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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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Corresponding Author:	Paolo E Angelini, MD Texas Heart Institute Houston, TX UNITED STATES
First Author:	Paolo E Angelini, MD
Order of Authors:	Paolo E Angelini, MD
	Raja Muthupillai
	Alberto Lopez
	Benjamin Cheong
	Carlo Uribe
	Eduardo Hernandez
	Stephanie Coulter
	Emerson Perin
	Silvana Molossi
	Federico Gentile
	Scott Flamm
	Giovanni Lorenz
	Flavio D'Ascenzi
	Jonathan Tobis
	Roberto Sarnari
	Antonio Corno
	James Furgerson
	Amedeo Chiribiri
	Adriana DM Villa
	Fulvio Orzan
	Pedro Brugada
	John Jefferies
	Pierre Aubry
	Jeffrey Towbin
	Gaetano Thiene
	Robert Tomanek
Manuscript Region of Origin:	North America
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). 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.
Suggested Reviewers:	Antonio Pelliccia ant.pelliccia@gmail.com

January 29, 2021

Dobromir Dobrev, MD, PhD
Editor-in-Chief, *International Journal of Cardiology – Heart & Vasculature*

Re: IJCJOURNAL-D-20-02676 – Angelini et al: Young athletes: Preventing sudden death by adopting a modern screening approach? A critical review and the opening of a debate

Dear Dr. Dobrev:

Enclosed is the above-named manuscript, which the authors hope will be suitable for publication in *International Journal of Cardiology – Heart & Vasculature.* This is an original manuscript that is the result of the collegial, collaborative efforts of a large, multicenter group of European and American authorities and practicing professionals in sports cardiology.

We have transferred the manuscript to *IJC Heart & Vasculature* on the advice of the editor of *International Journal of Cardiology.* We were instructed to respond to the reviewers' comments as usual and to submit those changes to your journal. Our point-by-point response to those comments is included as part of this submission. We understand that the Article Publishing Charge is waived.

We appreciate the opportunity to revise the work and to submit it to your journal. Please address all correspondence to me at the address shown on the title page. The authors appreciate your consideration and look forward to the reviewers' decision.

Sincerely yours,
Paolo Angelini, MD

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RESPONSE TO REVIEW
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REVIEWER #1
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COMMENT: This article is the result of a meeting of a large group of sports cardiologists, who have come up with a proposal, outlined here, for a new method to evaluate risk of SCD in athletes. It states clearly that prevention of SCD in athletes is a central role of the sports cardiologist. The new method involves the use of cardiac MRI imaging. There is logic in this, as explained in the text. The lesions detected by MRI may be the lesions which are most likely to cause death during sport (coronary lesions, ARVC, HCM), and less likely to cause death during rest or sleep.

RESPONSE: Thank you for correctly stating and appreciating the nature and relevance of our paper.

COMMENT: In essence my central criticism of this paper as it stands is that non-sports cardiologists have not apparently had much input in this albeit thoughtful proposal, and throughout, the premise and discussion needs to be more responsive to those who are not primarily motivated by and employed directly within this field.

RESPONSE: You suggest that the prevention of SCD in athletes is also, or is mainly, a matter for general cardiologists and the public to discuss and approve, in addition to specialists' (ie, sports cardiologists') conclusions. We firmly agree that the effective screening of athletes is a subject for all of the cardiology community (and the population at large) to discuss and jointly subscribe, ideally after formal discussion and consideration. The basic discussion should be about:
1. Although SCD in athletes is rare, it could, and probably should, be prevented by a better method that history and physical at primary screening;
2. Potential causes of death are likely much better known by cardiac MRI than by H&P-based screening;
3. Knowing the potential causes at screening is a much more hopeful study paradigm that awaiting tragic events/autopsy without being able to prevent them.

These are points we already made in the text. For example:
1. In the introduction: Limitations of current theory and practice in prevention (pages 8 and 9);
2. The value of establishing objective and reliable methods to identify probable high risk for SCD in athletes, by a generalized s-MRI (Sections 3.1 and 3.2, pages 11-15);
3. MRI (the "virtual autopsy") is as accurate as physical autopsy, and its timing is optimal (ahead of tragedies) (page 14, Table 4).

The wider discussion should occur to inform the prospective study we are now proposing (Section 3.4): this paper is an introduction to the final study, based on our revealing S2P preliminary investigation. The text was improved in various places.

COMMENT: One of the major issues here is why to focus on athletes at all, not really addressed as a key question in table 4.

RESPONSE: Table 4 compares screening MRI with the specific objections recently presented by the Canadian Sport Cardiology community. We believe that obtaining solid descriptions of quantifiable risk factors directly from primary screening is more efficient and accurate than by using gradual and lengthy screening protocols. The need for and value of the proposed enhancement of the sports cardiology discipline should be discussed on the basis of a more definitive assessment of the incidence of hr-CVCs and their effective individual risk by using objective, quantitative mortality/prevalence data.

COMMENT: Clearly such deaths, in comparison to the vast majority of young sudden deaths, are often high profile, covered by media, and may have image and fiscal implications for media organisations and clubs. This issue is not avoided by this paper and I commend the authors for that.

RESPONSE: Thank you for the acknowledgement.

