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The effectiveness of screening history, physical exam, and ECG to detect potentially lethal cardiac disorders in athletes: A systematic review/meta-analysis

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Abstract

Background: The optimal cardiovascular preparticipation screen is debated. The purpose of this study was to perform a systematic review/meta-analysis of evidence comparing screening strategies.

Methods: PRIMSA guidelines were followed. Electronic databases were searched from January 1996 to November 2014 for articles examining the efficacy of screening with history and physical exam (PE) based on the American Heart Association (AHA) or similar recommendations and electrocardiogram (ECG). Pooled data was analyzed for sensitivity, specificity, false positive rates and positive and negative likelihood ratios. Secondary outcomes included rate of potentially lethal cardiovascular conditions detected with screening and the etiology of pathology discovered.

Results: Fifteen articles reporting on 47,137 athletes were reviewed. After meta-analysis the sensitivity and specificity of ECG was 94%/93%, history 20%/94%, and PE 9%/97%. The overall false positive rate of ECG (6%) was less than that of history (8%), or physical exam (10%). Positive likelihood ratios were ECG 14.8, history 3.22 and PE 2.93 and negative likelihood ratios were ECG 0.055, history 0.85, and PE 0.93. There were a total of 160 potentially lethal cardiovascular conditions detected for a rate of 0.3% or 1 in 294. The most common pathology was Wolff-Parkinson-White (67, 42%), Long QT Syndrome (18, 11%), hypertrophic cardiomyopathy (18, 11%), dilated cardiomyopathy (11, 7%), coronary artery disease or myocardial ischemia (9, 6%) and arrhythmogenic right ventricular cardiomyopathy (4, 3%).

Conclusions: The most effective strategy for screening for cardiovascular disease in athletes is ECG. It is 5 times more sensitive than history, 10 times more sensitive than physical exam, has higher positive likelihood ratio, lower negative likelihood ratio and a lower false positive rate. 12-lead ECG interpreted using modern criteria should be considered best practice in screening for cardiovascular disease in athletes while the use of history and physical alone as a screening tool should be reevaluated.

Keywords: Preparticipation exam; Athlete; Cardiovascular screening; ECG; Sudden cardiac death

Introduction

The preparticipation examination (PPE) or periodic health examination (PHE) is the practice of regularly screening athletes prior to participation in sport. PPEs have been common place in the United States for over 50 years, in some countries such as Italy for decades, and in other countries like England PPEs are not required. Although there are many objectives to the PPE, it is widely agreed that the primary purpose of the PPE is to screen for potentially life-threatening disorders [1–5]. Cardiovascular pathology leading to sudden cardiac death (SCD) is the most common medical cause of death in athletes [6–8]. Therefore, a large portion of effort during the PPE is directed toward screening for cardiovascular disease. Screening has traditionally consisted of a history and physical examination although the utility of this approach has been questioned [9,10]. More recently there has been interest in adding a resting 12-lead electrocardiogram (ECG) to the PPE to improve detection of conditions associated with SCD. ECG screening is supported by Italian data showing a 90% decrease in the rate of SCD with the inclusion of ECG as part of athlete screening [6], although other studies have questioned this result [11]. The debate regarding various screening strategies engenders passionate support on both sides. This paper examines the data related to preparticipation cardiovascular screening in

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athletes through a systematic review of existing studies. The sensitivity, specificity, and positive predictive value of history, physical exam and ECG in the individual studies are calculated and a meta-analysis of pooled data performed in an effort to better understand the value and limitations of these tests in order to guide rational evidence-based approaches for cardiovascular screening in athletes.

Methods

The Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRIMSA) guidelines were followed conducting and reporting this review.

Search strategy

Relevant articles were identified by searching the following electronic databases: Medline, CINAHL, Embase, SportDiscus, The Cochrane Library, and PEDro. Database entries were searched from January 1996 to November of 2014. Initial AHA recommendations for cardiovascular screening in athletes were published in 1996 [12]. Search terms used included ECG, athlete, screening, preparticipation, history, and physical. Keywords were searched individually and grouped. The reference lists of the relevant articles and ePublication lists of key journals were manually reviewed for additional pertinent studies.

Selection criteria

Inclusion criteria for this analysis required: (1) the study reported on the outcomes of cardiovascular screening in athletes using history, physical exam, and ECG; (2) the history questions and physical exam were based on the AHA recommendations or similar guidelines; and (3) ECGs were interpreted using modern standards defined as criteria attempting to account for the physiologic changes of training in the athletic heart. Non-English language reports, conference abstracts, and review or clinical commentary articles were excluded. Only manuscripts by the same authors using different case populations were included. The titles and abstracts of the articles were reviewed to determine eligibility for inclusion in the analysis. Where eligibility was unclear the full text article was retrieved and reviewed.

Assessment of study quality

A seven-item quality assessment checklist was developed to assess for risk of bias. The seven items assessed were: (1) participant selection criteria described, (2) representative sample, (3) data collected prospectively and had at least one positive finding, (4) modern ECG criteria used for screening, (5) cardiovascular screening history and physical exam similar to recommended AHA guidelines, (6) outcomes were reported by individual tests (history, physical exam, and ECG), and (7) abnormal screening tests were evaluated by appropriate diagnostic testing. For each item articles were assessed as having fulfilled or not fulfilled the criterion. Articles with a score of 7 were considered of highest quality. Articles with potential bias were not excluded.

Data extraction and synthesis

A data-extraction form was developed specifically for this review with data obtained from each study. Data was extracted by one author (KH) and checked for accuracy by the other authors. Acquired data included the total number of participants in the study as well as their sex, the number of true positives, true negatives, false positives and false negatives based on the total number of disorders identified in the study. If these data were not available in the article or could not be calculated from the data provided, the corresponding author was contacted and asked for additional information. In some cases one element (i.e. physical exam) could not be extracted but data from other elements (i.e. history and ECG) could and then these elements were included. In addition, the type of ECG criteria used and the total number of potentially serious cardiovascular abnormalities discovered as well as the specific types of pathology were extracted. After the primary data was obtained, the sensitivity, specificity, false positive, and positive predictive value (PPV) of each screening test was calculated based on the total disorders identified by history, physical exam, and ECG. A false negative rate was not be calculated because in the majority of studies only those identified as abnormal with initial screening received additional definitive work-up. Thus, there were likely additional cardiovascular abnormalities not detected by any of the screening methods.

Calculations and analysis were performed in either STATA 11.0 (College Station, TX) or Excel (Redmond, WA).

