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Can an EKG prevent sudden cardiac death in an athlete? A systematic review

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Can an EKG prevent sudden cardiac death in an athlete? A systematic review

Abstract
Background: Current U.S. recommendations for pre-participation screening do not include EKG. European protocol recommends EKG as part of screening and Italy has followed this standard since 1982. Five cardiac abnormalities, hypertrophic cardiomyopathy, coronary artery anomaly of wrong sinus origin, myocarditis, arrhythmogenic right ventricular cardiomyopathy, and ion channelopathies, are the most prevalent causes of sudden cardiac death in the U.S. Most of these cardiac abnormalities display intermittent EKG abnormalities. An athlete may have an abnormal EKG without any family history, symptoms, or physical exam findings of a cardiac abnormality. Could implementation of screening EKG with pre-participation physical exams for athletes uncover these abnormalities, therefore decreasing the number of sudden cardiac deaths during physical activity per year?

Hypothesis: An EKG can contribute to the pre-participation physical for athletes by detecting certain cardiac abnormalities that lead to sudden cardiac death.

Study Design: Systematic review of medical trials.

Methods: Exhaustive search of databases including Ovid Medline, Pubmed, Cinahl, and Evidence-Based Medicine Review Multifile.

Results: Five studies were found that evaluated the correlation between abnormal EKGs in athletes and the diagnosis of a cardiac abnormality that will cause sudden cardiac death. Only one study evaluated all participants with an echocardiogram as well as an EKG. A likelihood ratio of 3.04, sensitivity of 73%, and specificity of 76% was calculated using the information from this study.

Conclusion: Studies evaluated did not make a large impact on the diagnosis of hypertrophic cardiomyopathy or other cardiac abnormalities by EKG. However, cardiac abnormalities that cause sudden cardiac death were found with EKG alone, when history and physical exam findings were normal. EKGs should be incorporated into pre-participation screenings to prevent sudden cardiac death.

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Sudden Cardiac death, mass screening, EKG, athletes

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Can an EKG prevent sudden cardiac death in an athlete? A systematic review

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A Clinical Graduate Project Submitted to the Faculty of the
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Biography

Cynthia Meleán is a native of Kansas where she majored in Human Biology at KU. After completion of her undergraduate degree, she worked as a medical assistant for an interventional cardiologist. Cynthia moved, with her partner and their daughter, to Oregon to attend the Pacific University PA program. She enjoys hobbies such as glassblowing, photography, and volunteering. She also has a special interest in practicing medicine in underserved countries. During her studies at Pacific University she was able to travel to Africa for the first time and witness healthcare needs in Kenya.
Abstract

**Background:** Current U.S. recommendations for pre-participation screening do not include EKG. European protocol recommends EKG as part of screening and Italy has followed this standard since 1982. Five cardiac abnormalities, hypertrophic cardiomyopathy, coronary artery anomaly of wrong sinus origin, myocarditis, arrhythmogenic right ventricular cardiomyopathy, and ion channelopathies, are the most prevalent causes of sudden cardiac death in the U.S. Most of these cardiac abnormalities display intermittent EKG abnormalities. An athlete may have an abnormal EKG without any family history, symptoms, or physical exam findings of a cardiac abnormality. Could implementation of screening EKG with pre-participation physical exams for athletes uncover these abnormalities, therefore decreasing the number of sudden cardiac deaths during physical activity per year?

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**Keywords:** Sudden Cardiac death, mass screening, EKG, athletes
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To Dr.s Jaime and Martha Meleán, my parents: Thank you for instilling in me the endless love of medicine and the aspiration to make a difference in the world.
# Table of Contents

Biography ............................................................................................................................... 2
Abstract ................................................................................................................................. 3
Acknowledgements .............................................................................................................. 4
Table of Contents ................................................................................................................... 5
List of Tables .......................................................................................................................... 6
List of Abbreviations............................................................................................................... 6
Introduction and Background ............................................................................................... 7
Methods ................................................................................................................................. 16
Results ................................................................................................................................ 17
Discussion and Recommendations ....................................................................................... 21
Conclusion ............................................................................................................................. 25
Tables .................................................................................................................................. 26
References ............................................................................................................................ 33
List of Tables

Table I: Presentation and recommendations for structural cardiac abnormalities

Table II: Criteria for positive 12-Lead EKG

Table III: Trial Matrix

Table IV: Trial Results

List of Abbreviations

AHA..........................................................American Heart Association

CPK-MB..................................................creatinine phosphokinase-myocardial band

EKG..........................................................electrocardiogram

ESR..........................................................erythrocyte sedimentation rate

HCM..........................................................hypertrophic cardiomyopathy

ICD..........................................................implantable cardioverter-defibrillator

LBBB......................................................left bundle branch block

LVH.......................................................left ventricular hypertrophy

LQTS.....................................................long QT syndrome

LR........................................................likelihood ratio

MRI........................................................magnetic resonance imaging

RBBB....................................................right bundle branch block

SCD.......................................................sudden cardiac death

Tn-I.......................................................troponin-I

WPW.................................................Wolf-Parkinson-White Syndrome
Can an EKG prevent sudden cardiac death in an athlete?  
A systematic review.

Introduction

As medical providers we all work to prevent death while improving quality of life. Therefore, it is difficult to see a young athlete, allegedly in good health, die suddenly as it contradicts all efforts we work towards. Witnessing this unforeseen event draws out the question, “how?” Young athletes are required to receive routine medical screening, however, it is possible for certain pathologies to be silent until a fatal event. It seems as if there should be something the medical community should do to prevent the unforeseen theft of these lives.

