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Pre-participation Cardiovascular Screening in Young Competitive Athletes

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Abstract

Purpose of Review The purpose of this review was to highlight the current recommendations, data, and limitations for methods of cardiovascular screening in athletes.

Recent Findings While the history and physical (H&P) alone remains the cornerstone for pre-participation cardiovascular screening (PPCS) in athletes, the advent of modern electrocardiographic (ECG) screening criteria has drastically increased sensitivity and decreased false-positive rates for screening. Advanced imaging techniques remain an important component of secondary testing after an athlete has an abnormal initial screening exam; however, the use of imaging for universal screening has not been rigorously tested to date. Current disqualification guidelines have now begun to emphasize shared decision-making between the provider and athlete in situations of clinical equipoise.

Summary All major medical and sporting societies recommend PPCS using a focused medical history and physical examination for all competitive athletes, but there remains controversy about the role of ECG and advanced imaging in PPCS. Future research should focus on the creation of a randomized trial that is powered for mortality that can truly assess the utility of PPCS in athletes.

Keywords Athlete · Pre-participation screening · Cardiac screening · Electrocardiography · Echocardiography

Introduction

Pre-participation cardiovascular screening (PPCS) for competitive athletes is designed to screen for underlying cardiovascular abnormalities that may increase the risk of sudden cardiac death (SCD) during sport participation. While the overall incidence of SCD during athletic activities is rare, deaths among young, ostensibly healthy athletes are tragic with often devastating impacts on families and local communities.

All major medical and sporting societies recommend PPCS using a focused medical history and physical examination for all competitive athletes [1–4]. Concerns about unacceptable sensitivity and specificity of PPCS confined to history and physical alone have generated interest in the use of adjunct screening tools including 12-lead electrocardiography (ECG). At present, the role of ECG and other additions to the medical history and physical examination remain controversial with some major organizations supporting ECG use [1–3], and others recommending against widespread ECG-inclusive screening [4, 5]. Specific American consensus documents have been made for young (age 12–25) [6], and masters athletes [7], with age-specific recommendations for competitive athletes, and quality standards have been published by major organizations including the National Collegiate Athletic Association (NCAA) to ensure high-quality screening techniques [8].

While work over the last few decades has led to significant progress regarding the implementation of PPCS, several key questions remain unanswered. Most importantly, the impact of PPCS on the incidence of SCD has yet to be firmly established. In addition, PPCS practices both within the USA and across other nations remain heterogeneous and devoid of an accepted gold standard of care. This review was written to summarize current PPCS recommendations and to highlight the available data describing the diagnostic accuracy (sensitivity, specificity, false-positive rate), cost, and key limitations of current PPCS strategies.

This article is part of the Topical Collection on *Cardiovascular Care*

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Methods

In this review, we included all prominent studies using the Pubmed database from inception to January 2020, with a focus on more recent studies. We also performed a manual search of the references cited by major articles. Keywords in our search technique included "cardiovascular screening," "pre-participation screening," "athlete," "cost," "electrocardiography," "echocardiography," "shared decision making."

History and Physical

PPCS based on a focused medical H&P is recommended by numerous governing bodies including the American Heart Association/American College of Cardiology (AHA/ACC), European Society of Cardiology (ESC), International Olympic Committee (IOC), and Fédération Internationale de Football Association (FIFA) [1–4]. While multiple different screening methodologies have been proposed by various societies, a thorough H&P remains the backbone of pre-participation screening in athletes.

Most providers evaluate athletes using standardized personal and family history questionnaires with the pre-participation examination monograph (PPE-4) or the American Heart Association 14 (AHA-14) questions (Table 1). The American Heart Association initially recommended a comprehensive personal and family H&P in 1996 [9] and 2007 [10], and recently, the AHA questions were expanded from a 12-point to a 14-point evaluation in 2014 [6, 8]. Questions inclusive of personal and family medical history are designed to screen for the presence of congenital and genetic cardiovascular diseases that have been shown to increase the risk of adverse outcomes during exercise. Notably, the AHA-14 and PPE-4 monograph contain questions with slightly different wording and are compared in Table 1. The AHA-14 questions are simpler but less comprehensive than the PPE-4 monograph which may impact the performance of screening. The focused physical examination, as recommended by the AHA/ACC, is geared toward the diagnosis of specific forms of valvular disease (cardiac auscultation supine and standing), hypertrophic cardiomyopathy with left ventricular outflow tract obstruction (cardiac auscultation with Valsalva), aortic coarctation (simultaneous femoral and radial pulses), Marfan's disease (kyphoscoliosis, high-arched palate, pectus excavatum, arachnodactyly, arm span > height, hyperlaxity, myopia, mitral valve prolapse, aortic insufficiency), and systemic arterial hypertension (brachial artery blood pressure while sitting) in athletes.

