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Review

Canadian Cardiovascular Society Cardiovascular Screening of Competitive Athletes: The Utility of the Screening Electrocardiogram to Predict Sudden Cardiac Death

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ABSTRACT

Prevention of sudden cardiac arrest/death (SCA/D) among athletes is a universal goal, although the optimal strategy for its achievement is controversial, with the inclusion of the 12-lead electrocardiogram (ECG) at the center of the debate. The ECG exhibits superior sensitivity over history and physical examination to detect conditions associated with SCA/D. However, the identification of disease does not necessarily lead to a significant reduction in SCA/D. The "Canadian Cardiovascular Society/Canadian Heart Rhythm Society Joint Position Statement on the Cardiovascular Screening of Competitive Athletes" recommended against the routine performance of an ECG for the initial cardiovascular screening of competitive athletes. The incidence of SCA/D among athletes (<35 years of age), the risk of SCA/D during sport participation among individuals with abnormalities found on screening ECG, the efficacy of the ECG to identify conditions associated

RÉSUMÉ

La prévention de l'arrêt cardiaque soudain (ACS) et de la mort subite d'origine cardiaque (MSOC) chez l'athlète constitue un objectif universel, bien que la stratégie optimale pour sa réalisation soit controversée, l'inclusion de l'électrocardiogramme (ECG) à 12 dérivations se trouvant au centre du débat. Comparativement à l'anamnèse et à l'examen physique, l'ECG présente une sensibilité supérieure quand il s'agit de détecter les troubles associés à l'ACS et à la MSOC. Cependant, le dépistage d'un état pathologique ne se traduit pas nécessairement par une réduction significative des cas d'ACS et de MSOC. Dans l'énoncé de position conjoint de, la Société canadienne de cardiologie et de la Société canadienne de rythmologie sur le dépistage cardiovasculaire des athlètes de compétition, le recours systématique à un ECG pour le dépistage initial des troubles cardiovasculaires chez les athlètes de compétition est déconseillé.

Cardiac pathology is the leading medical cause of sudden death in athletes.[1,2] Cardiovascular screening is the systematic practice of medically evaluating athletes before participation in sports for the purpose of identifying (or raising suspicion of) health conditions and abnormalities for which continued exercise may lead to disease progression or sudden cardiac arrest or death (SCA/D).[3] SCA/D may be the first clinical manifestation of an underlying cardiovascular condition in this population. Cardiovascular screening offers the *promise* of the identification of young athletes potentially at risk of SCA/D because of an underlying *identifiable* cardiac condition that may increase their risk of SCA/D through systematic evaluation that may afford the opportunity to identify at-risk athletes who have yet to be identified via case finding. The goal of cardiovascular preparticipation screening is to detect cardiac conditions associated with SCA/D in athletes, with the intent of reducing risk by activity restriction or treatment. The presence of automated external defibrillators and emergency action plans in sport and community settings can

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with SCA/D, and the positive predictive value of an abnormal ECG to predict SCA/D are critically examined. This review presents the evidence informing the panel's recommendation.

L'incidence de l'ACS et de la MSOC chez l'athlète (< 35 ans), le risque qu'ils surviennent pendant la pratique d'activités sportives chez les sujets présentant des anomalies qu'un ECG a permis de détecter, l'efficacité du dépistage par ECG des troubles associés à l'ACS et à la MSOC, de même que la valeur prédictive d'un résultat d'ECG anormal au regard de ces deux entités cliniques sont l'objet d'un examen critique. Le présent article de synthèse expose les données probantes sur lesquelles se fonde la recommandation du groupe.

dramatically reduce the incidence of sudden cardiac death (SCD).[4] The "Canadian Cardiovascular Society/Canadian Heart Rhythm Society Joint Position Statement on the Cardiovascular Screening of Competitive Athletes" recommended against the routine performance of an electrocardiogram (ECG) for the initial cardiovascular screening of competitive athletes.[5] This article serves as a companion to that position statement. A Canadian position statement was required because of the significant heterogeneity noted in screening practice and attitudes by institutions across Canada.[6,7]