Sudden Cardiac Death (SCD) is an uncommon incident, only occurring in 0.61/100,000 persons per year in the U.S. By definition SCD is a death in which the patient had stable cardiac function until the event, and usually occurs less than one hour from symptom onset. Corrado et al determined the relative risk of sudden cardiac death was 2.8 times greater for an athlete compared to their non-athlete counterparts. In the U.S. the top five cardiac abnormalities that cause SCD are, in order of prevalence, hypertrophic cardiomyopathy, coronary artery anomalies of wrong sinus origin, myocarditis, arrhythmogenic right ventricular cardiomyopathy, and ion channelopathies such as Brugada Syndrome and Long QT Syndrome. It is shown that hypertrophic cardiomyopathy accounts for 1/3 of SCD a year. Other causes of SCD, including Wolf-Parkinson-White syndrome, Marfan Syndrome, cardiac sarcoidosis, blunt trauma to the chest, myxomatous mitral valve degeneration, premature atherosclerotic coronary artery disease, and aortic valve stenosis, will not be addressed in this paper.

Once a provider comes to the diagnosis of a cardiac abnormality, recommendations of activity level must be provided. The Bethesda Conference is a convention, sponsored by the American college of
Cardiology Foundation, in which representatives from various organizations, including cardiologists and other providers from the medical community, discusses the latest details of cardiovascular abnormalities in trained athletes. All information is reviewed and recommendations of activity level according to diagnosis are formulated. The U.S. as well as the European medical and athletic communities adheres to these guidelines. It is noted that these recommendations are specific for competitive athletes and not to be utilized with non-competitive recreational athletes. Table 1 outlines the recommendations from the last conference, held in November 2004, for each of the top five diagnoses that have the potential to cause SCD.

**Hypertrophic Cardiomyopathy**

Hypertrophic Cardiomyopathy is an idiopathic disease of the heart that has a familial link. It is considered an autosomal dominant disease that can also develop due to genetic mutations. The left ventricle and/or right ventricle develop asymmetrical hypertrophy without an obvious cause, like aortic stenosis. The apical portion of the left ventricle is most often the hypertrophic portion. Some patients will also have left ventricular stiffness and subsequent impaired filling. Patients may be asymptomatic or complain of symptoms such as dyspnea, angina, fatigue, syncope, or palpitations. On physical exam one will find a harsh systolic crescendo-decrescendo murmur between the apex and left sternal border. The murmur increases with the Valsalva maneuver or when standing from squatting, and decreases when squatting from standing, and with passive leg elevation, or handgrip. The murmur of hypertrophic cardiomyopathy is unlike the murmur of aortic stenosis, in that it does not radiate to the carotid arteries. It will, however, radiate to the lower sternal border, axillae, and to the base of the heart. One may also note mild cardiomegaly, apical systolic thrill and heave, brisk carotid upstroke, or an S4 heart sound on physical exam.

Electrocardiogram (EKG) may reveal left ventricular hypertrophy (LVH), ST and T-wave abnormalities, abnormal Q-waves, or atrial and ventricular arrhythmias. EKG is abnormal in 75%-95%
of patients with HCM. Echocardiogram is considered the gold standard test to diagnose hypertrophic cardiomyopathy, and will reveal an asymmetrically hypertrophied septum, a narrow left ventricular outflow tract, a small to normal sized left ventricle, or systolic anterior motion of the mitral valve.\textsuperscript{4} Treatment for hypertrophic cardiomyopathy is medical symptomatic treatment unless there is obstruction. Alcohol ablation, myectomy, pacemaker, or implantable cardioverter-defibrillator (ICD) would be considered depending on the severity of the obstruction and success of less invasive treatment options. It is recommended that digoxin be avoided unless atrial fibrillation develops or there is systolic dysfunction.\textsuperscript{4}

**Coronary artery anomalies of wrong sinus origin**

Coronary artery anomalies of wrong sinus origin are a congenital malformation of one of the coronary arteries. The anomalous artery originates on the opposite side of the aorta than intended. In the anomalous position the artery travels between the aorta and the pulmonary artery trunk. This positioning creates an angling and a slit-like opening of the vessel, which decreases blood flow through the artery.\textsuperscript{4}

Patients may present with exertional syncope, chest pain, dizziness, or symptomatic ventricular arrhythmias. Most often patients are asymptomatic, have normal EKGs, and no significant findings on physical exam. Identification of anomalies can be done using MRI or ultrafast computed tomography imaging, but coronary arteriography is considered the best diagnostic study.\textsuperscript{5} Treatment for this malformation is surgical bypass.

**Myocarditis**

Myocarditis occurs most commonly from a viral infection (coxsackievirus B), causing inflammation and necrosis of the myocardium, which also could implicate the endocardium, the pericardium, and the valves. Myocarditis may also result from adenovirus, parvovirus, drugs, or toxins like cocaine. It is hypothesized that the viral infection triggers an immune response that subsequently injures the
myocardium after the virus has cleared. Patients may present with symptoms of congestive heart failure, but most commonly are asymptomatic. Symptoms such as chest pain dizziness, syncope, palpitations, tachyarrhythmias or bradyarrhythmias may appear days to weeks after a febrile illness. On physical exam the patient may exhibit tachycardia, hypotension, fever, murmur of mitral or tricuspid regurgitation, S3 or S4 gallops. EKG abnormalities, such as ST segment and T-wave changes, conduction delays, left bundle branch block, AV block, supraventricular tachycardia, or ventricular ectopy are transient, and most often found in first 2 weeks of febrile illness. An echocardiogram will often reveal regional wall motion abnormalities, mitral or tricuspid regurgitation. Once the diagnosis is determined, serial echos will be closely scrutinized to determine progression of the disease. Erythrocyte sedimentation rate (ESR) will be elevated and may be used to monitor the course of the disease. Creatinine phosphokinase-myocardial band (CPK-MB) and cardiac troponin-I (cn-I) may also be elevated. Endomyocardial biopsy is the gold standard diagnostic test. However, biopsy is not required since it does not contribute toward the treatment of myocarditis, unless it becomes necessary to make a more specific diagnosis should the patient fail to respond to standard therapy. Patients with symptomatic myocarditis should be hospitalized for symptom control.2