Heterogeneity among studies was evaluated using coupled forest plots. Summary points for sensitivity and specificity were estimated using a bivariate random effects meta-analysis model. The use of a random effects meta-analysis model takes the heterogeneity into account and provides a conservative estimate of pooled sensitivity and specificity [13,14]. Secondary outcomes included the overall rates and types of cardiovascular pathology identified. Cardiovascular pathology rates were calculated using simple ratios.

Results

The literature search initially yielded 787 articles. 756 articles were immediately excluded. There were 31 articles that potentially met the inclusion criteria and these were downloaded for further review. Of those 31, 16 articles were excluded because the study screened only with ECG and did not screen with a cardiovascular history or physical exam [15–22] the athletes were screened with ECG, history and physical exam but the statistics needed were not in the article, could not be calculated from the information in the article, and the corresponding author either did not have the data or did not reply to inquires [23–25]; the cohort was pre-identified with cardiovascular disease [17,26]; there was not at least one positive finding in the cohort [27,28]; or the manuscript was a letter to the editor [29]. Fifteen studies were included for full review (Fig. 1).

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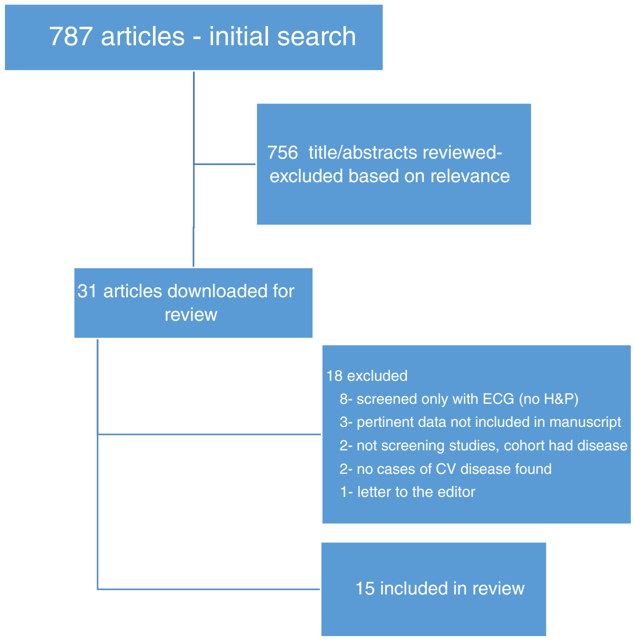

Fig. 1. Article selection.

Quality assessment

Overall, the quality assessment for the 15 articles ranged from 5 to 7. Three studies did not separate outcomes for history and physical exam and reported them together [30–32]. 10 of the 15 studies did not have a representative sample and looked at only a subset of the overall group of young athletes. Three looked primarily at high school athletes [33–35], 2 had only male or predominantly male participants [36–38], 2 examined only college athletes [39,40], and one study had a wider age range (5–39 years) than others [41]. However, taken in aggregate the group represented a broad and diverse population of athletes and was representative of screening in a wide array of settings.

Demographic data

A total of 47,137 athletes were screened. There were 29,658 (66%) males and 15,014 females (34%) excluding one manuscript that did not report on gender breakdown [31]. The group was ethnically and racially diverse (Table 1). The athletes screened were from Algeria, France, Germany, Greece, the Netherlands, Qatar, Spain, the United Kingdom, and the United States. The athletes ranged in age from 5 to 39 years and were primarily competitive athletes although some studies included active adolescents as well (Table 1).

Sensitivity, specificity, false positive rate and positive predictive value

The sensitivity, specificity, false positive rate and positive predictive values demonstrated in various studies are shown in Table 2. The combined false positive rates for history, physical exam, and ECG were 8%, 10%, and 6%, respectively. There was a wide range of false positive rates for ECG reflecting the different criteria used for interpretation (1%–19%). Likewise, there was a wide range of false positive rates for history ranging from 1% to 31%.

Meta-analysis of the fifteen studies (Table 3), showed ECG was the most accurate screening test with a pooled sensitivity of 94% (79%–98%), specificity of 93% (90%–96%), and a positive likelihood ratio of 14.8 (9.43–23.16) indicating that a positive ECG test largely increases the likelihood of disease. The pooled sensitivity decreased for history 20% (7%–44%) and physical exam 9% (3%–24%), and the specificity remained similar for history 94% (89%–96%) and physical exam 97% (95%–98%) compared to ECG. History 3.22 (1.3–8.01) and physical exam 2.93 (1.26–6.83) had similar positive likelihood ratios indicating that a positive result for either test suggests a small increase in the likelihood of disease. Figs. 2–4 show coupled forest plots of sensitivity and specificity for each test, with articles ranked in order of decreasing sensitivity.

Table 1
Demographics of individual studies.

Author	Year	N	Males	Females	Population	Country
Fuller	1997	5615	3375	2240	High school athletes	U.S.
Wilson	2008	2720			National and international junior athletes and active school children	U.K.
Bessem	2009	428	322	106	Athletes (22)	Netherlands
He via	2009	1220	1171	49	Athletes (23)	Spain
Baggish	2010	510	311	199	College athletes	U.S.
Magalski	2011	964	463	501	College athletes	U.S.
Wilson	2011	1220	1220	0	National level athletes	Qatar
Assanelli	2012	6634	5307	1327	Athletes (25.2)	Greece, Germany, France, Algeria
Snoek	2013	306	398	163	Students 16–35 median 18	Netherlands
Fudge	2014	1339	656	683	Active adolescents	U.S.
Price	2014	2017	1432	585	High school athletes	U.S.
Menagoflio	2014	1070	805	265	Regional, national, international	Switzerland
Alattar	2014	230	230	0	Organized sport	Dubai
Deligiannis	2014	22,205	13,546	8659	Competitive athletes	Greece
Anderson	2014	659	422	237	Adolescent athletes (15.4)	U.S.
Total		47,137	29,658	15,014		
			66%	34%		

Table 2
Sensitivity, specificity, false positive rate, and positive predictive value of individual studies.

