite yearly screening in 10 male MAs (2.8/1000 athlete-years) who had an abnormal cardiac screening, but cardiac functional tests (i.e. echocardiogram, electrocardiogram, nuclear) failed to detect the underlying CAD in most cases. It is useful to point out that 90% of athletes who had MACE had an FRS ≥10%. Therefore, the authors concluded that the use of computed coronary tomography angiography (CCTA) might be appropriate in MAs with an FRS ≥10% or a suspicious CV screening. The conception of the MASS study and enrolment began in 2015, before the emergence of the cornerstone papers of Merghani *et al.*[6] and Aengevaeren *et al.*,[7] which demonstrated an increased prevalence of calcified coronary atheromatic lesions in endurance MAs with a low atherosclerotic risk profile. Therefore, the use of CCTA was far from being established in this special population at the time of the study, even when mild abnormalities were found in the screening tests. In addition, the COVID-19 pandemic has negatively impacted the follow-up and reduced access to healthcare facilities. Nonetheless, the complex relationship between long-term endurance sport activity, CAD, and MACE is far from being completely understood. *De iure* physical activity and exercise are the best ways to improve the management of CV risk factors such as sedentary habits, obesity, dyslipidaemia, and hypertension and to decrease the risk of MACE; *de facto* different studies[6,7] have reported an increased prevalence of CAD, mostly calcified coronary plaques, in middle-aged MAs, even with a low CV risk profile. In 2017, Merghani *et al.*[6] included a population of 152 MAs (70% male, 54.4 ± 8.5 years) and 92 controls, all with a low FRS, who underwent a complete CV evaluation, including CCTA and FRS. While most participants (≥60%) of both groups had a normal coronary artery calcium (CAC) score, only male athletes showed a CAC ≥ 300 Agatston unit and a luminal stenosis ≥50%. Unexpectedly, the total years of training was the only independent variable associated with a higher CAC; sedentary controls mainly showed mixed morphology plaques.[6] In the same year, Aengevaeren *et al.*[7] evaluated 284 men (55 ± 7 years) and half of them showed CAC, with a median CAC score of 35.8 (interquartile range 9.3–145.8). Again, athletes with a lifelong exercise volume >2000 MET-min/week or practicing very vigorous intensity exercise (≥9 MET) showed a higher CAC score and prevalence of CAC. The most active athletes demonstrated a more benign composition of plaques, with a low prevalence of mixed plaques and more often only calcified plaques,

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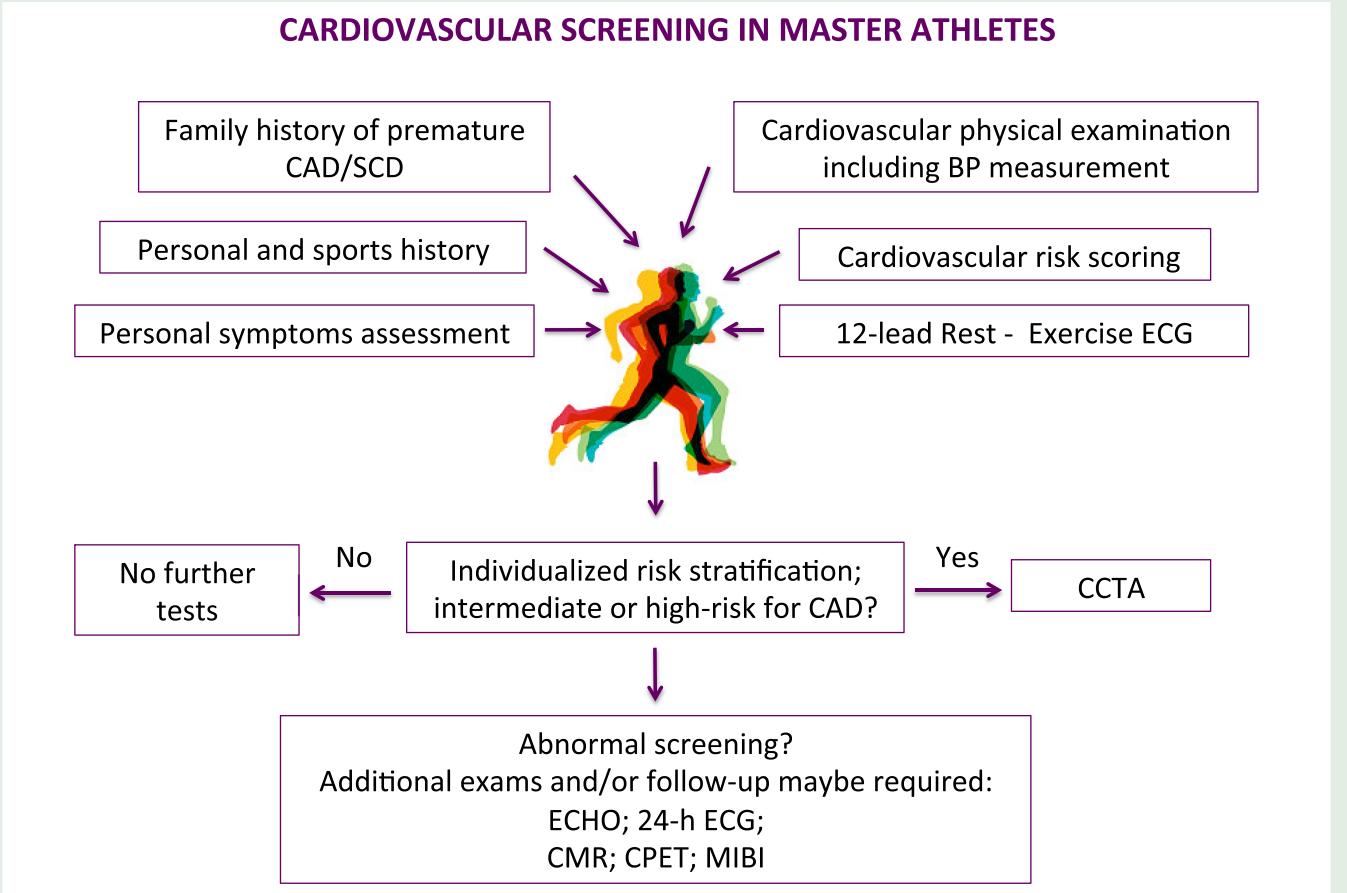