**Arrhythmogenic right ventricular cardiomyopathy**

Arrhythmogenic right ventricular cardiomyopathy is another disease that is autosomal dominant. In the disease process myocardial cells of the right ventricle are partially or totally replaced by adipose and fibrous tissue. These changes lead to reentrant ventricular tachycardia which appears in the EKG as a left bundle branch block. The EKG may also show inverted T-waves in right precordial leads and epsilon waves. Further imaging may reveal right ventricular dilation and poor contractility with a normal left ventricle. The diagnostic test of choice is MRI.4
Patients may experience palpitations or syncope, which can be treated with antiarrhythmics. However, if medications do not control symptoms, cryo-based or catheter-based radiofrequency ablation, ICD, or transplant must be considered.

**Ion channelopathies**

Ion channelopathies consist of a multitude of arrhythmic disorders, however, only two, Long QT Syndrome and Brugada Syndrome, are in the top five causes of sudden cardiac death. Long QT Syndrome may be idiopathic or acquired. The idiopathic type has a familial link and genetic mutations that affect the potassium and sodium channels. These mutations can occur on one or more of the five cardiac ion-channel genes, LQT1, LQT2, LQT3, LQT 5, and LQT6. There is believed to be a correlation between swimming and ventricular arrhythmias in LQT1. It is also found that LQT3 patients are at a greater risk for arrhythmias during rest. The prolonged QT segment is considered long when corrected QT is longer than 0.46 sec for males and 0.48 sec for females. Arrhythmias occur with adrenergic stimulation or may be induced by Valsalva Maneuver. Long QT can progress to T-wave alternans and ventricular tachycardia. The cardiac exercise stress test is considered the diagnostic test of choice. Some patients may present with syncope from the Torsade de pointes. If a patient has a family history of sudden cardiac death or symptoms, a beta-blocker is recommended at maximum doses. If the patient has a personal history of aborted sudden cardiac death ICD is recommended. A pacemaker or left-sided cervicothoracic sympathetic ganlionectomy are also treatment options depending upon the success of beta-blockers. Even with these treatments in place the Bethesda Conference recommends exclusion from all competitive sports.

Brugada Syndrome is the second type of ion channelopathy that is a common cause of sudden cardiac death. It is considered an autosomal dominant disease that has higher prevalence in Asian males. An EKG may show a right bundle branch block (RBBB) with ST elevation in anterior precordial leads V$_1$-V$_3$. However, these EKG findings which are the trademark pattern for Brugada Syndrome may be
intermittent. The diagnostic test of choice is electrophysiological testing. It is shown that the severity of the symptoms, such as syncope, correlates with the risk of sudden cardiac death. Hyperthermia is noted to elicit the typical Brugada Syndrome EKG pattern, predisposing patients to fever-induced polymorphic ventricular tachycardia. Treatment for Brugada syndrome is ICD.

Athletes Heart

An athlete who has rigorous training will experience structural cardiac remodeling to accommodate the physical activity of the body. These structural changes may look similar to hypertrophic cardiomyopathy, but are considered physiologic left ventricular hypertrophy. EKG abnormalities are present in 40% of elite athletes. Increase in vagal tone may cause bradycardia, sinus arrhythmias, sinoatrial block, multifocal atrial rhythms, junctional rhythms, first-degree AV block, Mobitz type I second-degree AV block, biphasic or inverted T-waves, or ST depression. All of these abnormalities will disappear with exercise. EKG may also reveal a notched p-wave, an increased R-wave or S-wave voltage, Q-waves, or repolarization abnormalities. Holter monitor may show frequent and/or complex ventricular tachyarrhythmias, which are consistent with myocarditis. Increased left ventricular wall thickness, enlarged ventricular and atrial cavity dimension, and increased calculated cardiac mass may appear on echocardiogram. Using echocardiography, a ‘grey zone’ is identified as the cardiac characteristics that are not completely diagnostic for HCM, dilated cardiomyopathy, or changes of an athlete’s heart. The grey zone is defined as left ventricular wall thickness of 13-15mm and/or left ventricular cavity enlargement ≥ 60mm. These findings make the definitive diagnosis of HCM in an athlete difficult. Further testing such as genotyping or MRI can result in a diagnosis. It is hypothesized that hypertrophy typical of an athlete’s heart does not do so at expense of the end diastolic left ventricular size, dilation of the left ventricle due to HCM is typically seen in end-stage HCM. It is also recommended that the athlete decondition for about 12 weeks with subsequent reevaluation. If, after
deconditioning, the cardiac changes show patterns of normalization, it can be deduced that the athlete has neither HCM nor dilated cardiomyopathy.26

