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Young athletes: Preventing sudden death by adopting a modern screening approach? A critical review and the opening of a debate



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ABSTRACT

Preventing sudden cardiac death (SCD) in athletes is a primary duty of sports cardiologists. Current recommendations for detecting high-risk cardiovascular conditions (hr-CVCs) are history and physical examination (H&P)-based. We discuss the effectiveness of H&P-based screening versus more-modern and accurate methods. In this position paper, we review current authoritative statements and suggest a novel alternative: screening MRI (s-MRI), supported by evidence from a preliminary population-based study (completed in 2018), and a prospective, controlled study in military recruits (in development).

We present: **1. Literature-Based Comparisons** (for diagnosing hr-CVCs): Two recent studies using traditional methods to identify hr-CVCs in >3,000 young athletes are compared with our s-MRI-based study of 5,169 adolescents. **2. Critical Review of Previous Results:** The reported incidence of SCD in athletes is presently based on retrospective, observational, and incomplete studies. H&P's screening value seems minimal for structural heart disease, versus echocardiography (which improves diagnosis for high-risk cardiomyopathies) and s-MRI (which also identifies high-risk coronary artery anomalies).

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Electrocardiography is valuable in screening for potentially high-risk electrophysiological anomalies. **3. Proposed Project:** We propose a prospective, controlled study (2 comparable large cohorts: one historical, one prospective) to compare: (1) diagnostic accuracy and resulting mortality-prevention performance of traditional screening methods versus questionnaire/electrocardiography/s-MRI, during 2-month periods of intense, structured exercise (in military recruits, in advanced state of preparation); (2) global costs and cost/efficiency between these two methods. This study should contribute significantly toward a comprehensive understanding of the incidence and causes of exercise-related mortality (including establishing a definition of hr-CVCs) while aiming to reduce mortality.

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1. Introduction

Sudden cardiac death (SCD) and sudden cardiac arrest (SCA) in athletes are unexpected and upsetting to the general population and to institutional promoters. Because both SCD and SCA are rare, they are inadequately addressed in the literature despite the anxiety and disappointment they elicit in the populace, the escalating pressure caused by media narratives, and the associated risks and mounting medico-legal liabilities. Even though current processes for prescreening young athletes before sports participation are inadequate, recent advancements in diagnostic methodologies signal that significant improvement is overdue but achievable.

Discussions on preventing SCD in athletes are persistently tentative and inconclusive, and they continue to be hindered by open, unresolved questions, including the following:

- 1. Is the issue big enough to justify spending more time and resources to pursue it?
2. Does the typical approach used by forensic pathologists to determine the causes of SCD in athletes—that a “plausible defect” found at autopsy of an SCD victim can automatically be assumed to be the cause of the final event—soundly establish true causative relationships [1]? Uncertainties that may cast doubt on this simple paradigm (which relies on pathology markers) include: Is there any myocardial scar? Any fat deposit? Any degree of myocardial disarray? Any ectopic coronary artery? Detailed criteria for determining severity are required for each of these.
3. Can we definitely establish that “exertion at maximal capacity” is the essential factor at the time of SCD in athletes? Is this true only in persons with preexisting high-risk cardiovascular conditions (hr-CVCs), or can it occur by chance, in anyone [2]?

- 4. If we identify and treat potential causes, could we claim that we can eradicate these horrendous tragedies on the athletic field [1–6]?
5. As a corollary to present theory and practice (“some anomalies of the heart cause SCD in athletes, and if we know about them we can prevent SCD”), can we favorably affect the incidence of SCD in athletes on the basis of a simple history and physical examination (H&P) and, possibly, resting electrocardiography (ECG) and echocardiography done only when justified by initial studies?

In this position paper, we present a critical review of current sports cardiology screening policies aimed at preventing SCD in athletes and propose an alternative, feasible, potentially more accurate, and efficient screening method based on magnetic resonance imaging (MRI). This is an attempt to widen the discussion in the medical community on optimal sports preparticipation screening and to lay the groundwork for a proposed study in military recruits that we believe will also have broad applicability to the athlete community.

2. Further facets of the debate: History of an ongoing process

As recently and strongly confirmed in a general statement from the American Heart Association [7], respected professionals, school systems, families, health organizations, and society at large support regular exercise to promote health and prevent disease, for at least the general population, despite an undoubtedly small, but definite, potential risk for negative and dramatic side effects.