COMMENT: However, a large study from the USA showed that the incidence of SCD in athletes is less than in non-athletes, (Maron, JACC 2014, table 2) whereas risk of suicide is ten times more likely in non-athletes, and population-based studies of young sudden death from Denmark (Heart Rhythm) and Australasia and New Zealand (NEJM) have shown that 95% of SCD in 1-35 year olds does not occur during exercise, indeed two thirds occur during sleep or rest.

RESPONSE: We understand your viewpoint, which aligns with concerns that a general physician can focus on, worried about the global picture of young-age mortality/suicides in particular. However, our paper is specifically about the prevention of SCD during exercise in young athletes and military recruits, and not in the mixed 1-to-35-year-old segment of the population, but in 12-to-35-year-olds (which sports cardiologists define as “the young”) and “during extreme exertion” (sports and military recruits). We do agree that anxiety and mental depression can be very serious concerns, but we can all accept that more than one issue can be simultaneously discussed and pursued in modern society. There is considerable interest in sports and military recruits from many in the medical and general communities. The “young athletes” we are mainly concerned with at this time are those in schools and sports who are at the highest risk for SCD during exertion. The age spectrum has been commonly agreed to be the 12-35 years, the time at which a person reaches maximal personal exercise capacity and activities and before the onset of risks related to coronary artery disease. The text was clarified and/or corrected on page 9, bottom paragraph; page 20, top paragraph; and Table 1. (the age spectrum).

COMMENT: If we take it that it is ethical to spend such a major focus on those in the population who, overall, are at lowest risk of a bad cardiovascular outcome, then the next step is to be sure that

this new screening program does not induce more harm than good. Previous studies of the effect of pre-participation screening in the UK and Israel have not showed a measurable benefit in reduction of SCD in sports.

RESPONSE: You have mentioned two important but limited papers:
1. The UK study (Malhotra et al; see Table 2) revealed that H&P plus echocardiography did not prevent SCD caused by coronary anomalies (poor diagnostic specificity) or HCM (poor monitoring of evolution of HCM over 10 years: one initial test may not be enough);
2. The Israel study used only primary H&P/ECG and did not have adequate population size/SCD events (and no reporting of the causes of SCD in the victims). All of these items are addressed in Table 2.

COMMENT: It is well known that any screening program causes harm as well as good. What efforts are planned to assess the harm, and the efficacy? Previous studies have been very weak in this regard. A number of people must be banned from the sport they love, to achieve the aims of this work. A large number will receive a diagnosis of uncertainty (borderline chamber sizes, LVNC etc) Clearly the plus side is that some people will have a curable lesion potentially fixed. However, others may have a curable lesion fixed when the benefit may be questionable, and of course therefore exposed to the risk of the cure itself. How many who are banned leave the sport and become depressed, even suicidal, or gain weight, adopt an unhealthy lifestyle? How many leave the country or state concerned and go play sport somewhere else? I expect that such questions can be addressed if such careful follow up is built into the proposed study.

RESPONSE: Yes, you are correct. Conversely, we firmly believe that inadequate screening implies high false positive and false negative diagnoses and can lead to secondary confusion and disappointment in some (how frequently?) cases. We believe that this is a major reason to carry out a large, controlled study establishing: 1. the real incidence of SCD during exertion and 2. the value of an improved screening when facing sound endpoints (mortality). We showed in Table 2 that H&P is not adequate in many cases in identifying the carriers of high-risk conditions, compared with cardiac MRI (which has the accuracy of autopsy, the gold standard for diagnosing structural heart conditions—albeit too late for the victim). As we reported from our previous study, only 1.5% of the general population studied by an MRI-based protocol had probable structural hr-CVCs, versus the 20% to 25% in H&P-based screening. In our tentative protocol, we promote a strict secondary evaluation by specialists in the at-risk candidates, for the concerns you indicate. The text in Sections 3.3 and 3.4 was further improved in covering such points.

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REVIEWER #2:

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COMMENT: In this document, Dr. Angelini and collaborators discuss a series of topics related to pre-participation cardiovascular screening in young athletes, and propose a novel approach largely

focused on the use of a modified protocol of cardiac magnetic resonance (s-MR). The authors raise some interesting questions and clinically relevant issues. However, I have some major concerns.

RESPONSE: We thank the reviewer for the fair representation and general approval of the attempt to improve general aims and methods.

COMMENT: The present manuscript is reportedly a Consensus document, but the meeting originating this consensus is only briefly reported in Section 3.2 (page 12). This should be reported in the introduction.

RESPONSE: The labeling of "Consensus" for this paper was a product of an editorial necessity. Actually, we did not aim on this occasion to establish a new set of definitive recommendations by an established representative body, but only to propose to the readership the fundamental questions to be here addressed, after a preliminary discussion by recognized experts: Do we want to maintain a sports cardiology discipline that lacks scientific and preventive value for the candidates and society? Consensus will come after the results of our proposed project become available, assuming confirmation of our initial thought that cardiac MRI is a much better screening means than the current H&P (as suggested by the initial results on our group's study in 5,169 adolescents) and likely effective in preventing SCD in athletes or recruits. We do understand that such an effort would require a huge commitment, with large public funding and substantial support by important institutions. The meeting in London was a preliminary evaluation of the current results of H&P primary screening and the presumed mortality risk reduction in a prospective controlled study. See Section 3.4, "The next -level study." The text was updated to clarify the aims, at those regards.