		Sensitivity (95% CI)			Specificity (95% CI)			False positive (95% CI)			Positive predictive value (95% CI)			
Author	Year	History	PE	ECG	History	PE	ECG	History	PE	ECG	History	PE	ECG	ECG criteria
Fuller	1997	0% (0%–45.9%)	17% (0.42%–64.1%)	83% (35.9%–99.6%)	97.9% (97.5%–98.3%)	96.9% (96.4%–97.3%)	97.5% (97%–97.9%)	2% (1.7%–2.5%)	3% (2.7%–3.6%)	2.5% (2.1%–2.9%)	0% (0%–3.16%)	0.57% (0.01%–3.14%)	3.4% (1.12%–7.81%)	No specific criteria
Wilson	2008	0% (0%–33.6%)	–	100% (66.4%–100%)	97.5% (96.9%–98.1%)	–	98.9% (98.4%–99.2%)	2.4% (1.9%–3.1%)	–	1.1% (0.7%–1.6%)	0% (0%–5.36%)	–	22.5% (10.8%–38.5%)	No specific criteria
Bessem	2009	25% (0.63%–80.6%)	0% (0%–60.2%)	75% (19.4%–99.4%)	94.8% (92.2%–96.7%)	97.4% (95.4%–98.7%)	92.5% (89.5%–94.8%)	5.2% (3.3%–7.8%)	2.6% (1.3%–4.6%)	7.5% (5.2%–10.5%)	4.3% (0.11%–21.9%)	0% (0%–28.5%)	8.6% (1.8%–23.1%)	Lausaunne criteria
Hevia	2009	0% (0%–45.9%)	0% (0%–45.9%)	100% (54.1%–100%)	99.1% (98.4%–99.5%)	99.6% (99.2%–99.9%)	93.9% (92.5%–95.3%)	0.9% (0.4%–1.6%)	0.3% (.08%–0.8%)	5.9% (4.7%–7.4%)	0% (0%–28.5%)	0% (0%–60.2%)	7.6% (2.84%–15.8%)	2005 ESC
Baggish	2010	0% (0%–70.8%)	33% (0.84%–90.6%)	66% (9.43%–99.2%)	95.8% (93.7%–97.4%)	97.8% (96.2%–98.9%)	84% (80.5%–87.1%)	4.1% (2.6%–6.3%)	2.2% (1.1%–3.8%)	15.9% (12.9%–19.4%)	0% (0%–16.1%)	8.33% (0.21%–38.5%)	2.4% (0.29%–8.43%)	2005 ESC
Magalski	2011	44% (13.7%–78.8%)	11% (0.28%–48.2%)	100% (66.4%–100%)	75.2% (72.4%–78%)	94.5% (92.8%–95.8%)	90.9% (89%–92.7%)	24.7% (22.0%–27.6%)	5% (4.2%–7.2%)	9% (7.3%–11.0%)	1.67% (0.46%–4.21%)	1.2% (0.05%–9.89%)	9.5% (4.42%–17.2%)	No specific criteria
Wilson	2011	42% (9.9%–81.6%)	–	100% (59%–100%)	82% (80.2%–84.5%)	–	91% (88.8%–92.2%)	17.6% (15.5%–19.8%)	–	9.4% (7.8%–11.2%)	1.4% (0.29%–4.01%)	–	5.8% (2.36%–11.6%)	No specific criteria
Assanelli	2012	74% (61.6%–85.6%)	–	100% (93.5%–100%)	98% (97.8%–98.5%)	–	97% (96.5%–97.3%)	2% (1.5%–2.2%)	–	3% (2.7%–3.5%)	26% (19.5%–33.6%)	–	21% (16.4%–26.7%)	2010 ESC

Snoek	2013	0% (0%–70.8%)	0% (0%–70.8%)	33% (0.84%–90.6%)	83% (79.1%–87.7%)	97% (95.3%–99.1%)	78% (73.1%–82.7%)	16.2% (12.3%–20.9%)	2.3% (0.9%–4.7%)	21.9% (17.3%–26.9%)	0% (0%–7.25%)	0% (0%–41%)	1.5% (0.04%–8.04%)	2010 ESC
Alattar	2014	50% (11.8%–88.2%)	0% (0%–45.9%)	100% (54.1%–100%)	90% (85.5%–93.7%)	97% (93.7%–98.7%)	81% (75.5%–86.1%)	9.8% (6.3%–14.5%)	3% (1.3%–6.3%)	19% (13.9%–24.5%)	12% (2.55%–31.2%)	0% (0%–41%)	12.5% (4.73%–25.2%)	ESC/Lausaunne
Deligiannis	2014	61% (42.1%–77.1%)	48% (30.8%–66.5%)	70% (51.3%–84.4%)	91% (90.5%–91.3%)	85% (84.6%–85.6%)	92% (91.4%–92.1%)	9% (8.7%–9.5%)	14.9% (14.4%–15.4%)	8% (7.9%–8.6%)	1% (0.6%–1.51%)	0.5% (0.28%–0.78%)	1.2% (0.79%–1.87%)	2010 ESC
Menagoflio	2014	0% (0%–60.2%)	0% (0%–60.2%)	100% (39.8%–100%)	98.7% (97.8%–99.3%)	98.6% (97.7%–99.2)	96.4% (95.1%–97.5%)	1.3% (0.7%–2.2%)	1.4% (0.7%–2.3%)	3.6% (2.5%–4.9%)	0% (0%–23.2%)	0% (0%–21.8%)	9.5% (2.66%–22.6%)	2010 ESC
Fudge	2014	40% (5.27%–85.3%)	0% (0%–52.2%)	100% (47.8%–100%)	68.5% (66%–71.1%)	90.3% (89%–92.2%)	94.9% (93.7%–96.1%)	31.4% (28.9%–34.0%)	9.3% (7.8%–11.0%)	5% (3.9%–6.3%)	0.47% (0.06%–1.71%)	0% (0%–2.93%)	6.9% (2.29%–15.5%)	Pre-Seattle
Price	2014	20% (0.50%–71.6%)	20% (0.51%–71.6%)	100% (47.8%–100%)	87.9% (86.4%–89.3%)	96.3% (95.4%–97.1%)	97.2% (96.3%–97.8%)	12% (10.7%–13.6%)	3.6% (2.9%–4.6%)	2.8% (21.5%–36.6%)	0.4% (0.01%–2.26%)	1% (0.03%–7.21%)	8.1% (2.67%–17.8%)	2010 ESC
Anderson	2014	20% (0.50%–71.6%)	20% (0.51%–71.6%)	80% (28.4%–99.5%)	92% (90%–94.3%)	96% (94.6%–97.6%)	89% (86.3%–91.3%)	8% (5.7%–10%)	3.6% (2.4%–5.4%)	11% (8.7%–13.7%)	2% (0.05%–10.4%)	4% (0.1%–20.4%)	5.3% (1.45%–12.9%)	No specific criteria
		48% (40%–55.8%)	23.6% (15.2%–33.8%)	90% (84.3%–94.2%)	92.3% (92.1%–92.5%)	89.6% (89.2%–89.9%)	93.8% (93.6%–94%)	7.7% (7.5%–7.9%)	10.4% (10.1%–10.8%)	6.2% (6.0%–6.4%)	2.1% (1.65%–2.6%)	0.5% (0.34%–0.84%)	4.7% (4.0%–5.5%)	

Table 3
Meta-analysis of pooled data.