Competitive sport or vigorous exertion can be a trigger for life-threatening arrhythmia or sudden cardiac arrest (SCA) in those with a susceptible underlying substrate. Young competitive athletes (<35 years) *may* have a higher relative risk of SCD compared with nonathletes of the same age, although there is conflicting literature. Data from the Italian screening experience reported an incidence of 1.9 deaths/100,000 athlete-years (AY) in athletes vs 0.79 deaths/100,000 AY in nonathletes, a 2.4-fold increase.[8] A French study also demonstrated that the relative risk of SCD was 4.5 times higher in competitive young athletes (0.98/100,000) compared with noncompetitive sports participants of the same age (0.22/100,000).[9] American high-school athletes were 2.7 times more likely to experience SCA than nonathletes (1.14/100,000 vs 0.31/100,000).[10] In contrast, in a nationwide registry from Denmark, athletes had a lower risk of SCD than nonathletes, with competitive and noncompetitive athletes exhibiting the same incidence of sport-related SCD.[11,12] Furthermore, nonathletes from Minnesota exhibited a higher incidence of SCD (1/39,454) vs athletes (1/120,614).[13]

The discord noted in the literature with respect to SCD in athletes vs nonathletes may reflect the imprecision of data collection. Incomplete ascertainment of details pertaining to the cause of death in studies that rely on media reports and insurance records and absent or limited autopsy data can result in inaccurate estimates.[14] The completeness of follow-up in nonathlete populations may be limited and less well documented compared with athlete populations, potentially leading to an underestimation of the rate of death in athlete populations and particularly in nonathlete populations. It is foreseeable that in both athlete and nonathlete populations the cause of death may be falsely credited to a cardiac etiology or cardiac deaths may incorrectly be assigned as noncardiac. The low overall incidence of SCA/D in athletes, the small absolute difference between SCD incidence in athletes and nonathletes, and the potential imprecision of estimates of SCD in nonathlete populations bring into question whether athletes are truly at a significantly higher risk of SCA/D vs nonathletes.

Despite these concerns, the observation that young athletes *may* be at a heightened risk of SCA/D compared with nonathletes provides one impetus for cardiovascular screening among athlete populations. There is consensus among the majority of international medical and sporting bodies that athletes should undergo some form of cardiovascular or preparticipation screening.[5,15-17] However, significant controversy exists regarding the optimal method to identify susceptible athletes, with the ECG at the center of the debate.[18]

Identification of disease does not necessarily lead to a reduction in SCA/D. The finding of an abnormality does not necessarily equate to lives saved. Among the population at risk (those who harbour subclinical cardiovascular disease), only a small fraction will ever have a cardiac event (SCA or SCD). Within the cohort of athletes with identified disease (~0.3% of all those screened[1,19]), a small proportion are destined to experience SCA, but the larger fraction will not experience SCA despite the presence of underlying disease. Moreover, of those who will experience SCA, many will occur at rest or in settings completely unrelated to sport activity.[20] In the 99.7% of athletes who do not have identifiable disease, the majority will not have SCA, but a small fraction with no detectable disease will still experience SCA (destined to experience SCA) (Fig. 1). Athletes with no identifiable disease but who experience SCA consist of 2 groups: (1) those with an underlying condition that predisposes them to SCA that is not readily detected with ECG-inclusive screening (ie, coronary artery anomalies, coronary artery disease [CAD], idiopathic ventricular fibrillation); and (2) those who have no discernable cardiac condition at the time of screening but will experience a SCA due to a condition that was not clinically detectable or not yet phenotypically expressed.[2]

Inherent in the supportive rationale for cardiovascular screening is the notion that athletes who are discovered to have disease associated with SCA/D and who are destined to experience SCA can be transitioned to those athletes who will not experience SCA/D via medical intervention or sport restriction.

It is imperative to distinguish the positive predictive value (PPV) of the ECG in diagnosing cardiac conditions vs the PPV of the ECG to determine the future absolute risk of SCA/D. Although diagnosing a relevant cardiac condition through screening may be of value, the ultimate goal is the reduction of SCA/D. There is no question that some athletes identified with disease via cardiovascular screening may develop symptoms, may experience SCA/D, and may have identifiable inherited conditions that may lead to additional diagnoses in family members (cascade screening). However, the majority will not. The ECG may be effective in detecting