COMMENT: The structure of the document is ambiguous and confusing. A clear statement summarizing the aim of the work is needed in the introduction. The main focus is apparently placed on promoting the use of MR in first-line cardiac screening. However, a variety of topics are briefly and superficially discussed in one or two sentences, without referring to previous evidence and not reaching any conclusion (e.g., page 8). Some claims are speculative and not supported by scientific data or previous evidence; a more balanced discussion is warranted.

RESPONSE: We did try to further improve the introduction according to the fair criticism of this reviewer (see revised Abstract and Introduction). The aim of this paper is to propose a more accurate and reliable method for effective screening of athletes (especially by introducing accurate and quantifiable parameters and valid mortality data endpoints). This is an open discussion and not yet the final recommendations on optimal screening. The article type was changed to reflect that this is only a "position paper," and not a conclusive agreement/consensus document. See: Title, Abstract, the 3 parts of the Discussion, and Section 3.4.

COMMENT: Other topics are not novel and add little to current knowledge (e.g., the incidence of sudden death in page 14). All these issues make the text difficult to follow. The language is sometimes too informal, which may not be appropriate for a consensus document.

RESPONSE: See our response to your second comment in regard to this not being a consensus document. The discussion of currently available data on mortality is a summary of an unconcluded topic in sports cardiology: At present, we don't definitively know the comprehensive mortality in sports or military activities, or the sample size required to reach statistical power on mortality endpoints (capable of enabling and justifying a definitive study on the value and accuracy of MRI-based screening). This section is to enable a documented discussion and planning. We agree that this is not a formal/final paper on the subject, as yet, but a condition to reach that end point. We have made some clarification of the process on pages 9-11 (Section on history of an ongoing process). Indeed, this is not a formal and final document to establish a new discipline in screening, but the proposal of new data (screening by MRI) and the basic terms of a required discussion (opinion essay).

COMMENT: As abovementioned, most of the document discusses cardiac magnetic resonance as a first-line tool for CV screening. It should be emphasized throughout the manuscript that echocardiography may provide very similar outcomes in a more cost-effective and accessible way. Targeted and limited echocardiographic exams have been proved useful in screening young athletes; the ostium of coronary arteries could be identified in up to 96% patients (Feinstein et al. Clin J Sport Med 1993;3:149-52; Weidenbener et al. Clin J Sport Med 1995;5:86-9; Wyman et al. J Am Soc Echocardiogr 2008;21:786-8; Grazioli et al. Rev Esp Cardiol 2014;67:701-5). Conversely, there might be some advantages of s-RM over echocardiography, but these have not been addressed. S-RM might be more sensitive in some cardiomyopathies with regional involvement (e.g., apical HCM), but it is very unlikely that this justifies the first-line use of s-MR. The study of myocardial fibrosis in s-MR could be of clinical value, but gadolinium was not administered in screened athletes of the S2P pilot study (reference 3). Therefore, it is unclear whether s-MR will provide additional benefits over a more convenient and widely available tool such as echocardiography. In this regard, the authors propose future studies to assess the role of s-MR (page 17); MR should be compared with a programme including echocardiography.

RESPONSE: The difference between echocardiography and s-MRI is discussed in the text, and specifically in Table 2 (comparison table between H&P, echo, and s-MRI) and the related discussion (at pages 13-14). The differences are related to accuracy, simplicity/reliability, timing requirement, and the ability to make a final diagnosis at one single initial screening encounter: all fundamental points for a screening program (different than in clinical diagnostic arena). New updates were added in the text on pages 13-14.

COMMENT: Some criteria for identifying high-risk individuals (Table 1) are misleading. Structural measurements (LVEDD, IVS) are classified as pathological if larger that the mean and one SD; this will classify as high-risk individuals >15% of a normal population, likely overdiagnosing patients with DCM (a two- or three-SD threshold might be more appropriate). I acknowledge that this Table only summarizes previous results, but should be considered as a source of bias when comparing these results to previous studies. Moreover, the Seattle criteria for ECG interpretation (reference 20) are no longer used; the International criteria are currently recommended (Sharma et al. EurHeartJ 2018;39:1466-1480).

RESPONSE: The paper is suggesting a method aimed at decreasing false final diagnoses (in terms of positive and negative results), while including criteria for identifying potentially high-risk conditions at primary screening. Our proposal is intrinsically calling for specialistic secondary follow-up evaluation of individual candidates for all borderline cases (in 1.5% of candidates only, a specialist will be called to give a clinical final decision). Especially for cardiomyopathies, adolescent phenotypes are frequently mild but will require careful follow-up (both clinical evaluation and imaging) in athletes. This point has been expanded with respect to the initial text (Table 1). We published quite precise quantitative data, especially in cardiomyopathies, whose normality ranges change according to age, sex, body weight, and race. Obviously, the final correlations with mortality risk will depend on screening results from large populations and mortality rates after strenuous physical activities. Echocardiography is not as accurate or apt to generate quantitative measurements as is screening MRI.

Thank you for the update on the new international criteria for Table 1; we have replaced the Seattle reference with the following:

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.

COMMENT: The left column in Table 4 summarizes some "objections to MRI screening" from reference 10; however, reference 10 does not even discusses magnetic resonance. Could the authors clarify?