	ECG	History	Physical
Sensitivity	94% (79%–98%)	20% (7%–44%)	9% (3%–24%)
Specificity	93% (90%–96%)	94% (89%–96%)	97% (95%–98%)
Positive likelihood ratio*	14.8 (9.43–23.16)	3.22 (1.3–8.01)	2.93 (1.26–6.83)
Negative likelihood ratio*	0.055 (0.012–0.25)	0.85 (0.68–1.07)	0.93 (0.85–1.03)

*Interpretation of likelihood ratios

Likelihood ratio	Interpretation
>10	Large and often conclusive increase in the likelihood of disease
5–10	Moderate increase in the likelihood of disease
2–5	Small increase in the likelihood of disease
1–2	Minimal increase in the likelihood of disease
1	No change in the likelihood of disease
0.5–1.0	Minimal decrease in the likelihood of disease
0.2–0.5	Small decrease in the likelihood of disease
0.1–0.2	Moderate decrease in the likelihood of disease
<0.1	Large and often conclusive decrease in the likelihood of disease

Cardiovascular pathology

There were 160 potentially lethal cardiovascular conditions identified in 47,137 athletes for a rate of 0.3% or 1 in every 294 athletes. Wolff-Parkinson-White (WPW) was the most frequently identified pathology (67, 42%), followed by Long QT Syndrome (LQTS) (18, 11%), hypertrophic cardiomyopathy (HCM) (18, 11%), dilated cardiomyopathy (11, 7%), coronary artery disease (CAD)/myocardial ischemia (MI) (9, 6%), and arrhythmogenic right ventricular cardiomyopathy (ARVC) (4, 3%). The rate of WPW was 1 in every 703 athletes while the rate of identified HCM and LQTS was 1 in 2618.

Discussion

The data on cardiovascular screening in a diverse population of over 47,000 athletes around the world is summarized by this systematic review. Cardiovascular screening examinations prior to participation in sport have a long history with various countries, states, and sporting organizations recommending or requiring differing elements. Most notably, the European Society of Cardiology (ESC), International Olympic Committee (IOC), Federation Internationale de Football Association (FIFA), and various U.S. professional sporting organizations recommend a cardiovascular screen inclusive of ECG [2,42], while the AHA recommends a 14-point personal and family history and

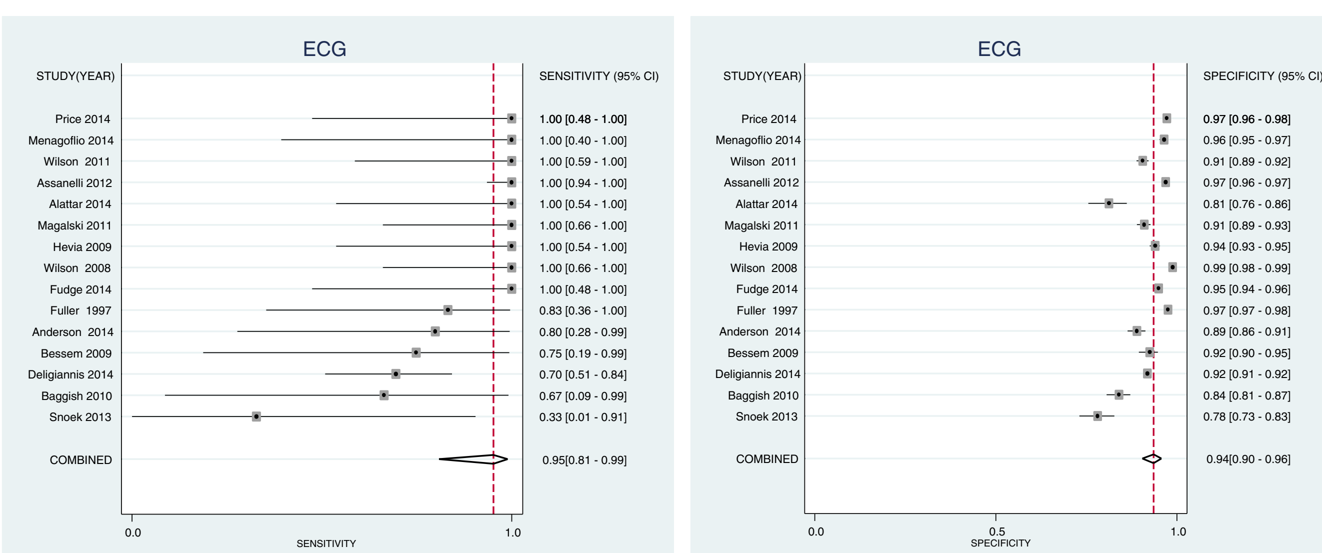

Fig. 2. Forest plot of sensitivity and specificity of ECG.

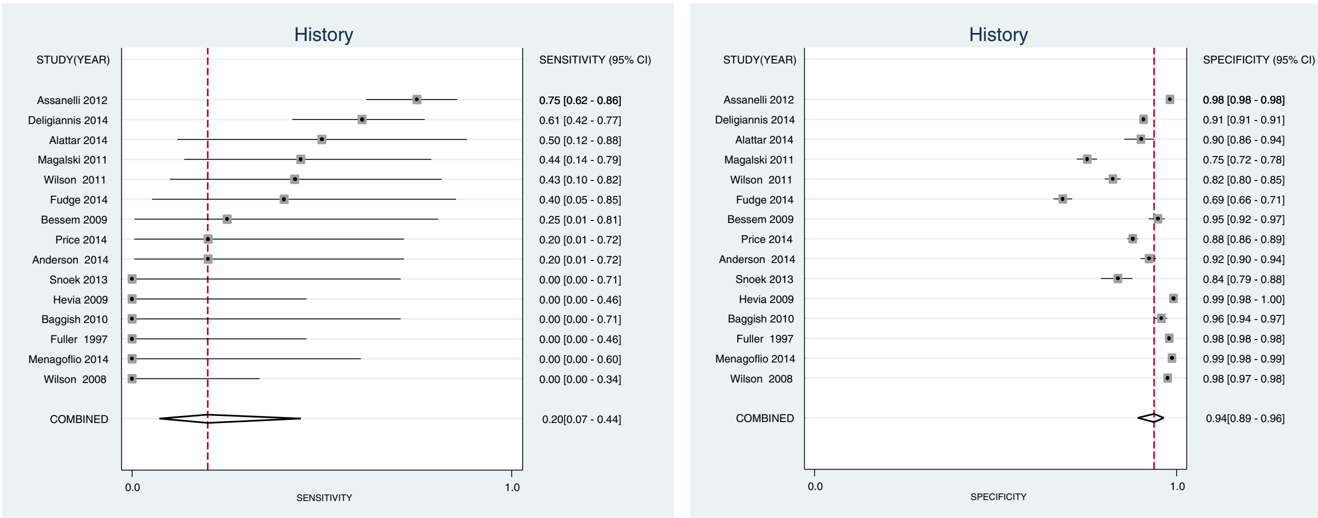

Fig. 3. Forest plot of sensitivity and specificity of history.

cardiovascular physical exam without an ECG [4]. While there is widespread agreement that cardiovascular screening in athletes is “justifiable, necessary, and compelling on the basis of ethical, legal and medical grounds” the AHA has cited concern regarding the high false positive rate of ECG [2,5]. However, as evidenced by this review, ECG actually has a lower false positive rate than either history or physical exam even when considering that 9 of the 15 studies used older criteria such as the 2005 or 2010 ESC criteria that have higher false positive rates than more recently defined standards for ECG interpretation in athletes. Newer ECG criteria such as the Seattle Criteria have decreased the false positive rate while retaining the sensitivity to detect pathologic conditions [43–47]. International collaboration will further refine and improve ECG criteria.