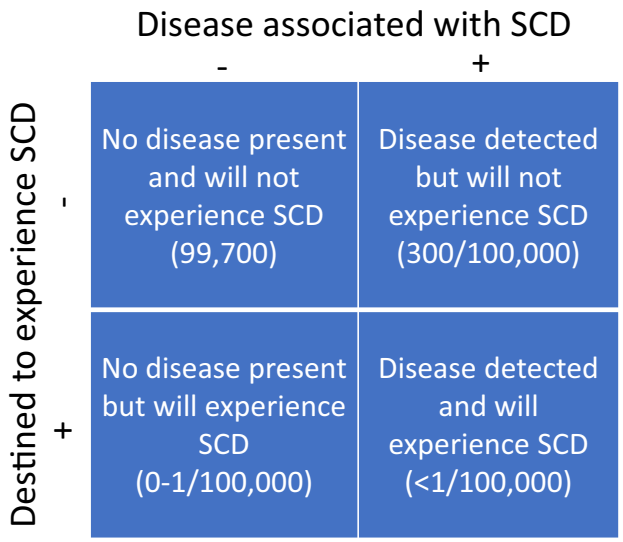

Figure 1. Potential outcomes for athletes with and without identifiable disease. The values presented within are based on a prevalence of 0.3% of conditions associated with SCD and an incidence of sports-related SCD of 1 in 100,000. SCD, sudden cardiac death.

disease, but does ECG-inclusive cardiovascular screening result in a reduction in SCA/D? The aim of this review is to go beyond reporting the ECG's ability to detect heart disease and investigate the potential for the ECG to reduce SCA/D.

Prevalence of Cardiovascular Diseases Associated With SCD and Incidence of SCD in Young Athlete Populations

The marked difference between the prevalence of conditions associated with SCA/D and the actual incidence of SCD among young athletes requires attention. The prevalence of cardiovascular diseases among athletes that may be associated with SCD is approximately 0.3%.[1,19] Although the distribution of the diagnoses may differ geographically between studies, the prevalence of approximately 0.3% remains relatively constant. Within a population of young Canadian athletes, the prevalence of disease was congruent with prior estimates at 0.52%.[21] In contrast, the reported incidence of SCD in young athletes varies greatly, with estimates ranging from 1/917,000 AY reported in Minnesota high school athletes to 1/5200 AY of National Collegiate Athletic Association Division I male basketball players, a difference of > 300-fold.[22,23] Among all National Collegiate Athletic Association athletes, the rate of SCD has remained similar over the last 10 years and is 1/53,7031 AY.[24] A 2017 meta-analysis of 21 studies comprising 437,156,081 AY found the incidence of sports-related SCD to be 0.72 per 100,000 (95% confidence interval [CI], 0.58-0.86) or 1 death per 138,889 AY.[25] There was no significant difference found between the incidence of sports-related SCDs in the United States (0.70 per 100,000; 95% CI, 0.47-0.93) and Europe (0.68 per 100,000; 95% CI, 0.51-0.86).[25] The risk of SCA during sport in a population of Canadian athletes aged 12 to 45 years was calculated to be 0.76 cases per 100,000 or 1/131,578 AY.[26]

Sudden Arrhythmic Death Syndrome as a Major Cause of SCD in Young Athlete Populations and Implications for Screening

Sudden arrhythmic death syndrome or autopsy-negative sudden unexplained death is defined as an SCD that remains unexplained after comprehensive postmortem and toxicology evaluation has ruled out noncardiac causes, and when the heart is morphologically normal on autopsy.[27] Sudden arrhythmic death syndrome has become increasingly recognized as a significant cause of SCD in young athlete populations, representing up to 50% of the total cardiac deaths.[20,24,28,29] However, only a small fraction (10%-34%) of sudden arrhythmic death syndrome occurs during or immediately after sport, with the majority of deaths occurring outside of sporting activity.[20,29,30] A proportion of sudden arrhythmic deaths are thought to be due to inherited arrhythmogenic diseases such as long QT syndrome (LQTS), short QT syndrome, Brugada syndrome, and catecholaminergic polymorphic ventricular tachycardia, in addition to idiopathic ventricular fibrillation and repolarization syndromes. Extensive clinico-genetic evaluation of family members of those who have sudden arrhythmic death syndrome using a resting 12-lead ECG, ECG-stress testing, sodium channel provocation testing, advanced cardiac imaging, and genetic testing has found a cardiac diagnosis associated with SCD in up to approximately 50%.[20,31-33] However, the yield to establish a definitive diagnosis can be considerably lower. Bagnall et al.[20] found a definite diagnosis in a first-degree relative in 13% of the sudden arrhythmic death syndrome cases. Sudden arrhythmic death syndrome represents a challenge for ECG-inclusive cardiovascular screening because the majority of sudden arrhythmic death syndrome cases are not readily identified via a resting ECG. In a comprehensive study of families with sudden arrhythmic death syndrome, the yield of the ECG was 35% in identifying a putative cause of death for the proband.[34] However, the yield of the resting 12-lead ECG to identify potential etiologies of sudden arrhythmic death syndrome may be lower. In a comprehensive study of 303 families with sudden arrhythmic death syndrome, baseline investigations including resting 12-lead ECG, exercise ECG stress test, and echocardiogram yielded a diagnosis in only 5% of the cases.[30]