An essential difference between SCD in young athletes versus adults in the general population who are older than 35 years of age is that the young heart does not have the end-of-life anatom-

ical changes at autopsy that are often seen in older patients, such as coronary artery disease-related intimal plaque, ulceration of coronary lesions, or thrombosis: The heart of a young SCD victim typically looks just as it did before the precipitating event, so that the mechanism of SCD usually remains unknown. The general theory on SCD in young athletes is that existing anomalies and pathophysiological mechanisms worsen during strenuous exertion [8]—for example, in some coronary artery anomaly (CAA) cases, worsening stenosis and ischemia may occur with maximal exertion, leading to mortal arrhythmias; similarly, in some cardiomyopathy (CMP) cases, which frequently include preexistent baseline myocardial fiber disarray or scarring, arrhythmias could be caused by exercise-induced tachycardia, reactive adrenergic surge, hemodynamic overload, or any combination of these.

In a recent update, while acknowledging the low quality of evidence supporting current approaches to routine sports preparticipation screening, a founding expert in this field, Professor Antonio Pelliccia [9], made several relevant observations. First and foremost, prophylactic protection and effective prevention of SCD are rights that belong to any citizen. Some modern governments recognize their intrinsic responsibility in this regard (as exemplified by Italian law since 1950). Thus, affordable screening should specifically aim at diagnosing hr-CVCs like CMP, CAAs, and ECG abnormalities that potentially predispose individuals to high risk during maximal exertion. Noting the inefficiency of standalone H&P, Dr. Pelliccia suggested that, although resting ECG (currently an established, routine test in Italy [9] and a few other countries) is limited by a low predictive value and a high rate of false-negative findings for structural heart conditions, stress ECG testing could nonetheless be useful in certain elite athletes (eg, those with CMP) [9].

While discussing such arguments, McKinney et al. [5], on behalf of the Canadian Cardiovascular Society/Canadian Heart Rhythm Society, stated recently that “Cardiovascular screening will never be able to detect all athletes at risk for SCD, irrespective of the screening strategy used. Automated external defibrillators and emergency action plans are proven tools to reduce SCD.” That point was made without consideration of the potential use of screening cardiac MRI (s-MRI), but it is the current position of many (apparently frustrated) sports cardiologists, specialists in SCD, and general practitioners involved in traditional precertification screening, who appear to favor taking aggressive care of SCD primarily as it occurs in the field. Incidentally, Johri et al. [10] did not report the prevalence or incidence of hr-CVCs or mortality in Canada, but only presented current Canadian methods for screening, while defining an established professional discipline in a comprehensive public-health system.

3. MRI-based screening: What does it provide, and how?

3.1. Preliminary screening study at the Texas heart Institute (2018)

In Houston, Texas, researchers at the Texas Heart Institute conducted the Screen to Prevent (S2P) preliminary 7-year study [3], which ultimately enrolled 5,169 middle- and high-school students (male and female, any race) from a general population. After providing written informed consent, all participants underwent standard H&P, a resting ECG, and an abbreviated electrocardiogram-gated cardiac MRI examination, without intravenous sedation or contrast administration, in a commercial MRI scanner (Philips, Achieva, Tesla 1.5) equipped with a 32-channel cardiac coil for signal reception. The imaging protocol consisted of two essential components: (1) Global left ventricular anatomy and function was evaluated by using a breath-held steady-state free precession cine imaging sequence acquired in standard orien-

tations (vertical long axis, four-chamber view, and left ventricular outflow tract) and, in a large continuous subseries, a complete sequence of short-axis tomographic sections was obtained; (2) The ostial locations and proximal courses of the coronary arteries were evaluated by using a targeted respiratory navigator-guided 3-D chest MRI with acquired voxel size of $0.7 \times 0.7 \times 1.5$ mm. No significant immediate or late side-effects from the MRI were reported [3]. Average testing time was 10–15 min. Mortality-based follow-up was not part of the program.

Per the S2P protocol, several factors related to compatibility with MRI were used as exclusion criteria, including having a pacemaker or defibrillator (although most newer devices are compatible with MRI imaging), having a previous experience of claustrophobia, or having a ferromagnetic metallic implant (one containing iron, nickel, or cobalt). A short screening protocol is much more tolerable than a long, clinical MRI test.

In the S2P study, only 1.47% of school-age sports participants were positive for hr-CVCs after one 30-minute screening session and thus required secondary evaluation for potential severe conditions [3]. This suggests that almost all young athletes (more than 98.5%) can be substantially reassured after a comprehensive discussion about their cardiac health. In Table 1, we present the criteria of probable high-risk factors, according to the S2P study protocol.

3.2. An updated collegial, critical discussion on screening

At a meeting organized by the Texas Heart Institute and King's College London in April 2019, 80 European and American invited authorities and practicing professionals in sports cardiology debated current concepts in preventing exercise-related SCD and the status of athlete preparticipation screening. At the meeting, these experts agreed by a two-thirds majority that the inclusion of s-MRI could significantly improve diagnostic precision over established routines (ie, H&P, ECG, and/or echocardiography) and that it would be likely to help prevent SCD in athletes. Notwithstanding such considerations, most of the audience expressed the need for a follow-up to our S2P study on the diagnostic accuracy of modern screening and its result in mortality prevention [3].