The screening history questions that are currently recommended are based on expert opinion. There is little research into how well different aged populations or cultures understand the questions or how different demographic groups answer the questions. In addition, there is concern that the typical history questions inquire about symptoms which are common place, subjective and not specific to those with cardiac disease. While chest pain or shortness of breath can be indicative of cardiovascular pathology, it can also be indicative of many other conditions including gastrointestinal, musculoskeletal, psychological or pulmonary issues. Studies looking at the number of AHA based history questions initially answered positive prior to physician review report positive rates of 35%–60% [23,30,34] while other studies report positive history responses as low as 1% [38,48].

This wide range of positive responses depends on whether the history questions are considered positive if answered affirmatively initially by the athlete or considered positive only after review by a physician or in combination with a normal ECG. When positive rates are reported after review by a physician it is often not possible to tell how many positive responses were disregarded because further testing

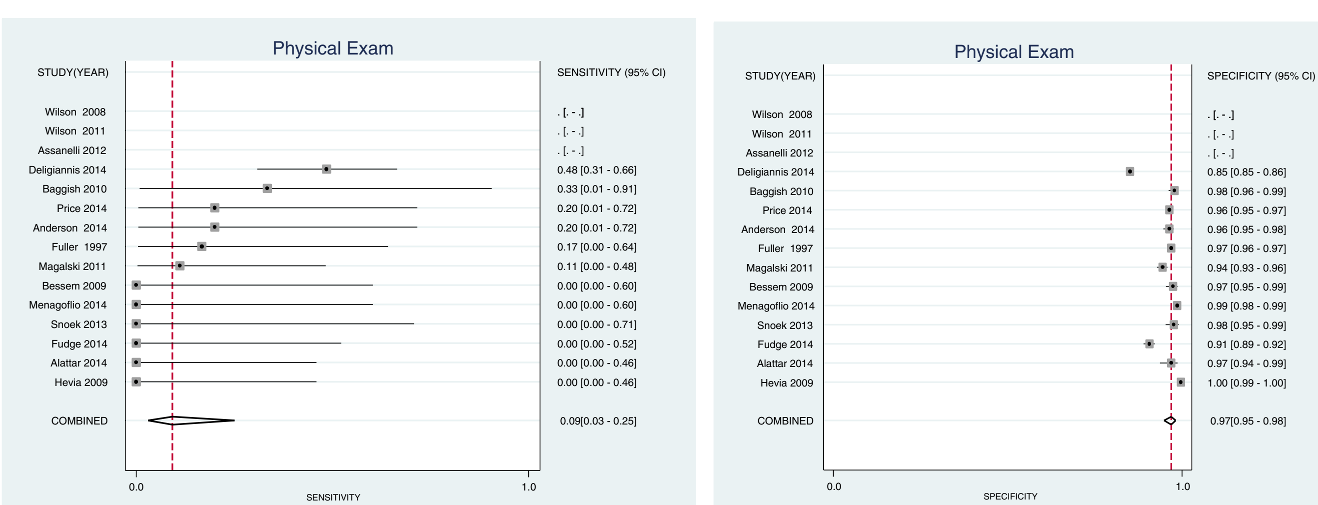

Fig. 4. Forest plot of sensitivity and specificity of physical.

in those athletes was deferred. There were 2 studies that performed echocardiograms in all athletes [39,40] and one that did echocardiography for all athletes in the first half of the 18 year study period [41]. In these studies the sensitivity of ECG (80%) was still superior compared to history (50%) and physical exam (33%). Although the screening questions may serve as a flag for further questioning, the ability to correctly differentiate positive versus negative responses by both experts and primary care physicians is unknown.

SCD is the presenting symptom in cardiovascular pathology in up to 80% of cases [49], therefore screening for prodromal symptoms by history will miss the overwhelming majority of cases. The 20% of athletes who do have warning signs preceding death may have symptoms which are non-specific and fairly ubiquitous making screening by history alone challenging. For example, abnormal history responses were initially reported in 68% of responses on the Pre-participation Physical Evaluation Monograph screening questions in a cardiovascular screen of active adolescents [34]. After review by a physician over half of these responses were not thought to be relevant and were disregarded, however in this study 31% of the total population screened still went on for further testing because of a positive history question [34]. In other studies 11%–15% of athletes reported a positive history of exertional chest pain [33,40], exercise associated dizziness (12%) [30], and exertional dyspnea (7%–15%) [33,40]. In contrast, some studies report a very low rate of positive responses to history questions [31,35,39,48]. The reason for the discrepancy between positive rates is likely due to differences in athlete population, manner in which the question is asked and understood, and the amount of overview done by a physician.

In this meta-analysis physical exam had the lowest sensitivity, the highest specificity, the lowest positive likelihood ratio and highest negative likelihood ratio. PE also had the highest false positive rate. The primary findings prompting further review on cardiovascular screening is a murmur or physical stigmata of Marfan's. The most common reason for secondary testing was a murmur on physical exam. The accuracy of auscultation to distinguish physiologic from pathologic murmurs compared to echocardiography for detection of cardiac pathology has been questioned [50].

The most common identified condition associated with SCD was WPW with an incidence of 1 in 703 athletes. This is consistent with reports of a prevalence of 1 to 4.5 per 1000 individuals [51]. In some studies HCM is reported as the leading cause of death in athletes in the United States with a reported prevalence of 1 in 500 in adults [8]. In other studies and in other countries it appears that HCM is a less common cause of SCD in athletes with autopsy-negative unexplained death or presumed arrhythmia being the most common cause of death [52–57]. In this systematic review of over 47,000 athletes screened there were 18 cases of HCM discovered for an incidence of 1 in 2618. ECG should detect over 90% of cases of HCM [58,59]. It is possible that some cases of HCM were missed and the actual prevalence of HCM is higher. Of the 12,353 cases that were screened with history, physical exam, ECG and echocardiogram, there was 1 case of HCM out of the 5 detected that was found only by echocardiogram. Because this review looked at pooled data from around the world and some reports have suggested that a large proportion of deaths in the US are due to HCM, the data was re-analyzed for screening studies in the US only. There were 11,104 US athletes screened and only 2 cases of HCM detected for a prevalence of HCM in the US of 1 in 5552. This data would suggest that HCM is less prevalent in athletes at screening than expected.