**Current Recommendations and the Italian Experience**

The American Heart Association (AHA) recommends a full evaluation prior to initial participation in a sport and to be repeated every two years for high school athletes, and every year for college athletes. A full evaluation consists of a 12-element screening survey that includes personal medical history and family medical history accompanied by a full physical exam. If one or more elements are positive, the AHA recommends further cardiovascular evaluation. The screening survey is comprised of the following points:

- **Personal history of**
  1. Exertional chest pain or discomfort
  2. Unexplained Syncope or near-syncope
  3. Excessive exertional and unexplained dyspnea/fatigue, associated with exercise
  4. Prior recognition of a heart murmur
  5. Elevated systemic blood pressure

- **Family history of:**
  6. Premature death (sudden and unexpected or otherwise) before age 50 years due to heart disease in ≥ 1 relative
  7. Disability from heart disease in a close relative < 50 years of age
  8. Specific knowledge of certain cardiac conditions in family members: hypertrophic or dilated cardiomyopathy, long-QT syndrome or other channelopathies, Marfan Syndrome, or clinically important arrhythmias

- **Physical Exam:**
  9. Heart murmur
  10. Femoral pulses to exclude aortic coarctation
  11. Physical stigmata of Marfan syndrome
  12. Brachial artery blood pressure in sitting position
This 12-element survey is essentially unchanged from the 1996 screening recommendations in spite of the fact that the in 2004/2005 the European Society of Cardiology and International Olympic Committee recommended EKGs as a part of preparticipation screening. It was determined that at a cost of 20 Euros for a history and physical examination a provider can include an EKG as part of the screening for a total of 30 Euros. The athlete or athletic team would be responsible for the cost and athletes under the age of 18 would provide payment through the National Health System. Should the EKG be abnormal the patient would be referred for further cardiac evaluation. Table II includes the parameters of an abnormal EKG.

Many researchers have followed the Veneto Region of Italian athletic population due to the implementation of EKGs as part of the sports screening in 1982. It is a state subsidized protocol. Italy is well-equipped to meet these requirements because there has been an abundance of physicians specialized in sports medicine. All physicians who will perform pre-participation screenings are required to have a post-graduate residency in sports medicine and sports cardiology. This allows medical centers to exist in which the sole purpose is to evaluate athletes. Corrado determined that after the standardization of EKGs with pre-participation physicals the prevalence of SCD due to HCM decreased. When compared with the non-athlete population it was noted that the prevalence of HCM did not decrease, only the SCD outcome in the athlete population decreased. Of 269 Italians under the age of 35 who died of sudden cardiac death during the year 1979 – 1996, 49 athletes and 220 non-athletes died. Only one of the athletes died as a result of HCM, opposed to 16 non-athlete deaths due to HCM. Arrhythmogenic right ventricular cardiomyopathy is now considered the most prevalent cause of SCD in Italy. Corrado performed another study examining the trends of SCD in Italy prior to standardized screening in 1979-1981, during early screening in 1982-1992, and throughout late screening 1993-2004. He concluded that the incidence of SCD in athletes aged 12-35 years old decreased overall by 89%.
The AHA explains that, legally requiring an EKG as part of a preparticipation physical would be a strain on the U.S. healthcare system’s finances and resources. However, if most of the causes of sudden cardiac death are silent until fatal, can a provider identify them with history and physical alone?
Methods

An exhaustive database search was performed using terms: sudden cardiac death, screening, EKG, and pre-participation physical. Databases used were Ovid Medline, Pubmed, Cinahl, and Evidence-Based Medicine Review Multifile. From these results trials written in English were selected and reviewed to identify if the subjects were athletes, whether EKGs were used as a screening test, and if an outcome of hypertrophic cardiomyopathy, anomalous coronary artery origin, myocarditis, arrhythmogenic right ventricular cardiomyopathy, or ion channelopathy was identified. Case studies and post mortem studies were eliminated. Each trial was critically appraised to determine validity. Table III outlines the relevance of each trial to the evaluation of EKGs in diagnosing cardiac abnormalities during pre-participation physicals. Two articles: “Cardiovascular pre-participation screening of young competitive athletes for prevention of sudden death in China” and “Prospective screening of 5,615 high school athletes for risk of sudden cardiac death” were eliminated since neither trial identified the number of athletes with a final diagnosis of the top five cardiac pathologies that could cause sudden cardiac death.
Results

Five trials were found to adhere with all specifications of this review. Table IV outlines each study and the corresponding outcomes.

In the first trial evaluated, Antonio Pelliccia et al \#1 evaluated the long term outcomes of abnormal EKGs in Italian athletes in a cohort study. Specifically he addressed, abnormal EKGs with deeply inverted T-waves (≥ 2mm in at least 3 leads) in athletes who had follow-up with serial EKGs and echocardiogram for 9 ± 7 years and had no current diagnosis of structural heart disease. These 81 athlete’s clinical courses were compared with 229 controls with normal EKGs. All subjects enrolled in the trial received an EKG and an echocardiogram. Eleven subjects of the abnormal EKG group were diagnosed with a cardiac disorder. In spite of a normal EKG four subjects were diagnosed with a cardiac disorder using echocardiogram. Seventy of the subjects with abnormal EKGs and 225 subjects with normal EKGs were determined to have normal cardiac function. Five athletes with abnormal EKGs were diagnosed with a hypertrophic, dilated, arrhythmogenic right ventricular cardiomyopathy. The clinical features of cardiomyopathy did not develop until 12 ± 5 years into follow-up. One of those five athletes died at the age of 24 due to arrhythmogenic right ventricular cardiomyopathy. No one in the control group developed cardiac symptoms nor was anyone diagnosed with cardiomyopathy. During the follow-up period, 27 of the subjects had normalization or decrease in abnormalities of their EKGs. 11 When compared with the gold standard test (echocardiogram) the calculated likelihood ratio is 3.04, providing a sensitivity of 73% and specificity of 76%.