Figure 1 Cardiovascular screening in the master athletes. CAD, coronary artery disease; CCTA, computed coronary tomography angiography; CMR, cardiac magnetic resonance; CPET, cardiopulmonary exercise test; MIBI, 99Tcm-sestamibi scintigraphy. Vector Image courtesy of FreeDigitalPhotos.net.

than less active individuals.[7] Both these articles were in favour of a more prevalent coronary calcification in asymptomatic MAs that should be considered as a benign phenotype, possibly in relation to a mechanical effect of increased haemodynamics of the coronary flow during exercise. Then came the very recent Master@Heart study, which prospectively enrolled 191 lifelong master endurance athletes, 191 late-onset athletes (who started practicing sport >30 years old), and 176 healthy non-athletes, who were 100% male, with a median age of 55 years, with a low CV risk profile, and who underwent CCTA.[8] That is when it all changed. When compared with healthy active controls with a similar low CV risk, lifelong endurance athletes did not show a more benign phenotype; in contrast, they showed more risk-prone coronary plaques, both calcific and non-calcific, even in proximal segments. Unexpectedly, lifelong endurance practice did not offer additional protection against CAD: it was associated with ≥1 non-calcified proximal plaque [odds ratio (OR) 2.80, 95% confidence interval (CI) 1.39–5.65] and ≥1 mixed plaque (OR 1.78, 95% CI 1.06–2.99) when compared with a healthy lifestyle, while late-onset athletes stood in the middle.[8] The Master@Heart lifelong athletes are a different population compared with those in previous studies,[4,6,7] as they have a higher CV fitness, are mostly cyclists, and the control population is composed of active individuals and not sedentary subjects. Apparently, in the Master@Heart study,[8] the relationship between the effects of exercise and the presence of coronary plaques demonstrates the presence of an adaptive response when an appropriate dose of exercise is delivered, while at the extremes (sedentary habit and lifelong endurance), it may become maladaptive. Are we sure that extreme endurance exercise is maladaptive and avoiding it will save athletes from MACEs? We do not have answers, but what the MASS study[4] teaches us today is that MAs are not protected from CAD, neither are we adequately screening them with first-line PPS. We must be aware that CAD can be present even in athletes with a low FRS; therefore, in the presence of a clinically suspicious or an abnormal PPS or a high-risk score, the presence of CAD must be ruled out (*Figure 1*), and CCTA offers the best way to evaluate the coronary tree, the presence of plaques, their morphology, and their extent.[8] Nowadays, CCTA is becoming the first-line investigation in the diagnosis of CAD and its haemodynamic impact with the use of the fractional flow reserve, with a sensitivity of 97% and a specificity of 78%, as reported by a recent meta-analysis.[9] But hopefully in the immediate future, quantitative imaging biomarkers might help us to better characterize tissue features to identify the vulnerable plaques and be more effective in decision-making. In fact, the probability of having an acute coronary syndrome is based on both adverse plaque characteristics and adverse haemodynamic characteristics, lesions with both components own the higher risk.[10] Longitudinal studies such as the MASS study are definitely urged in this special population to correctly evaluate the CV risk. An effective CV prevention is crucial for promoting an healthy CV ageing.

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