Recently, the AHA released new US blood pressure guidelines lowering the threshold for diagnosing hypertension (HTN) from ≥ 140/90 to ≥ 130/80 mmHg in adults and adolescents [11, 12]. However, the current guidelines for athletes define hypertension as ≥ 140/90 [13]. This may become significant in the future to reassess the impacts of HTN at a lower threshold in athletes as there recently has been significant exposure on HTN and the development of pathologic cardiovascular remodeling in athletes [14–16].

Diagnostic Accuracy

To date, there have been no studies assessing the H&P alone to detect cardiovascular conditions in athletes. Most studies have assessed history and physical along with other methods of screening (ECG, echocardiography, etc.). In 2010, Baggish et al. performed a prospective study of 510 collegiate athletes undergoing PPCS including a complete H&P in isolation, followed by ECG and then subsequent TTE screening as a gold standard to diagnose cardiac findings relevant to athletes. TTE identified 11/510 (2.2%) cardiac abnormalities relevant to sports participation risk in this study, and H&P alone detected abnormalities in 5/11 (45.5%) of these patients (sensitivity, 45.5% [95% CI, 16.8 to 76.2%]; specificity, 94.4% [CI, 92.0 to 96.2%]). In a recent meta-analysis of 15 studies from 1996 to 2014 by Harmon et al., the overall false-positive rates were 8% for history and 10% for the physical exam portions of the PPCS exam [17]. In a more recent study by Malholtra et al. assessing the utility of PPCS in 11,168 adolescent soccer players, a positive history was found in 2.2% of athletes with any cardiac condition, and 7.1% of athletes with a cardiac condition associated with SCD [18•]. The physical exam was positive in 28.5% of athletes with any cardiac condition, and 4.8% of athletes with a cardiac condition associated with SCD.

In studies of collegiate athletes, 27–37% of participants report a positive cardiovascular symptom or family history response during PPCS using the AHA 12-point or PPE-4 monograph [19, 20]. In contrast, 68% of high school athletes reported a positive history using the PPE-4 questions [21], and 22.5% reported a positive history using the new AHA-14 questions [22]. The new AHA-14 questions have a reported sensitivity of 18.8%, specificity of 68%, and positive predictive value of 0.3% in high school athletes [22]. While the H&P alone may be better than no PPCS, the significantly high false-positive rates call for refinement of questions based on the demographic and sport type of the athlete, and strengthens the argument for the potential role of other testing (i.e., ECG screening).

Limitations

While the history and physical remains the pinnacle screening system for athletes in the USA, significant limitations exist. For the physical exam portion of testing, there is significant heterogeneity in the ability of providers to diagnose cardiac conditions through cardiac auscultation [23, 24], and there still

Table 1 Comparison of AHA-14 questionnaire and PPE-4 monograph

AHA-14 questionnaire	PPE-4 monograph
Personal History	Heart Health Questions About You
1. Chest pain/discomfort/tightness/pressure related to exertion	6. Have you ever had discomfort, pain, tightness, or pressure in your chest during exercise?
2. Unexplained syncope/near syncope	5. Have you ever passed out or nearly passed out during or after exercise?
3. Excessive and unexplained dyspnea/ fatigue or palpitations, associated with exercise	12. Do you get more tired or short of breath more quickly than your friends during exercise? 10. Do you get lightheaded or feel more short of breath than expected during exercise? 7. Does your heart ever race or skip beats (irregular beats) during exercise?
4. Prior recognition of a heart murmur 5. Elevated systemic blood pressure	8. Has a doctor ever told you that you have any heart problems? If so, check all that apply: ▫ High blood pressure ▫ A heart murmur ▫ High cholesterol ▫ A heart infection ▫ Kawasaki disease Other: _______________
6. Prior restriction from sports	1. Has a doctor ever denied or restricted your participation in sports for any reason?
7. Prior testing for heart disease, ordered by a physician	9. Has a doctor ever ordered a test for your heart? (For example, ECG/EKG, echocardiogram) *11. Have you ever had an unexplained seizure?*
Family History	Heart Health Questions About Your family
8. Premature death (sudden and unexpected or otherwise) before 50 yrs. of age attributable to heart disease in >1 relative	13. Has any family member or relative died of heart problems or had an unexpected death before age 50 yrs. (including drowning, unexplained car accident, or sudden infant death syndrome)?
9. Disability from heart disease in a close relative < 50 yrs of age	
10. Hypertrophic or dilated cardiomyopathy, long QT syndrome or other ion channelopathies, Marfan syndrome, or clinically significant arrhythmias; specific knowledge of genetic cardiac condition in family member	14. Does anyone in your family have hypertrophic cardiomyopathy, Marfan syndrome, arrhythmogenic right ventricular cardiomyopathy, long QT syndrome, short QT syndrome, Brugada syndrome, or catecholaminergic polymorphic ventricular tachycardia? *15. Does anyone in your family have a heart problem, pacemaker, or implanted defibrillator?* *16. Has anyone in your family had unexplained fainting, unexplained seizures, or near drowning?*
Physical Examination	Physical Examination
11. Heart murmur	a. Heart • Murmurs (auscultation standing, supine, ± Valsalva) • Location of point of maximal impulse
12. Femoral pulses to exclude coarctation	b. Pulses • Simultaneous femoral and radial pulses
13. Physical stigmata of Marfan syndrome	c. Appearance • Marfan stigmata (kyphoscoliosis, high-arched palate, pectus excavatum, arachnodactyly, arm span > height, hyperlaxity, myopia, MVP, aortic insufficiency)
14. Brachial artery blood pressure (sitting position)	d. Blood pressure

Differences between the two questionnaires are italicized

remains extreme difficulty in the recognition and diagnosis of Marfan's syndrome [25].