The meeting attendees proposed that current, frequently accepted notions lack scientific support and called for further, updated discussion:

1. H&P and ECG are clearly inferior to s-MRI diagnostic accuracy, in terms of true-positive and especially true-negative results for any structural heart conditions, particularly for CAAs (Table 2) [2,3,6,11]. The only coronary anomalies of origin and course that may not be recognizable by the Texas Heart Institute s-MRI protocol (which covers only a 2-cm thick vertical segment at the aortic root) are the circumflex or left main artery originating from the right sinus of Valsalva with retro-aortic course. Because these are not hr-CVCs, we thought that the additional 3–5 min of s-MRI time needed to capture a longer segment was not justified [3].
2. Traditional approaches to cardiovascular screening and care of the athlete can be convoluted, such as that indicated in the Canadian “tiered approach” [10]. Such complex and prolonged approaches could potentially be exchanged for more straightforward methods that favor clarity and efficient timing while reducing comprehensive costs and, especially, false-negative diagnoses [3].
3. The s-MRI-based prevalence of probable hr-CVC factors is 1.5% in young general populations (Table 3) [3,12], or about 5 times higher than previously estimated on the basis of clinical and autopsy findings (0.3%) [8,10]. A recent in-depth literature review of SCD in athletes underscored a high prevalence of normal heart anatomy at autopsy completed by general (but not

Table 1
Diagnostic, probable high-risk criteria at MRI-based screening for elite athletes or military recruits.

Screening method	Criteria of probable high-risk conditions at primary screening stage
History	<ul style="list-style-type: none"> • History of syncope, sudden cardiac arrest, or aborted SCD (especially with associated angina pain) • Family history of SCD at age <35 years • In patients with potential hr-CVCs at screening MRI: exercise-limiting angina, dyspnea, dizziness
Physical exam	<ul style="list-style-type: none"> • Hypertension in upper extremities, with small pulses in lower extremities, and MRI evidence of coarctation of aorta • Systolic precordial murmur, increasing with Valsalva maneuver, and MRI evidence of HCM
ECCG	<ul style="list-style-type: none"> • As per international criteria [19]
Cardiac MRI	<ul style="list-style-type: none"> • HCM, by criterion 1a = IVS thicker than 1–2 SD above the normal average value for the patient’s group (see Angelini et al. [3], where one can find normality MRI tables for age, BMI, sex, race) • HCM criterion 1b = LV mass index greater than 1 SD from group’s MRI average (see Angelini et al. [3] for normality ranges) • Coarctation of aorta, ascending aorta aneurysm (Marfan-like?), with severity by measurements • DCM, by criterion 2a = LVEDD greater than 1 SD from average (see Angelini et al. [3] normality tables); criterion 2b = LVEF < 40% • Patients with positive Petersen anatomical criteria (MRI) for NCLV, with LVEF < 40%, and symptomatic for effort-related dyspnea (criterion 2c) • Coronary anomalies: ACAOS-IM of a main coronary artery, with ectopic origin and probable intramural course by criteria: (a) ectopic artery passing in front of the aorta, at the anterior aortic commissure, while (b) coursing to the proper sinus of Valsalva, about the sinotubular junction level on the vertical axis; (c) a more than 2:1 luminal ratio of long to short diameters in a cross-sectional proximal section

ACAOS-IM, anomalous origin of coronary artery from the opposite sinus of Valsalva with intramural course; BMI, body mass index; DCM, dilated cardiomyopathy; HCM, hypertrophic cardiomyopathy; hr-CVC, high-risk cardiovascular condition; IVS, interventricular septum; LV, left ventricle; LVEDD, left ventricular end diastolic diameter; LVEF, left ventricular ejection fraction; MRI, screening magnetic resonance imaging; NCLV, noncompaction left ventricle; SCD, sudden cardiac death.

Table 2
Prevalence of high-risk cardiovascular conditions in athletic candidates: comparison of results from 3 recent large prospective studies that used different protocols.