Interestingly, of the 47,137 cases screened there were no reports of coronary artery abnormalities. This is surprising because in studies reporting the etiology of SCD in athletes [8,52,53,60–62] or military recruits [55] SCD due to coronary artery abnormalities (CAA) represent between 6% and 27%. ECG would not be expected to detect CAA, however, screening with history and physical exam did not detect any CAA despite reports that 44% of athletes who died from CAA had prodromal symptoms such as syncope or chest pain [63]. Nearly a quarter of the total population was screened with echocardiogram in addition to history, physical exam and ECG and there were still no CAA detected. It is not clear which echocardiographic screening protocols were utilized and whether or not they were sufficient to identify CAAs. It is likely that the overall incidence of cardiac pathology found in this study is actually higher than stated because of undetected CAAs, as well as other disorders not routinely identified by history, physical exam, or ECG such as aortopathies and premature coronary atherosclerosis.

Strengths and limitations

The strengths of this review are that it combines data on the screening of 47,137 athletes with a measure of the quality of the studies and meta-analysis of pooled data. The findings reinforce the emerging body of literature supporting the effectiveness of ECG in screening for potentially lethal cardiac disease in athletes while also demonstrating the low relative of history and physical exam.

There were several limitations to this review. The meta-analysis did not have the level of data to investigate the interaction of several factors on the outcome. These factors include age group of the study populations or clinical experience of the diagnosing staff. The small number of studies included in this review also prevented stratification for sub-group analysis. Therefore conclusions cannot make on how these factors impact testing accuracy.

Another limitation to this study is the criteria used to evaluate ECG results. The various criteria used for screening included the Lausanne criteria, the ESC 2005 or 2010 criteria, or no specific published criteria but the authors of the study described what they considered physiologic versus pathologic findings [2,42,64]. A standardization of criteria would lead to more definitive screening results and reduce the potential for misclassification bias.

There was a moderate degree of heterogeneity among the estimates for specificity and sensitivity. This could have resulted from the diversity of study populations and study locations. The random-effects meta-analysis takes this into account and provides conservative estimates for pooled sensitivity and specificity estimates. However, future analysis of studies using similar ECG criteria for interpretation will likely decrease statistical heterogeneity. Finally, not all athletes were screened with definitive studies (echocardiogram, cardiac magnetic resonance imaging, genetic testing) and therefore pathology may have been missed. Thus, sensitivity and specificity were based on the total number of disorders identified in the study.

Conclusions

The purpose of this study was to perform a systematic review/meta-analysis of evidence comparing screening strategies. There were fifteen articles identified reporting on 47,137 athletes. The sensitivity of 12-lead ECG was much higher than both history and physical with similar sensitivity. In addition, the false positive rate of ECG (6%) was less than that of history (8%), or physical exam (10%). ECG had the highest positive likelihood ratios and lowest negative likelihood ratios. There were a total of 160 potentially lethal cardiovascular conditions detected for a rate of 0.3% which is consistent with other studies. The most common pathology identified was electrical disease and hypertrophic cardiomyopathy was a relatively infrequent finding. This meta-analysis suggests that electrical disease is more common cause of death than cardiomyopathies. This meta-analysis shows that ECG is the most effective strategy for screening for cardiovascular disease in athletes, and the use of history and physical exam alone as a screening tool should be reevaluated.

References

[1] American Academy of Family Physicians, American Academy of Pediatrics, American College of Sports Medicine, American Medical Society for Sports Medicine, American Orthopaedic Society for Sports Medicine, American Osteopathic Academy Of Sports Medicine. Preparticipation physical evaluation. 4th ed. American Academy of Pediatrics; 2010.

[2] Corrado D, Pelliccia A, Bjornstad HH, Vanhees L, Biffi A, Borjesson M, et al. Cardiovascular pre-participation screening of young competitive athletes for prevention of sudden death: Proposal for a common European protocol. Consensus Statement of the Study Group of Sport Cardiology of the Working Group of Cardiac Rehabilitation and Exercise Physiology and the Working Group of Myocardial and Pericardial Diseases of the European Society of Cardiology. Eur Heart J 2005;26:516–24.

[3] Ljungqvist A, Jenoure P, Engebretsen L, Alonso JM, Bahr R, Clough A, et al. The International Olympic Committee (IOC) Consensus Statement on periodic health evaluation of elite athletes March 2009. Br J Sports Med 2009;43:631–43.

[4] Maron BJ, Friedman RA, Kligfield P, Levine BD, Viskin S, Chaitman BR, et al. Assessment of the 12-lead electrocardiogram as a screening test for detection of cardiovascular disease in healthy general populations of young people (12–25 years of age): A scientific statement from the American Heart Association and the American College of Cardiology. J Am Coll Cardiol 2014;64:1479–514.

[5] Maron BJ, Thompson PD, Ackerman MJ, Balady G, Berger S, Cohen D, et al. Recommendations and considerations related to preparticipation screening for cardiovascular abnormalities in competitive athletes: 2007 update: A scientific statement from the American Heart Association Council on Nutrition, Physical Activity, and Metabolism: Endorsed by the American College of Cardiology Foundation. Circulation 2007;115:1643–5.

[6] Corrado D, Basso C, Pavei A, Michieli P, Schiavon M, Thiene G. Trends in sudden cardiovascular death in young competitive athletes after implementation of a preparticipation screening program. JAMA 2006;296:1593–601.

[7] Harmon KG, Asif IM, Klossner D, Drezner JA. Incidence of sudden cardiac death in National Collegiate Athletic Association athletes. Circulation 2011;123:1594–600.

[8] Maron BJ, Doerer JJ, Haas TS, Tierney DM, Mueller FO. Sudden deaths in young competitive athletes. Analysis of 1866 deaths in the United States, 1980–2006. Circulation 2009;119:1085–92.

[9] Drezner JA. Contemporary approaches to the identification of athletes at risk for sudden cardiac death. Curr Opin Cardiol 2008;23:494–501.

[10] Drezner JA, Levine BD, Vetter VL. Reframing the debate: Screening athletes to prevent sudden cardiac death. Heart Rhythm 2013;10:454–5.