The 12-Lead Resting ECG as a Screening Tool Compared With History and Physical Examination

The limited ability of history and physical examination components of cardiovascular screening to detect disease is not unexpected, because a significant proportion of athletes who may harbour underlying disease may be asymptomatic, may have not reported symptoms, or may not have had their reported symptoms appropriately evaluated. Additionally, the majority of causes of SCD are not readily identifiable by physical examination (sensitivity of 9% to detect disease).[29] Despite the limited ability of history to detect *disease*, personal and family history may play an important role in predicting *impending* SCD. There is considerable variability in reported antecedent symptoms; however, a notable proportion of young persons may be symptomatic before SCD. A large autopsy series of SCD in young athletes reported that 19% of

the victims were symptomatic before death.[29] In a Danish SCD registry of persons aged < 35 years, symptoms were reported before death in 35% of sudden arrhythmic death syndrome cases, 51% of hypertrophic cardiomyopathy (HCM) cases, and 79% of CAD cases.[35-37] However, in a UK study of 967 cases of sudden arrhythmic death syndrome, prodromal symptoms occurred < 10% of the time and only 4.2% had a positive family history.[38] The history component of cardiovascular screening may be insensitive to detect *disease* associated with SCA/D, but may potentially identify a proportion of symptomatic athletes or those with a family history of SCD who may be at risk for SCA/D. The history and physical examination components of cardiovascular screening have many limitations, but these are beyond the scope of the review and have been contextualized in the Canadian Cardiovascular Society/Canadian Heart Rhythm Society position statement.[5]

The ECG is often viewed as a singular screening tool, yet the ECG exhibits varying sensitivities and specificities for the multiple conditions associated with SCA/D. The relative sensitivity and specificity of the ECG may be influenced by the following variables: sex, race, age, volume of exercise, and type of sport (with sports that are associated with greater exercise-induced cardiac remodeling producing more training-related ECG changes.) A number of predisposing cardiac conditions associated with SCA/D are not readily identifiable by ECG (ie, coronary artery anomalies, CAD, catecholaminergic polymorphic ventricular tachycardia, idiopathic ventricular fibrillation, mitral valve prolapse, aortopathies, and idiopathic fibrosis) (Table 1). This important consideration is acknowledged in the "International Criteria for Electrocardiographic Interpretation in Athletes: Consensus Statement," "even if correctly interpreted, an ECG will not detect all conditions predisposing to SCD."[39] Furthermore, it should be recognized that a subset of individuals may have a concealed phenotype or a phenotype that has not been fully expressed at the time of ECG screening. For example, individuals with HCM and arrhythmogenic right ventricular cardiomyopathy (ARVC) may possess a normal ECG before phenotypically expressing the disease.[2] The reported sensitivities and

Table 1. Prevalence and causes of SCD in athletes

Inherited: structurally abnormal heart cardiomyopathies	Detectable by ECG	Reported sensitivity	Reported specificity in persons with the disease	Potential ECG findings
Arrhythmogenic right ventricular cardiomyopathy	✓	40-50	40-82	TWI, STD, epsilon waves, low precordial voltage (< 1.8 mV), PVCs
Dilated cardiomyopathy	✓	50	Low	TWI, STD, LBBB, IVCD, PVCs, q waves, low voltages
HCM	✓	90	90	TWI, STD, q waves, PVCs, IVCD
Idiopathic LVH/fibrosis	✓	High	Not specific	LVH
Left ventricular noncompaction	✓	87	Poor	TWI, STD, LBBB, IVCD, PVCs, q waves, LVH
Other				
Coronary artery abnormalities	✗	0	0	None
Valvular heart disease (bileaflet mitral valve prolapse syndrome, bicuspid aortic valve)	✗	0	0	None
Aortopathies (eg, ascending aortic aneurysm, Marfan syndrome)	✗	0	0	None
Inherited: structurally normal heart channelopathies				
Brugada syndrome	✓	High	High	Brugada pattern
Catecholaminergic polymorphic ventricular tachycardia; idiopathic ventricular fibrillation	✗	0	0	None
LQTS	✓	75*	95	QTC > 470 ms (male); > 480 ms (female)
Short QT syndrome	✓		95	QTC < 320 ms
WPW/ventricular pre-excitation	✓	100	100	Delta wave, short PR
Acquired: structurally abnormal heart				
Ischemic heart disease	✗	< 0.5	Low	q waves, TWI, PVCs, STD, LBBB, LAFB, AF
Myocarditis	~	25	Low	q waves, TWI, PVCs, AVB, LBBB
Acquired: structurally normal heart				
Commotio cordis	✗	0	0	None
Substance abuse	✗	0	0	None
Environmental factors (eg, hypothermia or hyperthermia, electrolyte disturbances)	✗	0	0	None