MG Wilson et al performed a study evaluating the benefit of 12-lead EKG with personal history, family history, and physical exam to screen for diseases that may cause sudden cardiac death. The MG Wilson trial evaluated the EKGs of 1,074 national and international junior athletes and 1,646 physically active schoolchildren. All subjects were in the age range of 10-20 years old. This
population represents a wide variety of ages and level of physical activity; however the type of sport in which each athlete participated was not specified. In the trial, only those subjects with an abnormal EKG received further cardiovascular evaluation including an echocardiogram. Diagnoses which were considered to increase risk of sudden cardiac death were: hypertrophic cardiomyopathy, long QT syndrome, Wolff-Parkinson-White syndrome, right ventricular outflow tract ventricular tachycardia, and arrhythmogenic right ventricular cardiomyopathy. The results of the study showed that, of the 1,074 junior athletes screened, only 20 subjects had a positive personal or family history, 25 had an abnormal EKG, 45 required additional evaluations, and 5 were subsequently diagnosed with a cardiac disease that had the potential to cause sudden cardiac death. Of the 1,646 schoolchildren 47 had a positive family or personal history, 15 had an abnormal EKG, 62 required further evaluation, and four were ultimately diagnosed with a cardiac disease that could lead to sudden cardiac death. It is further explained that the nine subjects who were diagnosed with a cardiac disease all had abnormal EKG’s and no subject had a positive family or personal history.  

Yuji Tanaka et al evaluated the usefulness and cost-effectiveness of a screening system using EKG in Japan compared to the US studies. Over an eight year period all seventh and tenth graders in Kagoshima, Japan, were screened with EKG and a medical history questionnaire. Only subjects with abnormal EKGs or a positive family history received further cardiac evaluation. Subjects were re-evaluated 3 years later. Of the original 68,503 students who underwent primary screening 30,696 had moved out of the area and were unavailable for follow-up. The remaining 37,807 were followed for six consecutive years. 632 students were previously diagnosed with heart disease prior to this study and eliminated. 1,876 students had abnormal EKGs requiring further diagnostic studies, 1,370 of whom were found not to have any cardiac abnormalities and 497 of whom were considered to be at low-risk. Nine students were diagnosed with high-risk diseases such as hypertrophic cardiomyopathy, left ventricular dilation, Wolff-Parkinson-White syndrome, primary pulmonary hypertension, and long
QT syndrome with torsade de pointes. None of the subjects diagnosed with hypertrophic
cardiomyopathy had a positive family history. Three of these nine subjects were athletes. One of the
high-risk subjects who was disqualified from his sport died at the age of 14 due to sudden cardiac
death while jogging. Two subjects in the low-risk group, each with normal EKGs, died during athletic
activities due to sudden cardiac death. 13

Antonio Pelliccia #2 also evaluated the efficiency of the Italian screening program for diagnosing
hypertrophic cardiomyopathy. A group of 4,485 elite Italian athletes were evaluated in this study
within two to eight months of initial screening. Through the standard screening each subject was
determined not to have a diagnosis of HCM, and each subject underwent the gold standard exam of
echocardiogram when diagnosing HCM. If needed the subject had cardiac magnetic resonance
imaging, coronary angiography, myocardial biopsy, electrophysiological study with programmed
ventricular stimulation, or genetic testing. In this study, 37 athletes were found to have physiological
left ventricular hypertrophy, consistent with the changes of in athlete’s heart. Of these 37 athletes 28
had abnormal EKGs. Two athletes had left ventricular dimensions that were consistent with the typical
athlete’s heart changes and non-obstructive HCM. Two athletes were later diagnosed with HCM. Of
these four athletes, three had abnormal EKGs, however, it is unclear which subjects had abnormal
EKGs. Four athletes were diagnosed with myocarditis, three with mitral valve prolapse, two with
Marfan syndrome, two with aortic valve disease, and 1 with arrhythmogenic right ventricular
cardiomyopathy. 14

Basavarajaiah et al evaluated 3,500 elite British athletes and the diagnosis of HCM. Asymptomatic
athletes aged 14-35 years were evaluated with EKG and echocardiogram. All athletes had a negative
family history for HCM and were involved in a variety of sports. Fifty-three of these athletes were
found to have a left ventricular wall thickness of greater than 12 mm, indicating left ventricular
hypertrophy. Echocardiogram testing revealed three athletes had a nondilated left ventricle, which may
be consistent with HCM, and EKG abnormalities including deep T-wave inversion in inferior and/or lateral leads, however, other features of HCM were not present and all further cardiac tests were all negative. One athlete underwent detraining for three months at which time echocardiogram and EKG abnormalities normalized. The other two athletes in question underwent genetic testing which was negative for HCM. Cardiac abnormalities other than HCM were diagnosed as result of this trial, six had WPW, nine had Long QT syndrome, five had mitral valve prolapse, two had atrial septal defect, three had bicuspid aortic valve, and one had a cortriatriatum. Twenty participants diagnosed with LVH also had deep T-wave inversion on EKG. Fifteen subjects had deep T-wave inversion in the absence of LVH. It is not stated if any of the group with normal echocardiograms had abnormal EKGS.\(^{15}\)
Discussion

It is shown that most of the pathologies that cause SCD will have an EKG abnormality and may not have an abnormal history or physical exam. Therefore, can an EKG contribute to a pre-participation physical? Each study, although flawed, was able to diagnose a cardiac abnormality when using EKG in addition to history and physical.