[11] Steinvil A, Chundadze T, Zeltser D, Rogowski O, Halkin A, Galily Y, et al. Mandatory electrocardiographic screening of athletes to reduce their risk for sudden death proven fact or wishful thinking? J Am Coll Cardiol 2011;57:1291–6.

[12] Maron BJ, Thompson PD, Puffer JC, McGrew CA, Strong WB, Douglas PS, et al. Cardiovascular preparticipation screening of competitive athletes. A statement for health professionals from the Sudden Death Committee (clinical cardiology) and Congenital Cardiac Defects Committee (cardiovascular disease in the young), American Heart Association. Circulation 1996;94:850–6.

[13] Harbord RM, Whiting P, Sterne JA, Egger M, Deeks JJ, Shang A, et al. An empirical comparison of methods for meta-analysis of diagnostic accuracy showed hierarchical models are necessary. J Clin Epidemiol 2008;61:1095–103.

[14] Harbord RM, Deeks JJ, Egger M, Whiting P, Sterne JA. A unification of models for meta-analysis of diagnostic accuracy studies. Biostatistics 2007;8:239–51.

[15] Ng CT, Chee TS, Ling LF, Lee YP, Ching CK, Chua TS, et al. Prevalence of hypertrophic cardiomyopathy on an electrocardiogram-based pre-participation screening programme in a young male South-East Asian population: Results from the Singapore Armed Forces Electrocardiogram and Echocardiogram screening protocol. Europace 2011;13:883–8.

[16] Koch S, Cassel M, Linne K, Mayer F, Scharhag J. ECG and echocardiographic findings in 10–15-year-old elite athletes. Eur J Prev Cardiol 2012;21:774–81.

[17] Rowin EJ, Maron BJ, Appelbaum E, Link MS, Gibson CM, Lesser JR, et al. Significance of false negative electrocardiograms in preparticipation screening of athletes for hypertrophic cardiomyopathy. Am J Cardiol 2012;110:1027–32.

[18] Grazioli G, Merino B, Montserrat S, Vidal B, Azqueta M, Pare C, et al. Usefulness of echocardiography in preparticipation screening of competitive athletes. Rev Esp Cardiol 2014;67:701–5.

[19] Heron N, Cupples M. The health profile of football/soccer players in Northern Ireland — A review of the UEFA pre-participation medical screening procedure. BMC Sports Sci Med Rehabil 2014;6:5 [1–7].

[20] Riding NR, Sharma S, Salah O, Khalil N, Carre F, George KP, et al. Systematic echocardiography is not efficacious when screening an ethnically diverse cohort of athletes in West Asia. Eur J Prev Cardiol 2013, http://dx.doi.org/10.1177/2047487313506549.

[21] Papadakis M, Carre F, Kervio G, Rawlins J, Panoulas VF, Chandra N, et al. The prevalence, distribution, and clinical outcomes of electrocardiographic repolarization patterns in male athletes of African/Afro-Caribbean origin. Eur Heart J 2011;32:2304–13.

[22] Marek J, Bufalino V, Davis J, Marek K, Gami A, Stephan W, et al. Feasibility and findings of large-scale electrocardiographic screening in young adults: Data from 32,561 subjects. Heart Rhythm 2011;8:1555–9.

[23] Zeltser I, Cannon B, Silvana L, Fenrich A, George J, Schleifer J, et al. Lessons learned from preparticipation cardiovascular screening in a state funded program. Am J Cardiol 2012;110:902–8.

[24] Schmied C, Di Paolo FM, Zerguini AY, Dvorak J, Pelliccia A. Screening athletes for cardiovascular disease in Africa: A challenging experience. Br J Sports Med 2013;47:579–84.

[25] Riding NR, Salah O, Sharma S, Carre F, George KP, Farooq A, et al. ECG and morphologic adaptations in Arabic athletes: Are the European Society of Cardiology's recommendations for the interpretation of the 12-lead ECG appropriate for this ethnicity? Br J Sports Med 2014;48:1138–43.