It is important to note that the majority of studies reporting the sensitivity and specificity of the ECG to identify a particular disease state are derived from highly enriched subpopulations of persons with established overt disease, as opposed to unselected screening populations, and are produced by expert readers.

AF, atrial fibrillation; AVB, atrioventricular block; ECG, electrocardiogram; HCM, hypertrophic cardiomyopathy; IVCD, intraventricular conduction delay; LAFB, left-anterior fascicular block; LBBB, left bundle branch block; LQTS, long QT syndrome; LVH, left ventricular hypertrophy; PVC, premature ventricular contraction; SCD, sudden cardiac death; STD, ST-segment depression; TWI, T-wave inversion; WPW, Wolff–Parkinson–White.

*Twenty-five percent of individuals with LQTS may have a normal QT interval or clinically concealed LQTS.

specificities of the ECG to detect certain cardiac conditions in healthy young athlete populations may not be as robust as in the cohorts of individuals with overt phenotypically manifest disease from which the sensitivities and specificities have been derived. For example, in a cohort of young individuals (mean age, 15.5 years) with borderline or definite ARVC, only 29% of the cohort had an abnormal ECG.[40]

Despite its limitations, the ECG exhibits superior sensitivity over history and physical examination to detect *disease* associated with SCD.[1,2] The high overall sensitivity of the ECG stems from the enhanced diagnostic yield of the ECG to detect asymptomatic electrical disease, such as Wolff–Parkinson–White (WPW)/ventricular pre-excitation, channelopathies, and occult cardiomyopathies such as HCM and ARVC[41] (Table 1). A meta-analysis of 15 ECG-inclusive cardiovascular screening studies comprising > 47,000 athletes demonstrated that the ECG possessed a sensitivity of 94% compared with history (20%) and physical examination (9%) to detect conditions *potentially* associated with SCA/D. It is important to note that in this meta-analysis, the ECG was used as the gold standard. The analysis did not evaluate the ECG's ability to predict SCA/D.[1] The ECG was more sensitive than echocardiography in a study of 11,168 English footballers, in whom the ECG-detected disease associated with SCD was 86% vs 29% for echocardiography.[2] Ventricular pre-excitation (WPW) represented 62% of the diagnoses found in this study. The potential magnitude of reduction in sports-related SCD is questionable because WPW is associated with a very low risk of SCA/D as the initial manifestation.[42]

The reported specificities of the ECG to discern cardiac pathology need to be interpreted with caution. In electrical diseases such as WPW, LQTS, short QT syndrome, and Brugada, the ECG is the sine qua non, and thus demonstrates high specificity. However, for cardiomyopathies such as HCM and ARVC, the specificity of the ECG is lower.[40] The ECG criteria may be specific for an individual with an overt and established cardiac diagnosis, but in the general screening population, the presence of an ECG abnormality is less specific.[40] The studies reporting the sensitivity and specificity of the ECG to identify a particular disease state are derived from highly enriched subpopulations of persons with established overt disease, as opposed to unselected screening populations. Additionally, studies are derived from tertiary centers with expert ECG interpretation. In screening populations, the presence of a positive ECG finding does not necessarily translate into disease identification (the ECG abnormality is not specific for the diagnosis of a condition with the exception of certain electrical diseases). For example, application of the 2017 International Criteria to a cohort of 4925 previously unscreened athletes resulted in 3.0% (146 athletes) being identified as having a positive ECG finding.[43] After expert evaluation, disease was confirmed in 15 athletes (HCM = 6, LQTS = 3, WPW = 6). The PPV for an abnormal ECG in this study to identify disease would be 0.102. Furthermore, in a study of 100 athletes with T-wave inversion who underwent expert clinical evaluation and genetic testing, 21 were ultimately diagnosed with a cardiac condition, with 77 of the 100 athletes having no condition identified after thorough clinical or genetic evaluation.[44] Thus, the reported PPV of the ECG pertaining to disease identification can be low, and an ECG abnormality may not be specific in diagnosing a cardiac condition (especially cardiomyopathies). The PPV of an abnormal ECG to predict SCA/D would be expected to be orders of magnitude less, because only a small fraction of those *with disease* will ever experience SCA/SCD.