When evaluating the value of a diagnostic test, EKG, there is a standard formula to determine the likelihood ratio. This calculated number indicates the importance and value of the test as a diagnostic tool. There are also a series of questions about a diagnostic test trial that help determine the validity of the trial itself. When evaluating each trial each question was addressed.

1. Was the gold standard test, as well as the diagnostic test in question, also performed on each subject? Were the clinicians evaluating each test blinded?

2. Did the patient sample provide a variety of characteristics that will be applied in clinical practice?

3. Was the decision to perform the gold standard test influenced by the results of the diagnostic test in question?

4. Were the methods of the trial presented with detail so they could be reproduced at a later date?

The likelihood ratio (LR) would then be calculated using the formula: \( LR = \frac{a}{a+c} \div \frac{b}{b+d} \), when \( a \) = subjects with a positive diagnostic test and confirmed diagnosis, \( b \) = subjects with a positive diagnostic test and no diagnosis, \( c \) = subjects with a negative diagnostic test, but a confirmed diagnosis using the gold standard test, \( d \) = subjects with a negative diagnostic test, and a confirmed absence of diagnosis using the gold standard test. If the LR is > 10 or < 0.1, then the diagnostic test can cause large changes
in the pretest probability of the target disorder, resulting in a high post-test probability. If the LR is 5-10 or 0.1-0.2, then the trial can cause moderate changes. If the LR is 2-5 or 0.2 to 0.5 the trial will cause small changes. If the LR is < 2 or > 0.5, then the trial can cause tiny changes. Finally, if the LR = 1.0, the trial will cause no change at all. Using the known pre-test probability and the calculated LR one can extrapolate the post-test probability using a likelihood ratio nomogram.16

Using the values from above a sensitivity and specificity of the diagnostic test can be calculated. Sensitivity = \( \frac{a}{a + c} \) and specificity = \( \frac{d}{b + d} \). Sensitivity is a measure of the number of patients who have a positive diagnosis and a positive test. Specificity is a measure of the number of patients who have a confirmed absence of the diagnosis and a negative test. If both sensitivity and specificity values are high, then the diagnostic test in question is considered to be a good one.15

Out of the five studies reviewed only one, Pelliccia #1, actually leads to an effective measurable comparison between a gold standard test, echocardiogram, and EKG. However, there is no pretest probability of HCM in athletes, since it is underreported, prohibiting a post-test probability calculation. The LR was calculated to be 3.04 indicating that these results will only make small changes in the prevalence of HCM in athletes. A sensitivity of 73% and specificity of 76% were calculated indicating EKG has a relatively high accuracy when evaluating for HCM.

Three of the studies, Pelliccia #1, Pelliccia #2, and Basavarajaiah, gave echocardiogram to all participants, at least suggesting that a comparison number between the results might be possible and/or useful, but Pelliccia #2 and Basavarajaiah did not provide sufficient information to calculate a likelihood ratio. Wilson and Tanaka did not give echocardiograms, which is clearly a questionable design flaw given that they purport to address whether the EKG would be a helpful tool when screening for a cardiac abnormality. Test results were also not accurately defined when reporting number of subjects diagnosed and correlation of number of subjects with abnormal EKGs.
In Tanaka two patients with normal EKGs died of SCD during athletic activities, but since no echos had been performed it is unclear as to whether the cause could have been detectable. The Tanaka study was also questionable from another standpoint in that it began with an extremely large sample size (69,033 students) but subsequently lost 30,696 students to follow up due to relocation. This extreme loss rate calls into question the validity of the study as there is no way to assess whether the relocated population was comprised of diagnostically significant subjects or how many of them died during sports activities.

Most studies provided the parameters for which they considered an EKG abnormal. However, Tanaka did not specify the study parameters. This presents another complication when comparing studies as the criteria may have varied. Replication of this study in the future is therefore made difficult.

Extensive evaluation may not detect an underlying cardiac abnormality, as was shown in the Italian population where 10 of 55 sudden cardiac deaths were athletes who had been fully evaluated in response to a suspicious screening EKG, history, or physical exam. In the Tanaka study 2 subjects with normal EKGs died suddenly while playing sports and one athlete who was restricted from competition died while jogging recreationally.

It is important to consider the fact that some of the subjects diagnosed with cardiac abnormalities had a normal history and physical exam. Had the current recommendation of history and physical alone been implemented no diagnoses would have been established and the subject may have experienced SCD. All subjects in Pelliccia #1 were asymptomatic. In the Wilson trial 67 subjects were referred for further cardiac evaluation due to a positive history or abnormal physical exam. Forty subjects were referred due to abnormal EKGs. All nine athletes diagnosed with cardiac abnormalities were asymptomatic and had a negative family history of SCD, but all nine had an abnormal EKG.

The U.S. via the AHA has determined that routine EKGs with pre-participation physicals is not a cost effective practice, but European countries in addition to some private entities routinely include EKG as
a screening tool to unearth cardiac abnormalities, and in the process preventing a number of sudden cardiac deaths. It is important to note Corrado’s evaluation of trends in the Italian population over 26 years found an overall decrease of SCD by 89%. 10
Conclusion

It would be appropriate for the U.S. to follow the example of other countries in implementing the maximum effort possible into these screening processes and increasing accessibility to a greater number of athletes. Even though it may not yet be feasible to require EKGs by legislation as it is in Italy, it should be employed as a guideline or recommendation.