RESPONSE: Thank you for catching this error. We inadvertently cited the wrong reference from the same group, and we have corrected this in Table 4 and in the text on page 19, top. The new citation is:

Dorian P, Goodman JM, Connelly KA. Policies to prevent sudden cardiac death in young athletes: challenging, but more testing is not the answer. JAHA 9 (8) (2020) e016332, https://doi.org/10.1161/JAHA.120.016332.

Each of the points mentioned as objections to MRI screening are extracted from this article published in response to a recent related paper from our group. We have updated the points and counterpoints of ours in the same Table 4.

COMMENT: The conclusions section should summarize data from the document, and should not introduce new topics (e.g., the use of machine learning). Moreover, I feel that discussing how could the military help to study athletes should not be done in the limitations section, but rather in a specific section.

RESPONSE: The reviewer's points are well taken. We have deleted the statement about machine learning in the Conclusion section (page 20), and we have pared down the discussion of the military in the Limitations section (page 19), while retaining the part of it that truly does address the military's limitations as a comparator group, given our intent to use that group in our next-level study.

COMMENT: What do the authors consider as "young"? Only in page 19 it is reported that the threshold is set at 32 years old. If so, which is the rationale for such threshold?

RESPONSE: The definition of a young population in sports cardiology was established empirically years ago as 12–35 years of age (Maron 2007 and Pelliccia 2018, both cited in this paper), and it is meant to distinguish specifically populations at sports activities-related risks: Sports-like activities generally start after the age of 12, and CAD-related cardiac events start manifesting more clearly after age 35 (especially in men), while exercise-related stress usually decreases at age 35. These points are clarified and made consistent in the revised text. See page 9, bottom paragraph; page 20, top paragraph; and Table 1.

COMMENT: Table 2 and 3 provide very similar data.

RESPONSE: The two tables do provide some similar data. Nonetheless, the tables have different purposes. The intent of Table 2 is to show an overall, high-level comparison among 3 recent, large prospective studies that are germane to this topic. The intent of Table 3 is to focus on one of those studies (our own) and to present greater detail by age group. Our study is foundational for the future proposed study described in this paper and is worth examining at a more detailed level. We prefer to keep both tables, and we hope the journal editor will agree.

COMMENT: References are incorrectly placed (at least, up to reference 9).

RESPONSE: Sorry! We are unclear as to what you mean by "incorrectly placed." If you could provide a bit more explanation, we are happy to try to correct whatever is wrong. We have regenerated the bibliography and, as far as we can tell, all references and DOIs are now correct.

COMMENT: The abstract provides a "methods section" that is not included in the main text.

RESPONSE: You are correct – this is not a typical original research paper. We have removed the reference to "Methods" in the Abstract, along with the other headings.

COMMENT: What is a "typical adult" (page 9, line 41)?

RESPONSE: We apologize for this vague terminology. By "typical adult," we meant adults in the general population who are older than 35 years of age, and we have corrected the text on page 9,

bottom, to say this. Age 35 years is when CAD-related cardiac events begin to manifest more clearly (especially in men), while exercise-related stress begins to decrease. We also made this correction on page 20, top paragraph.

REVIEW – POSITION PAPER

Young athletes: Preventing sudden death by adopting a modern screening approach?

A critical review and the opening of a debate

Paolo Angelini[1]*, Raja Muthupillai[2], Alberto Lopez[3], Benjamin Cheong[4], Carlo Uribe[5], Eduardo Hernandez[6], Stephanie Coulter[7], Emerson Perin[8], Silvana Molossi[9], Federico Gentile[10], Scott Flamm[11], Giovanni Lorenz[12], Flavio D'Ascenzi[13], Jonathan Tobis[14], Roberto Sarnari[15], Antonio Corno[16], James Furgerson[17], Amedeo Chiribiri[18], Adriana DM Villa[19], Fulvio Orzan[20], Pedro Brugada[21], John Jefferies[22], Pierre Aubry[23], Jeffrey Towbin[24], Gaetano Thiene[25], Robert Tomanek[26]

[1] Department of Cardiology, Texas Heart Institute, Houston, TX, USA. This author takes responsibility for all aspects of the reliability and freedom from bias of the data presented and their discussed interpretation.

[2] Department of Radiology, University of Houston, Houston, TX, USA. This author takes responsibility for all aspects of the reliability and freedom from bias of the data presented and their discussed interpretation.

[3] Electrophysiology Laboratory, Department of Cardiology, Texas Heart Institute, Houston, TX, USA. This author takes responsibility for all aspects of the reliability and freedom from bias of the data presented and their discussed interpretation.

[4] Department of Radiology, Texas Heart Institute, Houston, TX, USA. This author critically revised and gave final approval of the manuscript.

[5] Department of Cardiology, Texas Heart Institute, Houston, TX, USA. This author takes responsibility for all aspects of the reliability and freedom from bias of the data presented and their discussed interpretation.

[6] Department of Cardiology, Texas Heart Institute, Houston, TX, USA. This author critically revised and gave final approval of the manuscript.

[7] Department of Cardiology, Texas Heart Institute, Houston, TX, USA. This author critically revised and gave final approval of the manuscript.

[8] Department of Cardiology, Texas Heart Institute, Houston, TX, USA. This author critically revised and gave final approval of the manuscript.