The PPE-4 and AHA-14 questions are useful to providers as a framework for approaching young athletes; however, there is a significant false-positive rate [19–22] which can lead to unnecessary secondary testing. In a study by Fudge et al. of 1339 high school athletes in Seattle, the false-positive rate of the PPE-4 monograph was 31.3% [21]. A more recent study of 3620 high school athletes also showed that the positive predictive value of the AHA-14 questions was 0.3% [22]. Another significant limitation of the PPE-4 and AHA-14 is that the questions are based on expert opinion, and there is little data on how age, socioeconomic, or racial demographics affect responses to questions. These questions also require honest reporting from athletes who may be under significant societal or financial pressure to perform in their respective sport, and further data also suggests that there is not universal adherence or awareness of the AHA questions and PPE monograph on an institutional and national level [26–29].

Key Points

- A focused H&P represents the baseline standard of care for PPCS as currently recommended by all major cardiovascular and sporting governing societies.
- The AHA-14 and PPE-4 monograph are medical history questionnaires designed as guides for clinicians conducting PPCS.
- The H&P used in isolation as a screening tool is associated with high false-positive rates.
- Future studies should aim to derive evidence-based history questionnaires that account for factors (age, ethnicity, socioeconomic status, etc.) that may affect the accuracy of responses to questions.

Electrocardiography

Electrocardiographic screening for athletes is one of the most intensely debated quandaries in the field of sports cardiology. A history and physical examination with ECG screening is currently recommended by the European, FIFA, and IOC guidelines [1–3], whereas the current American Heart Association/American College of Cardiology (AHA/ACC) guidelines report that ECG screening in association with a comprehensive H&P may be considered in relatively small cohorts of healthy people with close physician follow-up (class IIb, level of evidence C), but do not recommend mandatory, universal ECG screening (class III, level of evidence C) [4]. Advocates for universal ECG screening argue that the addition of ECG to the H&P increases the detection of cardiovascular disease in athletes, and an estimated 60% of disorders associated with SCD may be detectable by ECG [30]. The primary driver for the inclusion of ECG screening in the European recommendations stems from experiences of the national screening program in Italy which showed a significant decrease in SCD after its inception in 1982 [31]. In 2006, Corrado et al. showed the annual incidence of SCD in Italian athletes decreased from 3.6/100,000 person-years in 1979–1980 to 0.4/100,000 person-years in 2003–2004 after the institution of mandatory PPCS in 1982 (89% reduction). While Israel is a European nation that also created a mandatory PPCS program in 1997, post-implementation data using their ECG screening program showed no difference in the risk of SCD [32].

There have been multiple iterations of ECG screening criteria in athletes since the first recommendations were proposed by the European Society of Cardiology (ESC) in 2005 (Fig. 1) [33, 34, 35•, 36, 37]. The biggest driver for the evolution of ECG screening guidelines was a series of NCAA papers reporting extremely high rates of abnormal ECGs and false-positive rates (> 10%) leading many critics to argue that universal ECG screening leads to too many inappropriate secondary tests and significant costs on the medical system (Table 2) [38–41]. After the first ESC criteria in 2005, which contained one table of potentially abnormal ECG patterns in athletes, the ESC proposed new criteria in 2010 and labeled ECG patterns as "Group 1" or "Group 2" [33]. The major difference from the 2005 and 2010 ESC criteria was the advent of a two-group system including ECG patterns that are normal training-related changes in Group 1 and training unrelated changes in Group 2. The 2010 ESC criteria unfortunately still had high false-positive rates, particularly in Black athletes [42–45]. In 2013, the Seattle Criteria were created and emphasized ethnic-specific ECG findings given the limitations found with the 2010 ESC criteria [34]. The next iteration of ECG guidelines was created in 2014 and called the Refined Criteria [36]. One of the major findings following publication of the Seattle Criteria was that isolated voltage criteria for atrial enlargement and left axis deviation led to a high proportion of abnormal ECGs and correlated poorly with underlying cardiac disorders in asymptomatic athletes [46, 47]. The authors of the Refined Criteria thereby created a group for borderline variants (only if 2 or more criteria are present warrants further investigation), which included multiple ECG changes found in the abnormal ECG group from the Seattle criteria (left atrial enlargement, right atrial enlargement, left axis deviation, right ventricular hypertrophy). The International Criteria are the most recent iteration of ECG guidelines and were created in 2017 [35•]. Notable changes in the International Criteria are the change of definition for pathologic q waves, recognition of juvenile T wave inversion (TWI) as a normal finding in athletes < 16 years, and addition of epsilon waves and TWI ≥ 1 mm in V5 or V6 alone to the "abnormal" category [48].