Disease Prevalence, Incidence of SCD, and ECG Performance in a Population

Separate from the diagnostic accuracy of the screening tool, the underlying incidence of SCA/D in a specific population is a major determinant of the potential number of lives that could theoretically be saved. Consider the following example: In a population of 1 million athletes in whom the prevalence of abnormal ECG findings is 5%, underlying disease associated with SCD is 0.3% and the incidence of SCD is 1/100,000/year, there would be 3000 young athletes harboring cardiovascular disease and 10 expected SCDs/year in the total population. By assuming the screening tool (the ECG) possesses 75% sensitivity and 95% specificity, 750 athletes with disease will not be identified and 2.5 of those would be *expected* to experience SCD. However, this process would yield approximately 50,000 false-positive screens, and although 2500 athletes with *true* disease would be identified, only 7.5 could potentially die of SCD and the other 2244.5 with disease would not be expected to experience SCD (Fig. 2). The potential effectiveness of screening with varying incidence of SCD and sensitivity and specificity of the screening tool are displayed in Supplemental Table S1.

ECG-inclusive preparticipation screening considerations

Not all cardiac conditions associated with SCA/D in young athletes possess equal risk of SCA/D. Furthermore, there is varying risk of SCA/D within the individual conditions themselves (not all those with HCM or ARVC are at similar risk of SCA/D or disease progression). In examining the impact of performing an ECG on the potential reduction of SCA/D, one must consider the ECG's ability to detect a particular disease and the risk of SCA that the specific disease/condition poses.

A normal ECG does not guarantee an absence of disease or event-free survival and can potentially result in false reassurance. In autopsy series of athletes in whom the cause of death is presumed to be cardiac in etiology, the victims of SCA/D infrequently had abnormal ECGs. Landry et al.[26] examined sports-related SCA/D (defined as death occurring during sports or within 1 hour after its cessation) in a population of athletes aged 12 to 45 years in Ontario, Canada, where no systemic cardiovascular screening is in place. Of the 13 competitive young athletes (<35 years of age) who experienced SCA not due to CAD, 2 had prior ECGs and echocardiograms that were normal. The etiologies of arrest were primary arrhythmic in 46.1% (n = 6), HCM in 15.3% (n = 2), coronary artery anomalies in 23.0% (n = 3), and commotio cordis in 15.3% (n = 2). Of the 6 athletes who survived the cardiac arrest (4 primary arrhythmic and 2 commotio cordis) who underwent subsequent investigations, only 1 had an abnormal ECG (T-wave inversions); however, no identifiable pathology was found on further testing). One of the deaths due to HCM had an ECG and echocardiogram before his SCD that were interpreted as normal.[26] In a study of 11,168 elite young English footballers screened with an ECG and echocardiogram at age 16 years, 8 sudden deaths