[9] Section of Pediatric Cardiology, Department of Pediatrics, Texas Children's Hospital, Baylor College of Medicine, Houston, TX, United States, Houston, TX, USA. This author critically revised and gave final approval of the manuscript.

[10] Centro Cardiologico Gentile, Naples, Italy. This author critically revised and gave final approval of the manuscript.

[11] Department of Radiology, Cleveland Clinic, Cleveland, OH, USA. This author critically revised and gave final approval of the manuscript.

[12] Department of Radiology, Wilford Hall Ambulatory Center, San Antonio Military Health System, Joint Base San Antonio, San Antonio, TX, USA. This author takes responsibility for all aspects of the reliability and freedom from bias of the data presented and their discussed interpretation.

[13] Division of Cardiology, University of Siena, Siena, Italy. This author critically revised and gave final approval of the manuscript.

[14] Department of Cardiology, University of California Los Angeles, Los Angeles, CA, USA. This author takes responsibility for all aspects of the reliability and freedom from bias of the data presented and their discussed interpretation.

[15] Department of Radiology, Northwestern University, Chicago, IL, USA. This author takes responsibility for all aspects of the reliability and freedom from bias of the data presented and their discussed interpretation.

[16] Department of Congenital Cardiac Surgery, Children's Memorial Hermann Hospital, UTHealth, Houston, TX, USA. This author takes responsibility for all aspects of the reliability and freedom from bias of the data presented and their discussed interpretation.

[17] Department of Cardio-Radiology, US Air Force Lackland Hospital, San Antonio, TX, USA. This author takes responsibility for all aspects of the reliability and freedom from bias of the data presented and their discussed interpretation.

[18] Department of Cardiovascular Imaging, School of Biomedical Engineering and Imaging Sciences, King's College London, United Kingdom. This author takes responsibility for all aspects of the reliability and freedom from bias of the data presented and their discussed interpretation.

[19] Department of Radiology, St. Thomas Hospital, King's College London, United Kingdom. This author takes responsibility for all aspects of the reliability and freedom from bias of the data presented and their discussed interpretation.

[20] Division of Cardiology, Department of Medical Sciences, University of Turin, Italy. This author critically revised and gave final approval of the manuscript.

[21] Cardiovascular Division, Free University of Brussels (UZ Brussel) VUB, Brussels, Belgium. This author takes responsibility for all aspects of the reliability and freedom from bias of the data presented and their discussed interpretation.

[22] The Cardiac Institute, University of Tennessee Health Science Center, Memphis, TN, USA. This author takes responsibility for all aspects of the reliability and freedom from bias of the data presented and their discussed interpretation.

[23] Department of Cardiology, Bichat Hospital, Paris, France. This author takes responsibility for all aspects of the reliability and freedom from bias of the data presented and their discussed interpretation.

[24] Division of Adult Cardiovascular Diseases, Methodist University of Tennessee Cardiovascular Institute and Department of Preventive Medicine, St Jude Children's Research Hospital, Memphis, TN, USA. This author takes responsibility for all aspects of the reliability and freedom from bias of the data presented and their discussed interpretation.

[25] Department of Pathologic Anatomy, University of Padua, Italy. This author takes responsibility for all aspects of the reliability and freedom from bias of the data presented and their discussed interpretation.

[26] Department of Anatomy and Cell Biology, University of Iowa, Iowa City, IA, USA. This author takes responsibility for all aspects of the reliability and freedom from bias of the data presented and their discussed interpretation.

*Corresponding author at: Department of Cardiology, Texas Heart Institute, 6624 Fannin Street, Suite 2780, Houston, TX 77030, USA. Phone: 713-790-9401; e-mail: pangelini@texasheart.com.

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Declaration of Competing Interest

None.

Keywords

Death, sudden, cardiac; heart defects, congenital; sports medicine; adolescent medicine; autopsy; diagnostic screening programs

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). 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.

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?

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 anatomical 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 magnetic resonance imaging (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-CVC 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 orientations (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 coronary MRI with acquired voxel size of 0.7 × 0.7 × 1.5 mm. No significant immediate or late side-effects from the MRI were reported [3]. Average testing time was 10–15 minutes. 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 minutes 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” shown in Figure 1 [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 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 screened versus unscreened athletes [13] and in military recruits [14] 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 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, and it 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-to-15-minute studies without involving physicians on the field—all while costing less than US $200 at dedicated, ideal-efficiency organizations [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 s-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 symptomatic mitral valve prolapse, ARVC, myocarditis, or HCM: all to be examined in quantification studies) [8, 9].

3.4. The next-level study

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 novel sports cardiology is established as a discipline: Such duty is potentially foundational, in view of the fact that preventing SCD in athletes during exertion is the primary calling for sports cardiologists [8].

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, 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, 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.

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 [3, 12]. In the few cases for which secondary testing is indicated (1.5% of a young population), it will most often be to evaluate the severity of identified potential hr-CVCs (especially those discovered by s-MRI or ECG), some of which could be disqualifying for certification. 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. In truth, there exists no other available, large, controlled, and uniform population that could be compared with athletes in depth (in terms of consistency of exercise program, data acquisition and quality, follow-up, and compulsory autopsy after SCD), if not the military.