	Malhotra et al. [2] (H&P, ECG, routine echo) n (%)	Williams et al. [6] (H&P, ECG, rare echo) n (%)	Angelini et al. [3] (H&P, ECG, s-MRI) n (%)
Sample size	11,168	3,620	5,169
hr-CVC	42 (0.38)	15 (0.41)	76 (1.47)
hr-CMP	6 (0.05)	2 (0.06)	14 (0.27)
DCM	1 (0.01)	0 (0.00)	11 (0.21)
HCM	5 (0.04)	2 (0.06)	3 (0.06)
hr-ACAOS-IM	2 (0.02)	1 (0.03)	23 (0.44)
R-ACAOS-IM	1 (0.01)	1 (0.03)	17 (0.33)
L-ACAOS-IM	1 (0.01)	0 (0.00)	6 (0.12)
ARVC	0 (0.00)	0 (0.00)	0 (0.00)
WPW	26 (0.23)	9 (0.25)	4 (0.08)

ARVC, arrhythmogenic right ventricular cardiomyopathy; DCM, dilated cardiomyopathy; H&P, history and physical examination; ECG, electrocardiogram; Echo, echocardiogram; HCM, hypertrophic cardiomyopathy; hr-ACAOS-IM, high-risk anomalous origin of coronary artery from the opposite sinus of Valsalva with intramural course; hr-CVC, high-risk cardiovascular condition; hr-CMP, high-risk cardiomyopathy; L-ACAOS-IM, left ACAOS from the right sinus with intramural course; R-ACAOS-IM, right ACAOS from the left sinus with intermural course; s-MRI, screening cardiac magnetic resonance imaging; WPW, Wolff-Parkinson-White syndrome.

Notice the differences in favor of the diagnostic accuracy of an s-MRI-based protocol, especially regarding CAAs and DCM (p value <0.01 for MRI-based versus the other screening methods). Prolonged QTc in the THI study (Bazett criteria, see Angelini et al. [3] in Table 3) was identified by using a Philips automatic ECG device (with an electrophysiologist’s confirmation), but we do not know the criteria or methods used by the other investigators, who report some 3-times-higher prevalence.

cardiovascular) pathologists [1]. Unfortunately, in reporting that in optimal hands only 10% of autopsies were normal, this group (University of Padua, Italy) emphasized the presence of conditions like myocardial scars, fat deposits, or myocardial bridges, even though lacking reliable quantifiable parameters for each.

4. Understanding the true incidence of SCD and agreeing that exercise (added to pre-existing cardiovascular conditions) is the critical factor in SCD in athletes will require a valid control group—for example, historical groups screened routinely according to standalone H&P-based policies. Autopsy of all victims would be strictly required.
5. Can a conclusive study dealing with all of these points (especially the true incidence of SCD in athletes) be realistic, feasible, and foundational for engendering a novel, more effective, and worthy discipline in sports cardiology?

3.3. Currently reported incidence and causes of SCD in athletes

The incidence of SCD in H&P-screened and unscreened athletes [13] is still inadequately assessed: for example, it is reported in similar populations to vary between 0.1% and 7%/100,000/year,

respectively (with lows in sedentary groups and peaks of 1/3,000/year [or 33/100,000/year] in male college basketball players [13]). An athlete with anomalous origin of the left coronary artery and intramural aortic course was considered to have a more than 300 times–higher risk for SCD compared with a noncarrier (or a sedentary person) [3,14].

Effort-related syncope with collapse (especially if preceded or followed by angina), SCA with recovery (including by proper and effective use of automatic implantable defibrillators), and SCD with unsuccessful resuscitation indicate essentially the same critical phenomenon—a sudden, life-threatening cardiac collapse—albeit with different final consequences [15]. Thus, we should advocate for prospective data collection and the publishing of outcomes related to these three emergencies. Also, the amount of exertion should be quantified and uniform, for fairness of comparison [9]. All of these factors explain in great part the inconsistency of SCD data in previous literature, on top of the variable quality of screening and the effectiveness of treatment policies.

Unlike s-MRI, H&P does not accurately identify most adolescents with structural hr-CVCs [3], such as high-risk CAAs (essentially those featuring intramural coronary course) and most cases of dilated or hypertrophic CMP at a young age [12,16]. Still, H&P

Table 3

Prevalence of potentially high-risk cardiovascular conditions: results from a study of middle-school and high-school adolescents screened with an s-MRI-based protocol.