Diagnostic Accuracy

The overall diagnostic accuracy of ECG screening to diagnose conditions leading to SCD has greatly improved with the evolution of ECG screening guidelines over the past decade (Table 2) [20–22, 33, 36, 38–42, 44, 45, 49–63]. Studies were included in Table 2 if they explicitly stated what ECG reading criteria were utilized, and diagnostic accuracy measures (sensitivity, specificity, false-positive rate) were only included if explicitly reported by each study, as many only include the abnormal ECG rate because not all athletes underwent TTE or

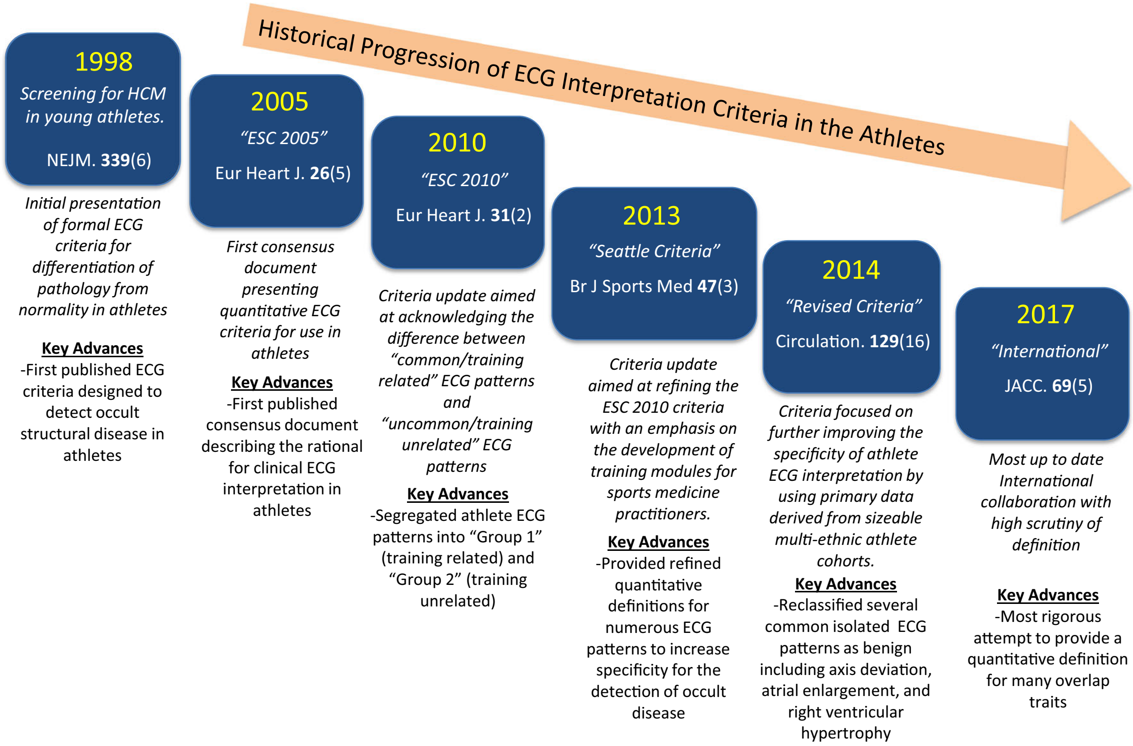

Fig. 1 Historical progression of ECG screening criteria in athletes. Abbreviations: Br J Sports Med, British Journal of Sports Medicine; ESC, European Society of Cardiology; Eur Hear J, European Heart Journal; HCM, hypertrophic cardiomyopathy; JACC, Journal of the American College of Cardiology; NEJM, New England Journal of Medicine

other "gold standard" tests to rule out cardiovascular abnormalities. Estimates from studies using the ESC 2010 criteria have shown significantly high rates of abnormal ECGs and false-positive rates (3–60%). With the evolution of the ECG screening guidelines, the International Criteria now have much lower false-positive rates of 1.3–6.8% depending on the population studied [56, 57, 64]. Two of three major studies have cited low false-positive rates for the International Criteria (1.3–1.5%); however, McClean et al. recently performed a study in 1304 Arab and Black athletes in Qatar and found a higher rate of 6.8%. These data suggest that the criteria could be further refined to be more inclusive of these populations. Recently, there has also been an interest in the diagnostic capability of ECG interpretation software to analyze an athlete's ECG. In a population of 5258 US collegiate athletes, Hyde et al. found a false-positive rate by experienced physicians using the Seattle Criteria of 2.8%, and a rate of 1.3% using the International Criteria. They also performed an analysis using the Cardea ECG interpretation software (©2018 Cardiac Insight Inc.) and found a false-positive rate of 5% using the Seattle Criteria and 2.3% using the International Criteria [56]. ECG interpretation software shows promise, but still has likely unacceptable increases in false-positive rates which could lead to significant costs from secondary testing.