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

These considerations are offered to the international sports cardiology and preventive medicine community to encourage a long-overdue discussion about the most appropriate and effective mode(s) of preparticipation screening for young athletes, as recurrently auspicated 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 it is now enabled by novel technology; rather, we propose to discuss the logic and feasibility of performing a large, prospective, and statistically valid study to enable a quality change in the discussion and to answer the fundamental question: “Is a more accurate study of the conditions predisposing to SCD able to 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 is expected to be required, in view of their novel educational needs and updated functions.

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

Author contributions

This review is the result of the collaborative efforts of a large, multicenter group. PA wrote the initial draft and accepts direct responsibility for the manuscript. All other authors made collegial, substantial contributions to the design of the work or to the analysis and interpretation of the text; critically revised the work for important intellectual content; and made editorial changes to the text before approving the submitted version. The authors state that the data from the literature reviewed in this article are reported correctly and that the opinions presented for discussion are their own.

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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	• 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	• 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
ECG	As per international criteria [19]
Cardiac MRI	• *HCM, by criterium 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 criterium 1b* = LV mass index >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 criterium 2a* = LVEDD >1 SD from average (see Angelini et al [3] normality tables); *criterium 2b* = LVEF <40%.
- Patients with positive Petersen anatomical criteria (MRI) for NCLV, with LVEF <40%, and symptomatic for effort-related dyspnea (*criterium 2c*).
- Coronary anomalies: ACAOS-IM of a main coronary artery, with ectopic origin and probably 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 sinutubular 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 prevalence data). Prolonged QTc in the THI study (Bazett criteria, see Angelini et al [3] in Table 3) was obtained by Philips automatic ECG reading (with electrophysiologist's confirmation), but we do not know the criteria used by the other investigators, who present some 3-times-higher prevalence.

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.

* 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].

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].

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 autoptic 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). Clearly, 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.

REVIEW – POSITION PAPER

Young athletes: Preventing sudden death by adopting a modern screening approach?

A critical review and the opening of a debate

Paolo Angelini[1]*, Raja Muthupillai[2], Alberto Lopez[3], Benjamin Cheong[4], Carlo Uribe[5], Eduardo Hernandez[6], Stephanie Coulter[7], Emerson Perin[8], Silvana Molossi[9], Federico Gentile[10], Scott Flamm[11], Giovanni Lorenz[12], Flavio D'Ascenzi[13], Jonathan Tobis[14], Roberto Sarnari[15], Antonio Corno[16], James Furgerson[17], Amedeo Chiribiri[18], Adriana DM Villa[19], Fulvio Orzan[20], Pedro Brugada[21], John Jefferies[22], Pierre Aubry[23], Jeffrey Towbin[24], Gaetano Thiene[25], Robert Tomanek[26]

[1] Department of Cardiology, Texas Heart Institute, Houston, TX, USA. This author takes responsibility for all aspects of the reliability and freedom from bias of the data presented and their discussed interpretation.

[2] Department of Radiology, University of Houston, Houston, TX, USA. This author takes responsibility for all aspects of the reliability and freedom from bias of the data presented and their discussed interpretation.

[3] Electrophysiology Laboratory, Department of Cardiology, Texas Heart Institute, Houston, TX, USA. This author takes responsibility for all aspects of the reliability and freedom from bias of the data presented and their discussed interpretation.

[4] Department of Radiology, Texas Heart Institute, Houston, TX, USA. This author critically revised and gave final approval of the manuscript.

[5] Department of Cardiology, Texas Heart Institute, Houston, TX, USA. This author takes responsibility for all aspects of the reliability and freedom from bias of the data presented and their discussed interpretation.

[6] Department of Cardiology, Texas Heart Institute, Houston, TX, USA. This author critically revised and gave final approval of the manuscript.

[7] Department of Cardiology, Texas Heart Institute, Houston, TX, USA. This author critically revised and gave final approval of the manuscript.

[8] Department of Cardiology, Texas Heart Institute, Houston, TX, USA. This author critically revised and gave final approval of the manuscript.

[9] Section of Pediatric Cardiology, Department of Pediatrics, Texas Children's Hospital, Baylor College of Medicine, Houston, TX, United States, Houston, TX, USA. This author critically revised and gave final approval of the manuscript.

[10] Centro Cardiologico Gentile, Naples, Italy. This author critically revised and gave final approval of the manuscript.

[11] Department of Radiology, Cleveland Clinic, Cleveland, OH, USA. This author critically revised and gave final approval of the manuscript.

[12] Department of Radiology, Wilford Hall Ambulatory Center, San Antonio Military Health System, Joint Base San Antonio, San Antonio, TX, USA. This author takes responsibility for all aspects of the reliability and freedom from bias of the data presented and their discussed interpretation.

[13] Division of Cardiology, University of Siena, Siena, Italy. This author critically revised and gave final approval of the manuscript.

[14] Department of Cardiology, University of California Los Angeles, Los Angeles, CA, USA. This author takes responsibility for all aspects of the reliability and freedom from bias of the data presented and their discussed interpretation.

[15] Department of Radiology, Northwestern University, Chicago, IL, USA. This author takes responsibility for all aspects of the reliability and freedom from bias of the data presented and their discussed interpretation.