Variable	Study population (N = 5,169)		11–14 years (n = 4310)	15–18 years (n = 859)
	n	% (95% CI)	n (%)	n (%)
Total hr-CVCs	76	1.47 (1.16–1.84)	62 (1.44)	14 (1.63)
hr-ACAOS-IM	23	0.44 (0.28–0.67)	20 (0.46)	3 (0.35)
L-ACAOS-IM	6	0.12 (0.04–0.25)	6 (0.14)	0 (0.00)
RSV	2	0.04 (0.01–0.10)	–	–
NCS	2	0.04 (0.01–0.10)	–	–
High-origin	2	0.04 (0.01–0.10)	–	–
R-ACAOS-IM	17	0.33 (0.19–0.53)	14 (0.32)	3 (0.35)
hr-CMP	14	0.27 (0.15–0.45)	6 (0.14)	8 (0.93)
DCM*	11	0.21 (0.11–0.38)	5 (0.12)	6 (0.70)
HCM	3	0.06 (0.01–0.17)	1 (0.02)	2 (0.23)
ECG hr-CVC	39	0.75 (0.54–1.03)	36 (0.84)	3 (0.35)
Brugada	1	0.02 (0.00–0.11)	0 (0.00)	1 (0.12)
WPW	4	0.08 (0.02–0.20)	4 (0.09)	0 (0.00)
QTc ≥ 470 ms	34	0.66 (0.46–0.92)	32 (0.74)	2 (0.23)
NCLV*	959	18.55 (17.5–19.64)	810 (18.79)	149 (17.35)

ACAOS-IM, anomalous origin of coronary artery from the opposite sinus of Valsalva with intramural course; CMP, cardiomyopathy; CVC, cardiovascular condition; DCM, dilated cardiomyopathy; ECG, electrocardiographic; HCM, hypertrophic cardiomyopathy; hr, high-risk; L-ACAOS-IM, left ACAOS from the right sinus with intramural course; NCLV, noncompaction left ventricle; NCS, noncoronary sinus; R-ACAOS, right ACAOS; RSV, right sinus of Valsava; WPW, Wolff-Parkinson-White anomaly.

Adapted with permission from Angelini P, Cheong BY, Lenge De Rosen VV, Lopez A, Uribe C, Masso AH, Ali SW, Davis BR, Muthupillai R, Willerson JT. High-risk cardiovascular conditions in sports-related sudden death: prevalence in 5,169 schoolchildren screened via cardiac magnetic resonance. *Tex Heart Inst J*. 2018;45:205–213 [3].

* Isolated NCLV by Petersen's criteria is not likely to be a high-risk condition in the young. In these 2 large cohorts (continuous series in 2 age groups: only the prevalence of CMP is different because of the apparent increase in DCM in the older adolescents (p value <0.01*). See Table 2 for aggregate results. As the origin and initial course of CAAs were well described in 99% of the MRI studies, the impact of potential false-positive and false-negative reporting could only be possible to validate by using autopsy data from the same subjects who die after MRI [2].

is quite valuable for identifying symptom severity and family history of SCD, which are important factors. Resting ECG alone can identify or create suspicion about potentially significant electrophysiological risk factors, such those related to prolonged QT, Wolf-Parkinson-White preexcitation, Brugada and other channelopathies, or arrhythmogenic right ventricular cardiomyopathies (ARVCs) [4,6,17]. Given such a complex population, the safest and most effective way to deal with electrophysiologically abnormal resting ECGs may be to directly refer these young athletes to specialized, dedicated centers for expert evaluation.

Echocardiography (especially the limited portable kind frequently done on the athletic field, which does not employ specialized physicians) can identify only major CMPs (quite rare in sports-practicing adolescent or young populations [Table 1]) and only occasionally hr-CAAs in individuals weighing more than 40 kg [12]. Additionally, noncompaction left ventricle (NCLV) could be relevant to identify at screening (an evolving topic of discussion), as it was recently found by MRI Petersen criteria to be present in 18.8% of a general adolescent population. NCLV could evolve into dilated CMP over years of sports training and competing, or just with aging [12]. The existence of NCLV in the general population was reported 12 times more frequently with s-MRI than with echocardiography in similar populations, as also compared with that in athletes (8.6 times more often with s-MRI: or 27.29 vs 3.16%, respectively) [7]; conversely, in reports of echocardiographic screening done for sports cardiology issues, NCLV was not even mentioned if the left ventricular ejection fraction was normal [2]. Our recent S2P s-MRI study in a large population included mention that dilated cardiomyopathy is almost 6 times more prevalent in 15–18-year-old adolescents than in 11–15-year-olds [3]. In the older cohort, most of the small group of adolescents with dilated cardiomyopathy also had NCLV (Petersen's criteria, data in preparation for publication).

For identifying hr-CAAs, s-MRI is much more precise and acceptable than competing screening imaging techniques, does not require ionizing radiation, contrast agents, or drugs, does not cause significant discomfort or side effects, and can be completed in 5–15-minute studies without involving physicians on the field [3,12].

Whereas a diagnosis of structural hr-CVC can be confidently obtained by s-MRI, the risk implicit in an individual form of CVC associated with clinical manifestations (especially syncope and SCA) needs to be confirmed by using specific secondary methods and interpreted by expert consultants (but this is strictly required in <1.5% of MRI-screened candidates found to have hr-CVCs such as ARVC, myocarditis, or HCM [3]). In particular, in athletes found to carry CAAs, we propose as relevant for additional secondary screening a computed tomography contrast angiography (the gold standard for noninvasive clinical study of CAAs). Late gadolinium enhancement by MRI or histological studies can be quite specific and may be indicated as secondary testing for some candidates at high risk for lethal ventricular arrhythmias (such as those caused by symptomatic mitral valve prolapse, ARVC, myocarditis, or HCM: all to be examined in quantification studies) [8,9].