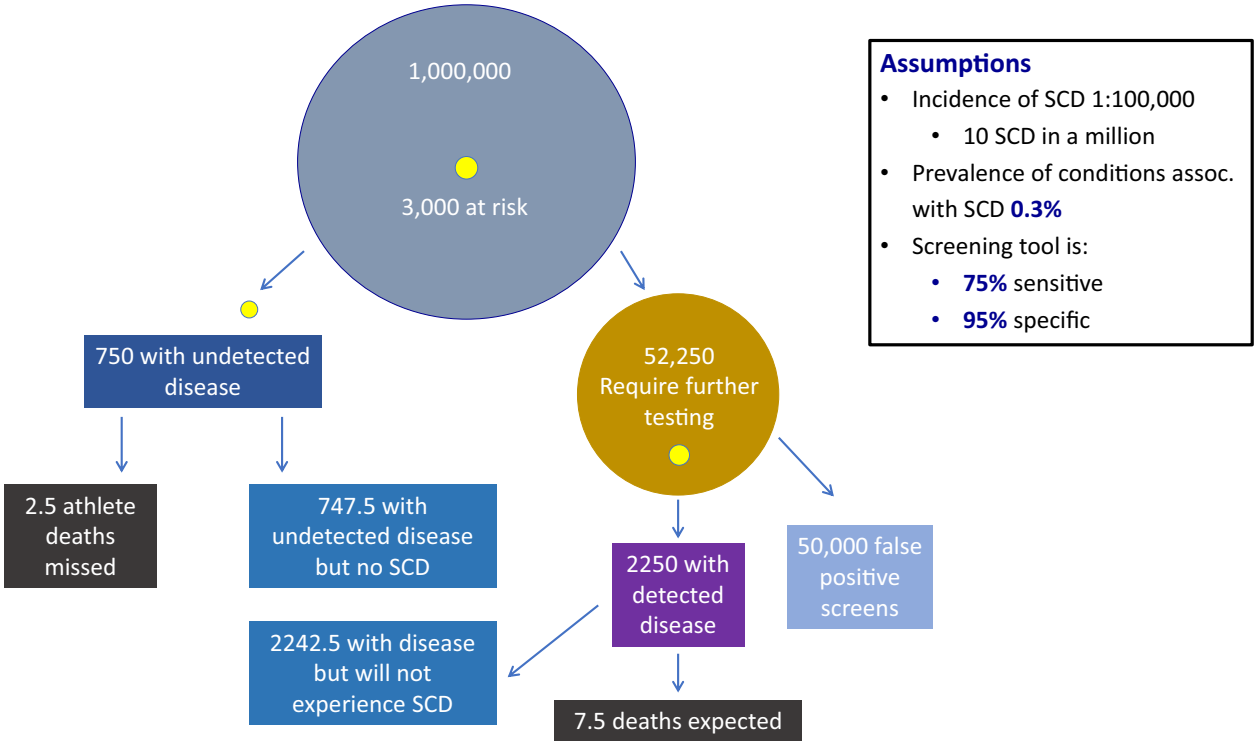

Figure 2. Interplay of disease prevalence, incidence of SCD, and diagnostic accuracy of the electrocardiogram (ECG). SCD, sudden cardiac death.

due to cardiac disease occurred (HCM, 3; ARVC, 2; dilated cardiomyopathy, 1; idiopathic left ventricular hypertrophy [LVH], 1; and sudden arrhythmic death syndrome, 1) with an incidence of 6.8/100,000 AY. Six of the 8 athletes who died had a normal ECG and echocardiogram at the time of screening (age 16 years), with a mean time of 6.8 years from screening to death.[2]

Refinement of ECG interpretation criteria has significantly reduced the number of false-positive ECG screens from 20% to 3%.[43] Despite the reduction in false-positive screens with improved ECG interpretation criteria, there are still significant costs associated with the subsequent secondary testing, evaluation, and long-term follow-up. The cost to identify a serious diagnosis using the 2017 International Criteria has been estimated at $26,405 USD.[43] Furthermore, a positive screening ECG may result in psychological distress, detrimental change in one's self worth and identity, loss of potential income, and potential difficulties in insurability.[45] Cardiologists less experienced at interpreting the ECGs of athletes are more likely to interpret an ECG as abnormal compared with experienced cardiologists (odds ratio, 1.44) and are more likely to refer athletes for secondary evaluation compared with experienced cardiologists (odds ratio, 4.74), thus potentially compounding costs and negative psychological impact.[46]

The Expected or Potential Number of Lives Saved by ECG-Inclusive Screening

There are no randomized data examining large populations of athletes screened with and without an ECG. To date, the evidence in support of ECG screening comes from a single experience in Veneto, Italy (with a known high incidence of ARVC within the region), where the annual incidence of SCD in athletes decreased by 89% (from 3.6/100,000 AY in pre-screening period to 0.4/100,000 AY after screening).[8] This marked reduction in SCD after the introduction of ECG-inclusive screening has not been reproduced in other jurisdictions.

To estimate the number of lives potentially saved via ECG-inclusive cardiovascular screening, 2 separate approaches were used: (1) using the incidence of sports-related SCD, combined with the reported causes of SCD from contemporary autopsy series, to calculate the number of cases of SCD that could be identified by ECG screening; and (2) estimating the risk of SCD on a per disease basis of conditions most commonly associated with SCD.

