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Editorial

New evidences recommend an active lifestyle in young HCM patients

Historically, after the pivotal investigations by BJ Maron, HCM has been considered the number 1 killer in young competitive athletes. Indeed, pioneering pathologic investigations from the Minneapolis Institute Foundation confirmed HCM as the most common substrate for sudden cardiac death (SCD) in young people engaged in vigorous sport activities [1].

Several mechanisms were postulated to explain the susceptibility to SCD in association with effort, including the epinephrine surge, which over a pathological substrate (i.e., myocardial disarray and scarring) may trigger ominous ventricular tachyarrhythmias. Furthermore, dehydration and electrolyte imbalance during intensive exercise further enhance the arrhythmic risk.

These early observations instilled the clinical perception that athletes dying suddenly were most commonly male, black, basketball players with HCM.

Only recently this tenet has been challenged by new pathologic investigations reporting a much lower proportion of SCDs attributable to HCM (6%–16%) [2,3].

Other than just pathologic reports, novel evidences derived from the clinical practice have challenged the perception of a detrimental effect of exercise and sport on the outcome of HCM.

Already in 1994, BJ Maron described a cohort of 14 patients (30–66 years), with fortuitus diagnosis of HCM, who competed in marathon, swimming, triathlon, basketball and football. Of note, none of these patients' developed symptoms, experienced disease progression or died suddenly [4]. As recently as in 2021, we described a cohort of 88 HCM-athletes, aged 31 ± 14 years, largely males, with low-risk profile, engaged in regular exercise training (≥6 h/week; >8 months/year), who had participated in competitions for 1 to 38 years (mean, 15 ± 10 years) [5]. During the follow-up of 1 to 22 years (mean 7 ± 5), 61 of the 81 patients quitted sport, as advised by their physicians, while 27 persisted in their usual, intensive training. Survival analyses showed no difference in mortality or a combined endpoint including cardiac events/symptoms among HCM patients who discontinued or persisted in vigorous activity [5]. Our results are in agreement with analysis performed by Hougaa et al. [6] in 121 patients with HCM, of whom 44 (36%) were actively engaged in sport. Kaplan Meier analysis showed no difference in age at first arrhythmic event between athletes vs. non-athletes HCM (log rank $p = 0.36$). Being an athlete was not a determinant for ventricular arrhythmias at univariate analysis, or when adjusted for global longitudinal strain and maximal LV wall thickness in multivariable analysis. Further reassurance was prompted by the prospective, observational ICD Sports Safety Registry [7]. Among 372 athletes receiving ICDs on the basis of standard criteria, 65 had HCM, and 13 (22%) of them were engaged in high-level and competitive sport. During a median follow-period of 31 months, there were no deaths or resuscitated tachyarrhythmias during or after sports participation. Of the 65 HCM patients, only one received an appropriate shock, during practice.

In conclusion, although evidence is still scarce, mounting number of observations suggest that the risk associated with exercise and sports in HCM patients is lower than estimated over a decade or two ago. In this context, there is great expectation for an ongoing study (LIVE-HCM, NCT02549664) planned to determine how active lifestyle and regular exercise program impact the well-being of individuals with genetic cardiovascular conditions including HCM. Moreover, the Dallas High Intensity Exercise for Increasing Fitness in Patients with Hypertrophic Cardiomyopathy (HIIT-HCM) Pilot Study has been designed to examine the efficacy of a supervised high-intensity exercise in adults with HCM.

Waiting for the results of these ongoing studies, we sought with great interest the report by .. in the current issue of the Journal [8], describing the effects of exercise training during childhood and adolescence in carriers of HCM-pathogenic genetic variants. Namely, in 187 participants with HCM or an HCM-causative genotype, the global amount of exercise training participated from childhood to the time of examination was compared with the morphologic features and diastolic functional properties examined by echocardiography. Notably, the magnitude of exercise training performed was correlated with a more favorable LV relaxation and filling profile and end-diastolic LV volume, when adjusting for the effects of age at examination, and presence of myocardial hypertrophy. This correlation was present even in patients with a clear HCM phenotype, but more evident in individuals with an HCM-causative genotype without LV hypertrophy, with best diastolic function seen in the genotype+ LVH- group. These results suggest that exercise training initiated during childhood and adolescence does have a positive effect on diastolic function in individuals with HCM and even more in those with HCM-causative genotype.

A support to these observations may be found in previous animal studies that showed a beneficial effect of exercise training on myocardial tissue structure and global cardiac stiffness [9]. Specifically, genetically modified mice with a HCM-causative variant undergoing regular exercise had myocyte organization similar to wild type mice, while sedentary HCM mice had significant myocyte disarray.

Support to this observation can be found also in human studies. Namely, in a large cohort of young HCM patients, Sheikh et al. observed that majority of athletes-HCM presented a larger LV cavity size and better diastolic function compared to sedentary HCM [10].

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Overall, these data suggest that exercise training had no apparent effect on worsening the focal fibrosis, but potentially reverts it towards normality in the early stages of cardiac development. If these results will be confirmed in further observations in larger cohort of HCM patients, it will become obvious that exercise training should be advised early in life of HCM individuals, before the phenotype development, in order to preserve the diastolic function later in life.

In consideration that majority of HCM patients are currently discouraged from participating in exercise programs and, as consequence, obesity and metabolic disorders are growing exponentially in these patients, it is time now for physicians to change their attitude and endorse, rather than restrict, participation in exercise programmes and sport in HCM patients, especially in those with HCM-causative genotype, as an essential lifestyle component and source of long-term benefits.

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Antonio Pelliccia*
Institute of Sport Medicine, Rome, Italy

* Corresponding author at: Institute of Sport Medicine, Largo Piero Gabrielli 1, Rome 00197, Italy.
E-mail address: antonio.pelliccia@coni.it.