Limitations

There are major limitations of ECG screening that have led many societies including the AHA/ACC to not recommend universal screening in athletes [4]. Opponents of ECG screening often cite the high costs of ECG, high false-positive rates leading to inappropriate secondary testing, lack of widespread expertise in the interpretation of an athlete's ECG, and the inability to detect important conditions such as congenital anomalous coronary artery as reasons why there should not be universal screening. Notably, with the evolution of the ECG screening criteria, the false-positive rate has drastically reduced from the initial 2010 ESC criteria to around 1.3–6.8% with the new International Criteria recommendations depending on the screening cohort [56, 57, 64]. The diagnostic accuracy of ECG screening continues to improve; however, critics still assert that the costs of the inappropriate secondary testing may outweigh the benefits of screening even at a low false-positive rate. While there have been significant strides in terms of mitigating the false-positive rate based on contemporary screening criteria, cost analyses for ECG screening continue to provide mixed results, with some papers favoring ECG screening [58, 65–67], and some suggesting inexcusably high costs [41, 68]. Even though ECG screening does in general cost more than an H&P alone, many diagnoses would have been missed in large-scale PPCS programs had ECG screening been omitted (HCM, ARVC, Long QT, Brugada

Table 2 Rates of abnormal ECGs and diagnostic accuracy measures for ECG interpretation guidelines

Author (year) [ref]	*N*	Abn ECG	Sens	Spec	FPR	Author (year) [ref]	*N*	Abn ECG	Sens	Spec	FPR
ESC 2005 Criteria						**Seattle Criteria**					
Baggish et al. (2010) [38]	510	16%	91%	83%	17%	Brosnan et al. (2014) [50]	1078	5%			4%
Le et al. (2010) [40]	658	35%				Sheikh et al. (2014) [36]	5505	10%	60% (WA) 70% (BA)	92% (WA) 79% (BA)	8% (WA) 21% (BA)
Hevia et al. (2011) [55]	1220	6%				Dunn et al. (2015) [20]	1596	6%			
Malhotra et al. (2011) [41]	1473	30%				Riding et al. (2015) [44]	2491	12%	100%	88%	11%
Fuller et al. (2016) [54]	874	11%				Wasfy et al. (2015) [62]	330	4%			3%
Snoek et al. (2015) [61]	561	21%				Drezner et al. (2016)* [53]	5258	4%	100%	97%	3%
ESC 2010 Criteria						Fuller et al. (2016) [54]	874	3%			
Corrado et al. (2010) [33]	1005	11%				Pickham et al. (2014) [59]	1417	6%			
Weiner et al. (2011) [63]	508	10%	91%	90%	10%	Dhutia et al. (2017) [52]	4925	6%			
Wilson et al. (2012) [45]	1220	10%			10%	Malhotra et al. (2019) [57]	11,168	4%	86%	96%	4%
Alattar et al. (2014) [49]	230	21%			18%	McClean et al. (2019) [64]	1304		62%	78%	22%
Brosnan et al. (2014) [50]	1078	17%			17%	Williams et al. (2019) [22]	3620	3%	88%	98%	2%
Chandra et al. (2014) [42]	4081	33%				**Refined Criteria**					
Deligiannis et al. (2014) [51]	22,205	8%				Sheikh et al. (2014) [36]	5505	7%	60% (WA) 70% (BA)	94% (WA) 84% (BA)	6% (WA) 16% (BA)
Fudge et al. (2014) [21]	1339	5%			5%	Riding et al. (2015) [44]	2491	5%	100%	94%	5%
Menafoglio et al. (2014) [58]	1070	4%				Fuller et al. (2016) [54]	874	3%	86%	97%	3%
Pickham et al. (2014) [59]	1417	26%				Dhutia et al. (2017) [52]	4925	4%			
Price et al. (2014) [60]	2017	3%				Malhotra et al. (2019) [57]	11,168	3%	86%	97%	3%
Sheikh et al. (2014) [36]	5505	22%	60% (WA) 70% (BA)	74% (WA) 40% (BA)	26% (WA) 60% (BA)	**International Criteria**					
Dunn et al. (2015) [20]	1596	27%				Dhutia et al. (2017) [52]	4925	3%			
Riding et al. (2015) [44]	2491	22%	100%	77%	22%	Hyde et al. (2019) [56]	5258	2%			1%
Snoek et al. (2015) [61]	561	12%				Malhotra et al. (2019) [57]	11,168	2%	86%	98%	2%
Wasfy et al. (2015) [62]	330	47%			46%	McClean et al. (2019) [64]	1304	8%	62%	93%	7%
Dhutia et al. (2017) [52]	4925	21%									
Malhotra et al. (2019) [57]	11,168	13%	86%	87%	13%						
McClean et al. (2019) [64]	1304		77%	59%	41%						