3.4. The next-level study

In truth, there exists no other available, large, controlled, and uniform population that could be compared with athletes in depth (in terms of age, consistency of exercise program and requirements for strenuous physical exertion, data acquisition and quality, follow-up, and compulsory autopsy after SCD), if not the military. However, similar to the situation with athletes, the incidence of SCD in military recruits is not adequately assessed. To our knowledge, the only related mortality rate assessment available was done by Eckard et al. [14], who quoted an annualized mortality rate in recruits of 13/100,000/year.

For these reasons, we are developing a prospective, controlled study in military recruits (with 2 large, analogous cohorts: 1 historical and 1 retrospective, or 2 parallel prospective) to compare: (1) diagnostic accuracy and resulting mortality-prevention performance of traditional H&P-based screening methods versus questionnaire/electrocardiography/s-MRI, during 2-month periods of intense, structured exercise; and (2) global costs and cost efficiency between these two approaches. Mandatory autopsy will be obtained in all casualties (any cause), which will enable a general validation of the MRI-versus-autopsy study. This study should contribute significantly to a comprehensive understanding of the

Table 4
Arguments against and in favor of preparticipation screening MRI.

Objections to MRI screening [18]	Support for MRI screening [3,12]
1. Only “treatable” causes should be screened.	1. There is no way to screen only for so-called treatable causes; we need to do accurate systematic screening and then individual evaluation of potential hr-CVCs.
2. The real incidence of SCD is unknown, but it is “extremely low.”	2. The real incidence of SCD can only be described by accurate methods used in all candidates (the denominator of carriers at risk is essential). In general, all mortality (in athletes especially) should be eliminated if possible.
3. The mechanisms of SCD are unknown.	3. The risks and mechanisms of SCD can be better studied in vivo, in individual cases identified by s-MRI screening, than by autoptotic study.
4. Screened adolescents will feel anxious and condemned or disabled by knowing the diagnosis; psychological impact follows.	4. Preparticipation-screened adolescents cannot feel anxious or condemned because of the risk, more than because of the clear explanation of an eventual issue (if any) and its treatment (frequently efficacious and available).
5. Mortality risk from hr-CVCs is low; finding an hr-CVC does not equate to finding mortality risk.	5. We need to describe the precise risk by accurately quantifying the severity of hr-CVCs and strict follow-up for mortality; s-MRI enables this job accurately, by primary-level protocol.
6. Mass screening of adolescents affects persons who will not be athletes.	6. We propose that only elite athletes be MRI-screened (high school, college, and professional athletes). We are interested in hr-CVCs, not all possible anatomical anomalies.
7. The role of exercise is unclear.	7. Most high-quality reports have found that 90% of SCD in athletes occurs during exertion: we could validate this by using a fixed-exercise program in military recruits (2 months long, advanced level).
8. Athletic screening is like “opening the Pandora’s box” while introducing or inventing previously unknown troubles.	8. Pandora was a curious girl, and she got in trouble, but athletes are serious and motivated, while looking for clarity and peace of mind (“How much can I push?”): they expect scientific evidence.
9. AED on the field with resuscitation is the primary and optimal policy for preventing death.	9. AED is welcome, but it may not be enough: Large surveys on mortality and irreversible brain damage rates after AED and out-of-hospital resuscitation quote 50–90% negative endpoints.

AED, automated external defibrillation; hr-CVC, high-risk cardiovascular condition; MRI, magnetic resonance imaging; SCD, sudden cardiac death. See text.

incidence and causes of exercise-related mortality (including establishing a definition of hr-CVCs) while aiming to reduce mortality.

As recently hypothesized for MRI-based preparticipation screening studies in US military recruits [3,12,14], it is possible that prospective, controlled studies could be used to fairly compare MRI-screened candidates with either sedentary recruits or historical cohorts of military recruits primarily studied only by H&P (effectively reducing or eliminating structural and ECG-based heart screening). It is important to clarify that MRI-based primary screening is particularly attractive in military recruits because it represents high-precision testing for structural CVCs, especially when combined with ECG screening for electrophysiological anomalies of potential consequence in a concise, accurate, comprehensive plan. Conversely, initial H&P screening will de facto lead to a 20–30% incidence of globally expensive, required secondary testing (usually ordered by primary physicians according to vague protocols and typically excluding asymptomatic carriers) [2,6,10] while essentially maintaining the limitation caused by false-negative initial diagnoses.