[16] Department of Congenital Cardiac Surgery, Children's Memorial Hermann Hospital, UTHealth, Houston, TX, USA. This author takes responsibility for all aspects of the reliability and freedom from bias of the data presented and their discussed interpretation.

[17] Department of Cardio-Radiology, US Air Force Lackland Hospital, San Antonio, TX, USA. This author takes responsibility for all aspects of the reliability and freedom from bias of the data presented and their discussed interpretation.

[18] Department of Cardiovascular Imaging, School of Biomedical Engineering and Imaging Sciences, King's College London, United Kingdom. This author takes responsibility for all aspects of the reliability and freedom from bias of the data presented and their discussed interpretation.

[19] Department of Radiology, St. Thomas Hospital, King's College London, United Kingdom. This author takes responsibility for all aspects of the reliability and freedom from bias of the data presented and their discussed interpretation.

[20] Division of Cardiology, Department of Medical Sciences, University of Turin, Italy. This author critically revised and gave final approval of the manuscript.

[21] Cardiovascular Division, Free University of Brussels (UZ Brussel) VUB, Brussels, Belgium. This author takes responsibility for all aspects of the reliability and freedom from bias of the data presented and their discussed interpretation.

[22] The Cardiac Institute, University of Tennessee Health Science Center, Memphis, TN, USA. This author takes responsibility for all aspects of the reliability and freedom from bias of the data presented and their discussed interpretation.

[23] Department of Cardiology, Bichat Hospital, Paris, France. This author takes responsibility for all aspects of the reliability and freedom from bias of the data presented and their discussed interpretation.

[24] Division of Adult Cardiovascular Diseases, Methodist University of Tennessee Cardiovascular Institute and Department of Preventive Medicine, St Jude Children's Research Hospital, Memphis, TN, USA. This author takes responsibility for all aspects of the reliability and freedom from bias of the data presented and their discussed interpretation.

[25] Department of Pathologic Anatomy, University of Padua, Italy. This author takes responsibility for all aspects of the reliability and freedom from bias of the data presented and their discussed interpretation.

[26] Department of Anatomy and Cell Biology, University of Iowa, Iowa City, IA, USA. This author takes responsibility for all aspects of the reliability and freedom from bias of the data presented and their discussed interpretation.

*Corresponding author at: Department of Cardiology, Texas Heart Institute, 6624 Fannin Street, Suite 2780, Houston, TX 77030, USA. Phone: 713-790-9401; e-mail: pangelini@texasheart.com.

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Declaration of Competing Interest

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Keywords

Death, sudden, cardiac; heart defects, congenital; sports medicine; adolescent medicine; autopsy; diagnostic screening programs

ABSTRACT

~~*Background:*~~ 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. ~~*Design:*~~ In this position paper, w~~W~~e review current~~ly held~~ 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). ~~*Methods*~~We present: ***1. Literature-Based Comparisons*** (for diagnosing hr-CVCs): Two r~~R~~ecent 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). Electrocardiography is valuable in screening for potentially high-risk electrophysiological anomalies. ***3. Proposed ~~Conclusive~~ Project:*** We ~~are~~ propos~~e~~ing a prospective, controlled study (2 comparable large cohorts: one historical, ~~and~~ 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.

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 aAny 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 ~~the factors we assume can cause SCD in a given individual~~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~~/or~~ echocardiography done only when justified by initial studies?

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 ~~recommend~~ 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. ~~School systems, families, health organizations, and society at large support athletic exercise, yet concerns remain about the hidden risks involved.~~

An essential difference between SCD in young athletes versus ~~typical~~ 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 anatomical changes at autopsy that are ~~typical of~~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, ~~severe coronary~~worsening stenosis and ischemia may occur ~~de novo~~ with maximal exertion, leading to mortal arrhythmias; similarly, in some cardiomyopathy (CMP) cases, which frequently include preexistent baseline myocardial fiber disarray or scarring~~s~~, 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 ~~and exercise-related ventricular arrhythmias~~) [9].

~~Along similar lines~~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 magnetic resonance imaging (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 ~~believe in~~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-CVC 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 ~~line for~~ 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 orientations (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 ~~were~~was obtained; (2) The ostial locations and proximal courses of the coronary arteries were evaluated by using a targeted respiratory navigator–guided 3-D coronary MRI with acquired voxel size of 0.7 × 0.7 × 1.5 mm. No significant immediate or late side-effects from the MRI were reported [3]. Average testing time was 10–15 minutes. 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), ~~a history or~~having a previous experience of claustrophobia, or ~~a~~having a ferro~~-~~magnetic metallic implant (one containing iron, nickel, or cobalt)~~, which could cause some degree of local heat or burning~~. 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 ~~probable~~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 ~~a new~~further, updated discussion~~, especially on the following recurrent subjects~~:

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]. ~~In contrast,~~ 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 minutes 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" shown in Figure 1 [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 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, ~~without including reliable severity~~ even though lacking reliable quantifiable parameters for each.