Abbreviations: *Abn ECG*, abnormal electrocardiography; *BA*, Black athletes; *FPR*, false-positive rate; *ref.*, reference; *Sens*, sensitivity; *Spec*, specificity; *WA*, white athletes

*Hyde et al. (2019) used the same cohort of 5258 college school athletes as Drezner et al. (2016), so repeated results not included in the Seattle Criteria section syndrome, Wolff-Parkinson-White syndrome) [18•]. Another significant limitation of ECG screening is the expertise needed to interpret an athlete's ECG, especially when so many guidelines and updates have been created over the last decade [33, 34, 35•, 36, 37]. Dhutia et al. performed a study of ECG interpretation of 400 young athlete's ECGs among 8 cardiologists (4 with experience in screening athletes), and found inexperienced cardiologists to be more likely to classify an ECG as abnormal (odds ratio = 1.44; 95% CI 1.03–2.02); they had a moderate level of interobserver reliability using 3 different ECG criteria ($\kappa = 0.40$–0.53), and had a higher cost of cardiovascular evaluation per athlete than experienced cardiologists ($175, 95% CI $142–$228 vs. $101, 95% CI $83–$131) [69•]. Finally, the age at which some cardiovascular abnormalities manifest on an ECG varies, so the optimal time of testing and indication for repeat testing remain unknown.

Key Points

- Universal ECG screening for athletes remains a controversial topic, and is currently recommended by European guidelines but not American guidelines.
- Current American guidelines endorse the addition of ECG to H&P in selected populations when there is appropriate clinician oversight and adequate resources to facilitate downstream testing.
- The evolution of ECG screening criteria has drastically reduced false-positive rates, while maintaining high sensitivity in athletes.
- High costs, inexperience of ECG readers, and uncertain diagnostic performance of ECG in some populations remain its greatest limitations.

Multimodality Imaging

Currently, no major sporting or professional societies, other than FIFA, recommend routine use of multimodality imaging as a component of PPCS. Nonetheless, multiple screening programs, universities, national teams, and professional teams have included imaging as a part of their routine screening process. A screening strategy utilizing multimodality imaging has not been rigorously tested or validated to date, so it remains unclear what impact it may have on the future of PPCS. The most common imaging modality considered to date has been transthoracic echocardiogram (TTE), and supporters suggest that a limited TTE-based strategy may enhance sensitivity of screening and potentially reduce the number of days lost to sport in athletes who undergo universal PPCS and are deemed to require a secondary cardiovascular workup.

While there is debate about the utility of multimodality imaging during routine PPCS of athletes, imaging remains a vital component of secondary testing when an athlete is determined to have an abnormal initial screening exam. Common indications requiring secondary imaging include history of unexplained prior syncope or a family history of sudden cardiac death in a first-degree relative, report of exertional chest discomfort or inappropriately labored breathing, and certain abnormal ECG findings as proposed by the recent International Criteria [35•]. Athletes that are deemed to require follow-up testing often undergo one or multiple cardiac imaging tests to assess valvular morphology/function, myocardial structure/function, and coronary anatomy.

Diagnostic Accuracy

The majority of PPCS studies have included TTE as the "gold standard" to assess the diagnostic capability of a H&P only or H&P with ECG screening strategy. Baggish et al. performed a prospective study of 510 collegiate athletes undergoing PPCS including a complete H&P, ECG, and TTE from 2006 to 2008, and found 3 athletes (0.6%) with a major structural abnormality identified by echocardiography (moderate pulmonic stenosis, hypertrophic cardiomyopathy, myocarditis) who all had abnormal findings on H&P and/or ECG screening [38]. Magalski et al. performed a subsequent study of 964 collegiate athletes from 2004 to 2009 with TTE as component of PPCS with H&P and ECG screening, and found 1 athlete (0.1%) with a major structural abnormality by echocardiography (Ebstein's anomaly with mild-to-moderate tricuspid regurgitation) [39]. Notably, this athlete was also found to have Wolff-Parkinson-White syndrome, so there were no major diagnoses isolated by TTE that had normal H&P and ECG. Rizzo et al. performed a larger study of 3100 soccer players who underwent PPCS in Italy with TTE screening added onto the mandated H&P and ECG, and found 56 athletes (1.8%) with cardiac structural abnormalities [70]. Of these, 4 (0.1%) were determined to be clinically significant conditions (HCM in 2 athletes, biscupid aortic valve with aortic dilation, large ASD), and all 4 had abnormal H&P and/or ECG. In the largest study including TTE as a component of PPCS to date, Malhotra et al. performed comprehensive screening (H&P, ECG, TTE) on 11,168 adolescent soccer players, and found 42 athletes (0.38%) with conditions associated with SCD [18•]. Of these, 4 athletes had negative H&P and ECG screening, but positive echocardiograms (1 ARVC, 2 coronary anomalies, 1 bicuspid aortic valve). Therefore, there are few cases in these previous studies with normal H&P and ECG and abnormal TTE, which questions potential utilities for TTE in front-line universal screening.