3.5. Cost considerations

Discussing the cost of alternative forms of primary screening is quite important, especially because states, schools, and health insurance companies require them. Large, dedicated primary screening centers could be conveniently and cost-effectively organized to facilitate s-MRI-based assessment of large populations of athletes (preferentially more than 20 per day in the MRI unit) at a reasonable and affordable cost—less than US \$200 at dedicated, ideal-efficiency organizations [3,12]. In the few cases for which secondary testing is indicated (1.5% of a young population), it will be for expert evaluation of the severity of identified potential hr-CVCs (especially those discovered by s-MRI or ECG), some of which could be disqualifying for certification or require intervention. A recent counterpoint discussion by members of the Canadian Sport Medicine Society raised the main points they favor against using s-MRI (summarized in Table 4) [18].

4. Limitations

The present review and discussion of a promising future is limited by several factors that will have to be addressed in any forthcoming study protocol.

In particular, using US military recruits and athletes as equivalent comparators is an imprecise but necessary simplification: The two populations will need to be described in many subclasses (by age, sex, type of sports/physical exertion, preliminary screening and follow-up environments) that could modify the risk for SCA or SCD.

That said, athletes undoubtedly comprise a more complex population [9] with essential differences, including the competitive nature of their involvement, additional emotional stress as related to competitions, variable medical care, and data acquisition style and depth. These factors and others will have to be considered by sports cardiologists if applying the new substantial and systematic evidence we hope to be able to offer soon.

Finally, it is important to note that here we are specifically discussing recruits and athletes who are 12–35 years of age. Older individuals are likely to have additional confounding pathologies (especially acquired coronary disease that progresses with age) and different precipitating factors, like more-limited exercise protocols or marathon-like exertion.

5. Conclusions

The need to prevent SCA and SCD in athletes and in military recruits is at the base of a wished-for new order in which sports cardiology is established as a new and effective discipline. Such duty is potentially foundational, if one accepts that preventing SCD in athletes during exertion is the primary calling for sports cardiologists [8].

The considerations presented herein are offered to the cardiology community in general, and to international sports cardiology and preventive medicine societies, to encourage a long-overdue discussion about the most appropriate and effective mode(s) of preparticipation screening for young athletes, as recurrently auspiciously.

cated by the general public, the media, sport cardiologists and medico-legal representatives. We understand that reaching a consensus will not be easy, especially in light of the differing points of view of the various established health organizations and professionals currently involved in traditional primary screening.

At present, we are not ready to automatically endorse a change in the guidelines for athlete preparticipation screening just because novel technologies are now available; rather, we propose to discuss the logic and feasibility of performing a large, prospective, and statistically sound study to validate a quality change in the discussion and to answer the fundamental question: "Would a more accurate study of the conditions predisposing to SCD substantially reduce SCD during sports?"

If MRI-based testing should ultimately become the preferred plan of action for preparticipation screening, the formation of a new curriculum and teaching focus for sports cardiologists and consultants will be required, in view of their novel educational needs and updated functions.

Declaration of Competing Interest

The authors report no relationships that could be construed as a conflict of interest.