The results suggest that to include EKG with pre-participation physicals would have positive impact on the diagnosis of cardiac abnormalities that cause sudden cardiac death. Although the studies reviewed are too vague to be conclusive. This is an area that requires further study with trials that compare echocardiogram with EKG in all of the participants, follow-up subjects closely, and report exact results of each group.
Table 1. Presentation and recommendations for structural cardiac abnormalities

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Symptoms</th>
<th>Physical Exam Findings</th>
<th>EKG Findings</th>
<th>Gold Standard Test</th>
<th>36th Bethesda Recommendations</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Hypertrophic Cardiomyopathy</td>
<td>- Asymptomatic - dyspnea - angina - fatigue - syncope - palpitations</td>
<td>- harsh systolic crescendo-decrescendo murmur between the apex and left sternal border increasing with Valsalva Maneuver - mild cardiomegaly - apical systolic thrill and heave - brisk carotid upstroke - S4 heart sound</td>
<td>- LVH - ST and T-wave abnormalities - abnormal Q-waves in inferior and/or lateral leads - atrial arrhythmias and/or - ventricular arrhythmias</td>
<td>Echocardiogram</td>
<td>Exclusion from competitive sports, with possible exception of low intensity (class IA)</td>
</tr>
<tr>
<td>2. Coronary artery anomalies of the wrong sinus origin</td>
<td>- exertional syncope - chest pain - dizziness</td>
<td>normal</td>
<td>- normal - arrhythmias</td>
<td>Coronary arteriography</td>
<td>- Exclusion from all competitive sports until three months after successful bypass, if no evidence of ischemia, ventricular or tachyarrhythmias, or dysfunction during maximal exercise testing - if previous myocardial infarction follow recommendations for coronary artery disease</td>
</tr>
<tr>
<td>Myocarditis</td>
<td>- Asymptomatic - chest pain - dizziness - syncope - palpitations</td>
<td>- tachycardia - hypotension - fever - murmur of mitral or</td>
<td>- ST segment changes - T-wave changes - conduction</td>
<td>Biopsy</td>
<td>- Withdraw from competitive sports for six months after onset of clinical presentation</td>
</tr>
<tr>
<td>Condition</td>
<td>Symptoms</td>
<td>Electrocardiographic Findings</td>
<td>Imaging</td>
<td>Restrictions</td>
<td></td>
</tr>
<tr>
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<td></td>
</tr>
<tr>
<td>Arrhythmogenic right ventricular cardiomyopathy</td>
<td>- shortness of breath&lt;br&gt;- peripheral edema&lt;br&gt;- tricuspid regurgitation&lt;br&gt;- S₃ or S₄ gallops</td>
<td>- delays&lt;br&gt;- left bundle branch block&lt;br&gt;- AV block&lt;br&gt;- supraventricular tachycardia&lt;br&gt;- ventricular ectopy</td>
<td>Cardiac MRI</td>
<td>- May return to sports once inflammatory and heart failure serum markers, EKG, LV function, wall motion, cardiac dimensions, and holter monitor readings have normalized&lt;br&gt;- Exclusion from competitive sports except low intensity sports (class IA)</td>
<td></td>
</tr>
<tr>
<td>Ion Channelopathies: a) Long QT syndrome</td>
<td>- Palpitations&lt;br&gt;- syncope</td>
<td>- ventricular tachyarrhythmias&lt;br&gt;- LBBB&lt;br&gt;- T-wave inversion in precordial leads V₁-V₃&lt;br&gt;- epsilon waves</td>
<td>Exercise stress testing</td>
<td>- Restriction to class IA sports if history of out-of-hospital cardiac arrest or suspected long QT precipitated syncope&lt;br&gt;- Restriction to class IA sports if asymptomatic with baseline QT prolongation&lt;br&gt;- No restrictions for genotype-positive/phenotype-negative long QT syndrome patients&lt;br&gt;- Restriction from competitive swimming for patients with LQT1&lt;br&gt;- Restriction from contact sports if patient has an ICD/pacemaker due to risk of damage to pacemaker system&lt;br&gt;- Restriction to class IA if ICD present</td>
<td></td>
</tr>
</tbody>
</table>