Limitations

The major limitations associated with multimodality cardiovascular imaging are the potential for false-positive results in athletes with inconclusive imaging, false-negative results in athletes with conditions associated with normal echocardiographic imaging, cost of imaging, clinical expertise needed to interpret images, and the time needed to acquire accurate images.

Key Points

- A screening strategy incorporating multimodality imaging for PPCS in athletes has not been rigorously tested to date and is therefore not recommended.
- Multimodality imaging as a component of PPCS is currently not advised by any major society, other than FIFA, who currently requires a TTE prior to all World Cup events.
- Multimodality imaging plays an important role as secondary or "downstream" testing following the identification of abnormal H&P and/or ECG findings.

Costs of Pre-participation Screening

One of the major barriers to the advent of universal PPCS in athletes is the significant cost associated with obtaining a cardiac diagnosis that could prevent SCD. The majority of previous studies have focused on the costs associated with H&P + ECG screening techniques. Cost-based estimates are inherently difficult to compare given that they vary widely based on the definition of a positive cardiac diagnosis, country-based cost estimates of screening, and if the analyses were performed on a specific population (e.g., young athletes, high school, college) or were estimates based on the number of athletes in a large population. The majority of cost is also driven by secondary testing, which varies considerably across healthcare systems.

There are three major prior cohort studies that have estimated the actual cost for H&P + ECG screening in elite athletes. One early study by Malhotra et al. in 1473 Division I athletes at the University of Virginia projected the cost per cardiac finding based on H&P alone was $68,745 vs. $68,893 with an H&P + ECG screening technique, so therefore concluded that there was no discrete benefit of adding ECG to H&P alone screening [41]. Menafoglio et al. also performed a study in 1070 Swiss athletes aged 14–35 in 2015, and found that the cost per cardiac diagnosis for H&P alone was estimated at $14,434 vs. $15,746 with H&P + ECG screening (converting CHF to dollars using conversion estimates) [58]. A total of 4 athletes (0.4%) in their study were found to have a cardiovascular condition that could potentially lead to SCD, and all of them had abnormal ECG screening leading to secondary testing. Therefore, the authors concluded that the most cost-effective method of PPCS may be ECG screening without H&P, but a method of cardiovascular screening with H&P + ECG is feasible in Switzerland at a reasonable cost. Dhutia et al. examined the costs to screen 4925 primarily Caucasian male, elite soccer athletes using the 2010 ESC criteria, Seattle Criteria, or Refined Criteria [65]. They found the total cost per serious diagnosis associated with SCD was $35,993 using the 2010 ESC criteria, $30,251 using the Seattle criteria, and $28,510 using the Refined criteria with costs of secondary testing based on the 2014/2015 UK National Health Services tariff payment system.

Larger population-based studies have also yielded mixed results. Wheeler et al. combined 2 prior studies to derive cost-based estimates in a population of 3.7 million high school and college athletes in a high-risk activity [66]. Their projections showed that the addition of ECG to an H&P alone screening technique saves 2.06 life-years per 1000 athletes at an incremental cost of $89 per athlete with a cost-effectiveness ratio of $42,900 per life-year saved. Fuller et al. also performed a population-based analysis in high school athletes and found a benefit of adding ECG to an H&P alone technique [67]. They calculated the cost per life year saved to be $84,000 with H&P and $44,000 for 12-lead ECG. In contrast, Schoenbaum et al. performed a large population-based estimate in young athletes and compared H&P alone vs. H&P + ECG vs. ECG only techniques and found that an ECG after a negative H&P led to an incremental cost-effectiveness of $68,800/QALY, so concluded that adding ECG to PPCS was not cost effective [68]. Another study by Leslie et al. using ECG to screen adolescents initiating stimulant medications (8 years of age) and adolescents participating in sports (14 years of age) projected an incremental cost-effectiveness of screening between $91,000 and $204,000 per life year, so concluded that the cost of ECG screening in these cohorts is high compared to the health-related benefits [71].

To assess the potential costs associated with a nationwide US screening system in high school and college athletes, Halkin et al. created a cost-projection model using an initial Italian study [31] and applied this model to US college and high school athletes using Medicare estimates for cost [72]. Their estimates projected that a 20-year program of H&P + ECG screening would cost between $51 and 69 billion, with a cost per life saved between $10.6 and 14.4 million. While this study importantly projects the costs associated with universal screening, a cost in isolation has little value. It is vital to extrapolate these findings to the overall healthcare budget and see what areas of healthcare may be constrained if universal PPCS is mandated.