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References

- [1] G. Thiene, S. Rizzo, M. Schiavon, et al., Structurally normal hearts are uncommonly associated with sudden deaths in athletes and young people, *J. Am. Coll. Cardiol.* 73 (23) (2019) 3031–3032, <https://doi.org/10.1016/j.jacc.2019.03.497>.
- [2] A. Malhotra, H. Dhutia, G. Finocchiaro, et al., Outcomes of cardiac screening in adolescent soccer players, *N. Engl. J. Med.* 379 (6) (2018) 524–534, <https://doi.org/10.1056/NEJMoa1714719>.
- [3] P. Angelini, B.Y. Cheong, V.V. Lenge De Rosen, et al., High-risk cardiovascular conditions in sports-related sudden death: Prevalence in 5,169 schoolchildren screened via cardiac magnetic resonance, *Tex. Heart Inst. J.* 45 (4) (2018) 205–213, <https://doi.org/10.14503/THIJ-18-6645>.
- [4] B.J. Maron, P.D. Thompson, M.S. Maron, There is no reason to adopt ECGs and abandon American Heart Association/American College of Cardiology history and physical screening for detection of cardiovascular disease in the young, *J. Am. Heart Assoc.* 8 (14) (2019), <https://doi.org/10.1161/JAHA.119.013007> e013007.
- [5] J. McKinney, A.M. Johri, P. Poirier, et al., Canadian Cardiovascular Society cardiovascular screening of competitive athletes: the utility of the screening electrocardiogram to predict sudden cardiac death, *Can. J. Cardiol.* 35 (11) (2019) 1557–1566, <https://doi.org/10.1016/j.cjca.2019.08.023>.
- [6] E.A. Williams, H.F. Pelto, B.G. Toresdahl, et al., Performance of the American Heart Association (AHA) 14-point evaluation versus electrocardiography for the cardiovascular screening of high school athletes: a prospective study, *J. Am. Heart Assoc.* 8 (14) (2019), <https://doi.org/10.1161/JAHA.119.012235> e012235.
- [7] S.B. Ross, K. Jones, B. Blanch, et al., A systematic review and meta-analysis of the prevalence of left ventricular non-compaction in adults, *Eur. Heart J.* 41 (14) (2020) 1428–1436, <https://doi.org/10.1093/eurheartj/ehz317>.
- [8] B.J. Maron, P.D. Thompson, M.J. Ackerman, et al., Recommendations and considerations related to preparticipation screening for cardiovascular abnormalities in competitive athletes: 2007 update: a scientific statement from the American Heart Association Council on Nutrition, Physical Activity, and Metabolism: endorsed by the American College of Cardiology Foundation, *Circulation* 115 (12) (2007) 1643–1655, <https://doi.org/10.1161/CIRCULATIONAHA.107.181423>.
- [9] A. Pelliccia, The cardiovascular screening programs in athletes: from the Italian experience to a global strategy, in: P. Thompson, A. Fernandez (Eds.), *Exercise and Sports Cardiology, Volume 3: Exercise Risks, Cardiac Arrhythmias and Unusual Problems in Athletes*, World Scientific Publishing Co Pte Ltd, London, UK, 2018, pp. 15–29.
- [10] A.M. Johri, P. Poirier, P. Dorian, et al., Canadian Cardiovascular Society/Canadian Heart Rhythm Society joint position statement on the cardiovascular screening of competitive athletes, *Can. J. Cardiol.* 35 (1) (2019) 1–11, <https://doi.org/10.1016/j.cjca.2018.10.016>.
- [11] D. Corrado, C. Basso, A. Pavei, P. Michieli, M. Schiavon, G. Thiene, Trends in sudden cardiovascular death in young competitive athletes after implementation of a preparticipation screening program, *JAMA* 296 (13) (2006) 1593–1601, <https://doi.org/10.1001/jama.296.13.1593>.
- [12] P. Angelini, R. Muthupillai, B. Cheong, R. Paisley, We have plenty of reasons to propose new, updated policies for preventing sudden cardiac death in young athletes, *J. Am. Heart Assoc.* 9 (8) (2020), <https://doi.org/10.1161/JAHA.119.014368> e014368.
- [13] K.G. Harmon, J.A. Drezner, M.G. Wilson, S. Sharma, Incidence of sudden cardiac death in athletes: a state-of-the-art review, *Br. J. Sports Med.* 48 (15) (2014) 1185–1192, <https://doi.org/10.1136/bjsports-2014-093872>.
- [14] R.E. Eckart, S.L. Scoville, C.L. Campbell, et al., Sudden death in young adults: a 25-year review of autopsies in military recruits, *Ann. Intern. Med.* 141 (11) (2004) 829–834, <https://doi.org/10.7326/0003-4819-141-11-200412070-00005>.
- [15] A. Lofti, L.W. Klein, R.S. Hira, et al., SCAI expert consensus statement on out of hospital cardiac arrest, *Catheter. Cardiovasc. Interv.* (2020) 1–18, <https://doi.org/10.1002/ccd.28990>.
- [16] P. Angelini, C. Uribe, Anatomic spectrum of left coronary artery anomalies and associated mechanisms of coronary insufficiency, *Catheter. Cardiovasc. Interv.* 92 (2) (2018) 313–321, <https://doi.org/10.1002/ccd.27656>.
- [17] C. Pappone, G. Ciconte, F. Manguso, et al., Assessing the malignant ventricular arrhythmic substrate in patients with Brugada syndrome, *J. Am. Coll. Cardiol.* 71 (15) (2018) 1631–1646, <https://doi.org/10.1016/j.jacc.2018.02.022>.
- [18] P. Dorian, J.M. Goodman, K.A. Connelly, Policies to prevent sudden cardiac death in young athletes: challenging, but more testing is not the answer, *J. Am. Heart Assoc.* 9 (8) (2020), <https://doi.org/10.1161/JAHA.120.016332> e016332.
- [19] J.A. Drezner, S. Sharma, A. Baggish, et al., International criteria for electrocardiographic interpretation in athletes: consensus statement, *Br. J. Sports Med.* 51 (9) (2017) 704–731, <https://doi.org/10.1136/bjsports-2016-097331>.