4. Understanding the true incidence of SCD and ~~proving~~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, ~~sedentary people with similar hr-CVC prevalence (a similar general population of unscreened candidates de facto involved in sports) or~~ historical groups ~~routinely~~ screened routinely ~~by~~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 screened versus unscreened athletes [13] and in military recruits [14] 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~~) from the same population, on the basis of outcomes in US military recruits observed during basic training activities~~) [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. ~~In particular, updated mortality data on SCD should be added to the incidence of SCA (inclusive of late neurological residua) and must include qualifying data on preliminary screening (preexisting conditions) and on quality of resuscitation efforts in the field.~~ 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 ~~the~~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 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 ~~routinely and~~ 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, and it 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-to-15-minute studies without involving physicians on the field—all while costing less than US $200 at ~~quite feasible,~~ dedicated, ideal-efficiency organizations [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 s-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 symptomatic mitral valve prolapse, ARVC, myocarditis, or HCM: all to be examined in quantification studies) [8, 9].

3.4. The next-level study

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 novel sports cardiology is established as a discipline: Such duty is potentially foundational, in view of the fact that preventing SCD in athletes during exertion is the primary calling for sports cardiologists [8].

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, 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, secondary ~~expensive~~ 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.

Discussing the cost of ~~novel~~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 [3, 12]. In the few cases for which

secondary testing is indicated (1.5% of a young population), it will most often be to evaluate the severity of identified potential hr-CVCs (especially those discovered by s-MRI or ECG), some of which could be disqualifying for certification. 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 ~~and resulting publications~~.

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. In truth, there exists no other available, large, controlled, and uniform population that could be compared with athletes ~~and studied~~ in depth (in terms of consistency of exercise program, data acquisition and quality, follow-up, and compulsory autopsy after SCD~~). The military could provide an unprecedented preliminary database with an exceptionally robust control cohort~~), if not the military.

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 ~~when~~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 ~~younger than 32~~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

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

~~Incidentally, artificial intelligence and machine learning techniques may one day enable more efficient, consistent, and inexpensive interpretation of radiological screening images .~~ At present, we are not ready to automatically endorse a change in the guidelines for athlete preparticipation screening just because it is now enabled by novel technology; rather, we propose to discuss the logic and feasibility of performing a large, prospective, and statistically valid study to enable a quality change in the discussion and to answer the fundamental question: “Is a more accurate study of the conditions predisposing to SCD able to 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 is expected to be required, in view of their novel educational needs and updated functions.

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Author contributions

This review is the result of the collaborative efforts of a large, multicenter group. PA wrote the initial draft and accepts direct responsibility for the manuscript. All other authors made collegial, substantial contributions to the design of the work or to the analysis and interpretation of the text; critically revised the work for important intellectual content; and made editorial changes to the text before approving the submitted version. The authors state that the data from the literature reviewed in this article are reported correctly and that the opinions presented for discussion are their own.

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Table 1

Diagnostic, probable *high-risk criteria* at MRI-based screening for elite athletes or military recruits ~~(preliminary simplified recommendations)~~

Screening method	Criteria of probable high-risk conditions at primary screening stage
History	• History of syncope, sudden cardiac arrest, or aborted SCD (especially with associated angina pain) • Family history of SCD at age <35~~2~~ years • In patients with potential hr-CVCs at screening MRI: exercise-limiting angina, dyspnea, dizziness
Physical exam	• 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
ECG	As per international ~~Seattle~~ criteria [19]
Cardiac MRI	• *HCM, by criterium 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 criterium 1b* = LV mass index >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 criterium 2a* = ~~above~~ LVEDD >1 SD from average (see Angelini et al [3] normality tables); *criterium 2b* = LVEF <40%.
- Patients with positive Petersen anatomical criteria (MRI) for NCLV, with LVEF <40%, and symptomatic for effort-related dyspnea (~~*preliminary*~~ *criterium 2c*).
- Coronary anomalies: ACAOS-IM of a main coronary artery, with ectopic origin and probably 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 sinutubular 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~~with~~ 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 prevalence data). Prolonged QTc in the THI study (Bazett criteria, see Angelini et al [3] in Table 3) was obtained by Philips automatic ECG reading (with electrophysiologist's confirmation), but we do not know the criteria used by the other investigators, who present some 3-times-higher prevalence.

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.

* 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].

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].

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 autoptic study.
4. Screened adolescents will feel anxious and condemned or disabled by knowing the diagnosis; psychological impact follows.	4. Preparticipation-screened adolescents ~~may~~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 ~~presently~~ propose that only elite athletes be MRI-screened (high school, college, and professional athletes). Clearly, we are interested in hr-CVCs, not all possible anatomical anomalies.
7. The role of exercise is unclear.	7. Most ~~good~~high-quality reports have found that 90% of SCD in athletes occurs during exertion: we could ~~clarify~~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.

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List of all Authors: Paolo Angelini[1]*, Raja Muthupillai[2], Alberto Lopez[3], Benjamin Cheong[4], Carlo Uribe[5], Eduardo Hernandez[6], Stephanie Coulter[7], Emerson Perin[8], Silvana Molossi[9], Federico Gentile[10], Scott Flamm[11], Giovanni Lorenz[12], Flavio D'Ascenzi[13], Jonathan Tobis[14], Roberto Sarnari[15], Antonio Corno[16], James Furgerson[17], Amedeo Chiribiri[18], Adriana DM Villa[19], Fulvio Orzan[20], Pedro Brugada[21], John Jefferies[22], Pierre Aubry[23], Jeffrey Towbin[24], Gaetano Thiene[25], Robert Tomanek[26]

Corresponding Author: Paolo Angelini

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Highlights