Ion - Asymptomatic - Right bundle | Electrophysiology | Restriction to class IA |
<p>| Channelopathies: b) Brugada syndrome | -syncope | branch block (RBBB) with ST elevation in anterior precordial leads V₁-V₃ -inverted T-wave in precordial leads -ST up sloping coved type in right precordial leads | gical testing | sports, even if ICD present |</p>
<table>
<thead>
<tr>
<th>EKG Interval</th>
<th>EKG Finding</th>
<th>Diagnosis</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>P-wave</strong></td>
<td>Negative portion of the P-wave in lead $V_1 \geq 0.1$ mV in depth and $\geq 0.04$ s in duration</td>
<td>Left atrial enlargement</td>
</tr>
<tr>
<td></td>
<td>Peaked P-wave in leads II and III or $V_1 \geq 0.25$ mV in amplitude</td>
<td>Right atrial enlargement</td>
</tr>
<tr>
<td><strong>QRS Complex</strong></td>
<td>Right $\geq +120^\circ$ or left $-30^\circ$ to $-90^\circ$</td>
<td>Frontal plane axis deviation</td>
</tr>
<tr>
<td></td>
<td>Amplitude of R or S wave in standard lead $\geq 2$ mV, S-wave in lead $V_1$ or $V_2 \geq 3$ mV, or R wave in lead $V_5$ or $V_6 \geq 3$ mV</td>
<td>Increased voltage</td>
</tr>
<tr>
<td></td>
<td>Abnormal Q-waves $\geq 0.04$ s in duration or $\geq 25%$ of the height of the ensuing R wave or QS pattern in 2 or more leads</td>
<td>Q-wave</td>
</tr>
<tr>
<td></td>
<td>QRS duration $\geq 0.12$ s R or R’ wave in lead $V_1 \geq 0.5$ mV in amplitude and R/S ratio $\geq 1$</td>
<td>Right or Left bundle branch block</td>
</tr>
<tr>
<td><strong>ST-segment, T-waves, and QT interval</strong></td>
<td>ST-segment depression or T-wave flattening or inversion in 2 or more leads</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Prolongation of heart rate corrected QT interval $&gt;0.44$ s in males and $&gt;0.46$ s in females</td>
<td>Long QT Syndrome</td>
</tr>
<tr>
<td><strong>Rhythm and conduction abnormalities</strong></td>
<td>Premature ventricular beat (PVC) or more severe arrhythmias</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Supraventricular tachycardia, atrial flutter, or atrial fibrillation</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Short PR interval (&lt;0.12 s) with or without ‘delta’ wave</td>
<td>Wolff-Parkinson-White Syndrome</td>
</tr>
<tr>
<td></td>
<td>Sinus bradycardia with resting heart rate $\leq 40$ bpm, PR $\geq 0.21$ s</td>
<td>First, second, or third atroventricular block</td>
</tr>
</tbody>
</table>
Table III. Trial Matrix

<table>
<thead>
<tr>
<th>Author/ Title/ Journal</th>
<th>Yr. published</th>
<th>Patients/ Population</th>
<th>Interventtion</th>
<th>Comparison</th>
<th>Outcome</th>
<th>Study type</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pelliccia/ Outcomes in athletes with marked ECG repolarization abnormalities/ The New England Journal of Medicine</td>
<td>2008</td>
<td>Athletes during the years 1979-2001 who had repolarization abnormalities and control group of athletes during 1980-2000 who had normal EKGS</td>
<td>EKG</td>
<td>Echocardiogram</td>
<td>Cardiac abnormality diagnosis</td>
<td>Cohort</td>
</tr>
<tr>
<td>Wilson/ Efficacy of personal symptom and family history questionnaires when screening for inherited cardiac pathologies: the role of electrocardiography/ British Journal of Sports Medicine</td>
<td>2007</td>
<td>Athletes and active schoolchildren under age 35</td>
<td>EKG</td>
<td>Cardiac evaluation if abnormal EKG</td>
<td>Cardiac abnormality diagnosis</td>
<td>Prospecti ve</td>
</tr>
<tr>
<td>Tanaka/ Usefulness and cost effectiveness of cardiovascular screening of young adolescents/ Medicine and Science in Sports and Exercise</td>
<td>2005</td>
<td>7th and 10th graders in Kagoshima, Japan during 1989-1997</td>
<td>EKG</td>
<td>Cardiac evaluation if abnormal EKG</td>
<td>Cardiac abnormality diagnosis</td>
<td>Prospecti ve</td>
</tr>
<tr>
<td>Pelliccia/ Evidence for the efficacy of the Italian national pre-participation screening programme for identification of hypertrophic</td>
<td>2006</td>
<td>Elite Italian athletes</td>
<td>EKG</td>
<td>Echocardiogram</td>
<td>Cardiac abnormality diagnosis</td>
<td>Prospecti ve</td>
</tr>
<tr>
<td>Basavarajaiah/Prevalence of hypertrophic cardiomyopathy in highly trained athletes/Journal of the American College of Cardiology</td>
<td>2007</td>
<td>Asymptomatic elite athletes from 1996-2006</td>
<td>EKG</td>
<td>Echocardiogram</td>
<td>HCM diagnosis</td>
<td>Prospective</td>
</tr>
</tbody>
</table>
### Table IV. Trial Results

<table>
<thead>
<tr>
<th>Trial</th>
<th>Number of subjects in Trial</th>
<th>Number of subjects with abnormal EKG</th>
<th>Hypertrophic Cardiomyopathy</th>
<th>Coronary Artery Anomalies of Wrong Sinus Origin</th>
<th>Myocarditis</th>
<th>Arrhythmogenic Right Ventricular Cardiomyopathy</th>
<th>Ion Channelopathies: Long QT Syndrome or Brugada Syndrome</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pelliccia #1</td>
<td>310</td>
<td>81 (11)</td>
<td>3 diagnoses, including 1 aborted sudden cardiac death</td>
<td>NA</td>
<td>NA</td>
<td>1 Fatality</td>
<td>NA</td>
</tr>
<tr>
<td>Wilson</td>
<td>2720</td>
<td>40 (9)</td>
<td>0</td>
<td>NA</td>
<td>NA</td>
<td>1</td>
<td>3</td>
</tr>
<tr>
<td>Tanaka</td>
<td>37,807</td>
<td>1,876 (9)</td>
<td>5 including 1 sudden cardiac death</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
<td>1</td>
</tr>
<tr>
<td>Pelliccia #2</td>
<td>4,450</td>
<td>31 (14)</td>
<td>2</td>
<td>NA</td>
<td>4</td>
<td>1</td>
<td>NA</td>
</tr>
<tr>
<td>Basavarajaiah</td>
<td>3,500</td>
<td>35 (26)</td>
<td>0</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
<td>9</td>
</tr>
</tbody>
</table>

(Parentheses) indicates total number of subjects diagnosed with a cardiac abnormality
References