Key Points

- The majority of cost associated with PPCS is generated by the secondary testing performed after initial abnormal screening and varies widely across different healthcare systems.
- Cost-effectiveness studies assessing the addition of ECG screening to H&P alone have yielded mixed results to date.
- The consideration of what areas of the overall US healthcare budget would be constrained by adapting universal PPCS should be considered when making future decisions about the implementation of any universal PPCS programs.

Disqualification from Sport and Shared Decision-making

Guidelines have been created to assist providers with risk stratification and the determination of subsequent competitive sport eligibility among athletes diagnosed with cardiovascular disease during screening [73–80]. The first consensus guidelines were established by an expert panel sponsored by the ACC in 1985 from the Bethesda Conference #16 [80]. Since then, there have been 3 iterations of the North American guidelines (Bethesda #26-1994, Bethesda #36- 2005, AHA/ACC guidelines- 2015), as well as parallel consensus statements from the ESC in 2005 and more recently the European Association of Preventive Cardiology (EAPC) has released 3 disease-specific consensus documents [73–79].

While previous guidelines provided discrete binary recommendations whether athletes should be able to participate in sport or be disqualified, there has recently been a call to action for guideline documents to focus on shared decision-making between an athlete and their sports provider [81, 82]. In December 2015, the AHA/ACC released a new consensus guideline for disqualification from sport that was an update from its previous statement from the 2005 Bethesda Conference [76, 80]. This new guideline document represented a pivotal paradigm shift for the practice of sports cardiology. Specifically, the historical approach to eligibility which endorsed a binary "yes" or "no" decision-making strategy was replaced by a more nuanced approach that provided athletes and their physicians with the opportunity to approach this topic using a shared decision-making model. Current AHA/ACC guidelines now utilize the contemporary format of a 3 class of recommendation system associated with level of evidence for each recommendation with class I signifying participation in sports is recommended, class IIa and IIb suggesting sport participation is reasonable or may be considered, and class III indicating that participation in sport is not recommended. While class IIa and IIb recommendations demonstrate scientific and clinical uncertainty, this allows providers to use shared decision-making with an athlete to make individualized recommendations. The 2015 AHA/ACC guidelines presented a total of 84 class II recommendations among the 253 possible cardiovascular diagnoses or clinical scenarios. While the term "shared decision-making" was not discretely used in this guideline document, an individualized approach to care for the athlete is implied and should be considered with the new format of recommendations. In parallel with the North American guidelines, the 3 new European consensus statements from the EAPC have also moved to a more contemporary approach providing multiple classes of recommendation that support an approach of shared decision-making [73, 77, 79].

The use of a shared decision-making strategy represents a paradigm shift in the field of sports medicine but comes with inherent challenges. As athletes are now empowered to work with their providers to make individualized decisions about sport participation, more athletes with established cardiovascular disease are likely to partake in competitive sports. Many diseases that previously led to automatic disqualification are associated with varying degrees of risk ranging from trivial to high. At present, tools to quantify risk of SCD during exercise for an individual athlete with newly established disease are lacking. Generation of strategies to define risk are needed. The implementation of shared decision-making also brings new challenges. If an athlete with cardiovascular disease chooses to accept the risk and to participate in sport without consensus from physicians, schools, and organizations, what process should ensue to define the appropriate course of action? Is there a role for involving the legal system in the deliberation of controversial cases? While there are tangible benefits to application of shared decision-making for athletes with cardiovascular disease, this approach brings inherent complexity to a previously simplistic binary decision-making process.

Key Points

- The use of shared decision-making for athletes with some forms of cardiovascular disease is now supported by American and European guidelines, which represents a departure from the previous binary "yes" or "no" recommendations.
- While shared decision-making is now considered standard of care, its impact has yet to be rigorously defined.
- Shared decision-making introduces new challenges including unquantifiable risk for cohorts that were previously restricted and potential medico-legal implications when there is a disagreement between the athlete and other stakeholders.

Conclusion

Over the last decade, there have been significant advances in the scientific knowledge surrounding pre-participation cardiovascular screening in athletes, which have completely reshaped the field. The H&P remains the foundation of PPCS and is supported by all major sporting societies and governing bodies. Universal inclusion of ECG to H&P is currently recommended by the European guidelines while American guidelines suggest that ECG should only be considered in relatively small cohorts of healthy young people when there is adequate clinical oversight and financial resources. Multimodality imaging is currently not recommended for universal PPCS and has not been rigorously validated to date. The advent of shared decision-making in disqualification guidelines means that more athletes with cardiovascular disease may choose to partake in sport, which is a practice with completely undefined outcomes. Future research should look to refine current H&P and ECG screening techniques, and to create a definitive large-scale study that is powered to address the impact of PPCS on the incidence of sudden death.

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Compliance with Ethical Standards

Conflict of Interest Bradley Petek declares that he has no conflict of interest.

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Human and Animal Rights and Informed Consent This article does not contain any studies with human or animal subjects performed by any of the authors.

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