[26] Corrado D, Basso C, Schiavon M, Thiene G. Screening for hypertrophic cardiomyopathy in young athletes. N Engl J Med 1998;339:364–9.
[27] Mesihovic-Dinarevic S, Kulic M, Kreso A. Cardiovascular screening in young athletes in Sarajevo Canton. Bosn J Basic Med Sci 2010;10:227–33.
[28] Yim ES, Basilico F, Corrado G. Early screening for cardiovascular abnormalities with preparticipation echocardiography: Utility of focused physician-operated echocardiography in preparticipation screening of athletes. J Ultrasound Med 2014;33:307–13.
[29] Efthimiadis GK, Mezilis N, Meditskou S, Giannakoulas G, Karvounis H, Pliakos C, et al. Preparticipation cardiovascular screening in competitive athletes: The case in a Greek population. Scand J Med Sci Sports 2009;19:297–8.
[30] Snoek JA, Jongman JK, Brandon T, Berkel SV, Hof AW. Performance of the Lausanne questionnaire and the 2010 European Society of Cardiology criteria for ECG interpretation in athletes. Eur J Prev Cardiol 2013 [Epub ahead of print].
[31] Wilson MG, Basavarajaiah S, Whyte GP, Cox S, Loosemore M, Sharma S. Efficacy of personal symptom and family history questionnaires when screening for inherited cardiac pathologies: The role of electrocardiography. Br J Sports Med 2008;42:207–11.
[32] Wilson MG, Chatard JC, Carre F, Hamilton B, Whyte GP, Sharma S, et al. Prevalence of electrocardiographic abnormalities in West-Asian and African male athletes. Br J Sports Med 2012;46:341–7.
[33] Anderson JB, Grenier M, Edwards NM, Madsen NL, Czosek RJ, Spar DS, et al. Usefulness of combined history, physical examination, electrocardiogram, and limited echocardiogram in screening adolescent athletes for risk for sudden cardiac death. Am J Cardiol 2014;114:1763–7.
[34] Fudge J, Harmon KG, Owens DS, Prutkin JM, Salerno JC, Asif IM, et al. Cardiovascular screening in adolescents and young adults: A prospective study comparing the pre-participation physical evaluation monograph 4th edition and ECG. Br J Sports Med 2014;48:1172–8.
[35] Fuller CM, McNulty CM, Spring DA, Arger KM, Bruce SS, Chryssos BE, et al. Prospective screening of 5,615 high school athletes for risk of sudden cardiac death. Med Sci Sports Exerc 1997;29:1131–8.
[36] Alattar A, Ghani S, Mahdy N, Hussain H, Maffulli N. Pre-participation musculoskeletal and cardiac screening of male athletes in the United Arab Emirates. Transl Med UniSa 2014;9:43–9.
[37] Assanelli D, Levaggi R, Carre F, Sharma S, Deligiannis A, Mellwig KP, et al. Cost-effectiveness of pre-participation screening of athletes with ECG in Europe and Algeria. Intern Emerg Med 2014 [Epub ahead of print].
[38] Hevia AC, Fernandez MM, Palacio JM, Martin EH, Castro MG, Reguero JJ. ECG as a part of the preparticipation screening programme: An old and still present international dilemma. Br J Sports Med 2011;45:776–9.
[39] Baggish AL, Hutter AM, Wang F, Yared K, Weiner RB, Kupperman E, et al. Cardiovascular screening in college athletes with and without electrocardiography: A cross-sectional study. Ann Intern Med 2010;152:269–75.
[40] Magalski A, McCoy M, Zabel M, Magee LM, Goeke J, Main ML, et al. Cardiovascular screening with electrocardiography and echocardiography in collegiate athletes. Am J Med 2011;124:511–8.
[41] Deligiannis AP, Kouidi EJ, Koutlianos NA, Karagiannis V, Anifanti MA, Tsorbatzoglou K, et al. Eighteen years' experience applying old and current strategies in the pre-participation cardiovascular screening of athletes. Hellenic J Cardiol 2014;55:32–41.
[42] Bille K, Figueiras D, Schamasch P, Kappenberger L, Brenner JI, Meijboom FJ, et al. Sudden cardiac death in athletes: The Lausanne recommendations. Eur J Cardiovasc Prev Rehabil 2006;13:859–75.
[43] Bessem B, de Bruijn MC, Nieuwland W. The ECG of high-level junior soccer players: Comparing the ESC vs. the Seattle criteria. Br J Sports Med 2014, http://dx.doi.org/10.1136/bjsports-2013-093245.
[44] Wasfy MM, DeLuca J, Wang F, Berkstresser B, Ackerman KE, Eisman A, et al. ECG findings in competitive rowers: Normative data and the prevalence of abnormalities using contemporary screening recommendations. Br J Sports Med 2014, http://dx.doi.org/10.1136/bjsports-2014-093919.
[45] Pickham D, Zarafshar S, Sani D, Kumar N, Froelicher V. Comparison of three ECG criteria for athlete pre-participation screening. J Electrocardiol 2014;47:769–74.
[46] Exeter DJ, Elley CR, Fulcher ML, Lee AC, Drezner JA, Asif IM. Standardised criteria improve accuracy of ECG interpretation in competitive athletes: A randomised controlled trial. Br J Sports Med 2014;48:1167–71.
[47] Sheikh N, Papadakis M, Ghani S, Zaidi A, Gati S, Adami PE, et al. Comparison of electrocardiographic criteria for the detection of cardiac abnormalities in elite black and white athletes. Circulation 2014;129:1637–49.
[48] Menafoglio A, Di Valentino M, Segatto JM, Siragusa P, Pezzoli R, Maggi M, et al. Costs and yield of a 15-month preparticipation cardiovascular examination with ECG in 1070 young athletes in Switzerland: Implications for routine ECG screening. Br J Sports Med 2014;48:1157–61.
[49] Maron BJ, Shirani J, Poliac LC, Mathenge R, Roberts WC, Mueller FO. Sudden death in young competitive athletes. Clinical, demographic, and pathological profiles. JAMA 1996;276:199–204.
[50] Guntheroth WG. Innocent murmurs: A suspect diagnosis in non-pregnant adults. Am J Cardiol 2009;104:735–7.
[51] Rao AL, Salerno JC, Asif IM, Drezner JA. Evaluation and management of Wolff-Parkinson-White in athletes. Sports Health 2014;6:326–32.
[52] Harmon KG, Drezner JA, Maleszewski JJ, Lopez-Anderson M, Owens D, Prutkin JM, et al. Pathogeneses of sudden cardiac death in National Collegiate Athletic Association athletes. Circ Arrhythm Electrophysiol 2014;7:198–204.
[53] Holst AG, Winkel BG, Theilade J, Kristensen IB, Thomsen JL, Ottesen GL, et al. Incidence and etiology of sports-related sudden cardiac death in Denmark — Implications for preparticipation screening. Heart Rhythm 2010;7:1365–71.
[54] Puranik R, Chow CK, Duflou JA, Kilborn MJ, McGuire MA. Sudden death in the young. Heart Rhythm 2005;2:1277–82.
[55] Eckart RE, Scoville SL, Campbell CL, Shry EA, Stajduhar KC, Potter RN, et al. Sudden death in young adults: A 25-year review of autopsies in military recruits. Ann Intern Med 2004;141:829–34.
[56] Eckart RE, Shry EA, Burke AP, McNear JA, Appel DA, Castillo-Rojas LM, et al. Sudden death in young adults: An autopsy-based series of a population undergoing active surveillance. J Am Coll Cardiol 2011;58:1254–61.
[57] Margey R, Roy A, Tobin S, O'Keane CJ, McGorrian C, Morris V, et al. Sudden cardiac death in 14- to 35-year olds in Ireland from 2005 to 2007: A retrospective registry. Europace 2011;13:1411–8.
[58] Ryan MP, Cleland JG, French JA, Joshi J, Choudhury L, Chojnowska L, et al. The standard electrocardiogram as a screening test for hypertrophic cardiomyopathy. Am J Cardiol 1995;76:689–94.
[59] Maron BJ, Roberts WC, Epstein SE. Sudden death in hypertrophic cardiomyopathy: A profile of 78 patients. Circulation 1982;65:1388–94.
[60] Corrado D, Basso C, Rizzoli G, Schiavon M, Thiene G. Does sports activity enhance the risk of sudden death in adolescents and young adults? J Am Coll Cardiol 2003;42:1959–63.
[61] de Noronha SV, Sharma S, Papadakis M, Desai S, Whyte G, Sheppard MN. Aetiology of sudden cardiac death in athletes in the United Kingdom: A pathological study. Heart 2009;95:1409–14.
[62] Suarez-Mier MP, Aguilera B, Mosquera RM, Sanchez-de-Leon MS. Pathology of sudden death during recreational sports in Spain. Forensic Sci Int 2013;226:188–96.
[63] Basso C, Maron BJ, Corrado D, Thiene G. Clinical profile of congenital coronary artery anomalies with origin from the wrong aortic sinus leading to sudden death in young competitive athletes. J Am Coll Cardiol 2000;35:1493–501.
[64] Corrado D, Pelliccia A, Heidbuchel H, Sharma S, Link M, Basso C, et al. Recommendations for interpretation of 12-lead electrocardiogram in the athlete. Eur Heart J 2010;31:243–59.