Approach 1: estimating the number of potential deaths that could be identified by ECG based on incidence of sports-related SCD, prevalence of disease from autopsy series of sports-related SCD, and sensitivity of the ECG to detect the specific conditions

An incidence of sports-related SCD of 0.72/100,000 or 7.2 per 1,000,000 was used.[25] The etiologies of SCD from 3 large autopsy series (Landry et al.,[26] Bagnall et al.,[20] Finocchiaro et al.[29]) were compiled to provide an estimate of the prevalence that each condition contributed to SCD. The proportion of the pooled weighted individual conditions was then multiplied by 7.2 (number of deaths per 1,000,000) to arrive at an estimate of how many deaths per million were due to each condition. The sensitivity of the ECG to detect the specific condition was then multiplied by the expected number of deaths for that specific condition to identify the number of deaths potentially identifiable by ECG screening. The total number of deaths expected to be identified for each

condition was summed and expressed as a percentage of 7.2 per 1,000,000.

On the basis of the etiologies of sports-related SCD reported in the 3 autopsy series with the assumption that the resting 12-lead ECG exhibits 100% sensitivity for all conditions that are detectable by an ECG, 53.1% (3.8/7.2 per 1,000,000) of the deaths could have been detected with a prescreening ECG. If more conservative sensitivities from the current literature for the specific conditions are used, then it would be estimated that the ECG would be able to detect 24.3% (1.7/7.2 per 1,000,000) of all of the deaths. A significant proportion of sports-related SCD observed in the study by Finocchiaro et al.[29] were attributed to idiopathic LVH or idiopathic left ventricular fibrosis. The ability and diagnostic accuracy of the ECG to detect these conditions in a cardiovascular screening setting are undefined. For idiopathic LVH, it would be assumed that the ECG would not be specific because isolated LVH is considered a normal variant in isolation as per the 2017 International ECG Recommendations.[47] Removing the study by Finocchiaro et al.[29] and combining the studies by Landry et al.[26] and Bagnall et al.[20] result in 34.2% of the deaths *potentially* being identifiable by the ECG. It is important to note that in the study by Landry et al.,[26] the actual number of deaths that could have been identified with a screening ECG would have been at maximum 25% (there were 2 deaths each attributed to HCM and sudden arrhythmic death syndrome; the 1 abnormal ECG resulted in normal downstream testing). This also assumes that the 2 sudden arrhythmic death syndrome deaths would have been detected by the ECG, which is less probable.[26] In this analysis, the majority (65.8%-75.2%) of deaths occurring during sport would *not* be readily identifiable with a resting ECG. The absolute number of sports-related SCD that are identifiable with a cardiovascular screening ECG is estimated at 1.7 to 2.5 per 1,000,000 (Table 2). The percentage of sports-related SCD based on etiology from autopsy series that could be identified by ECG is presented in Figure 3.

Table 2. Number of sports-related SCDs per million that potentially can be identifiable by ECG

Cause of death	Percentage of SCD	Expected percentage detected by ECG	Potential number of SCD per million identified by ECG
Aortic dissection	3.1%	0	0
ARVC	12.5%	50	0.45
CAD*	15.6%	0	0.00
DCM	3.1%	50	0.11
HCM	12.5%	90	0.81
Myocarditis	6.3%	25	0.11
SADS	39.1%	35†	0.98
Commotio cordis*	3.1%	0	0
Coronary artery anomaly*	4.7%	0	0
Total	100%		2.5/7.2‡

ARVC, arrhythmogenic right ventricular cardiomyopathy; CAD, coronary artery disease; DCM, dilated cardiomyopathy; ECG, electrocardiogram; HCM, hypertrophic cardiomyopathy; SADS, sudden arrhythmic death syndrome; SCD, sudden cardiac death.

* It is assumed the coronary artery anomalies, CAD, and commotio cordis are not readily identifiable on a resting ECG.

† A 35% sensitivity was used for sudden arrhythmic death syndrome based on the study by Kumar et al.[32]

‡ The 7.2 deaths per million is based on a meta-analysis of incidence of sports-related SCD.[23]

Approach 2: estimating the risk of SCD on a per disease basis and the number needed to screen to prevent 1 death

The prevalence and risk of SCD for the most common conditions identifiable by ECG (ARVC, HCM, LQTS, and WPW syndrome) can be estimated. The *sensitivity* and *specificity* of the ECG are then applied to the prevalence of disease to calculate the proportion of athletes at risk of death per year during sport and overall. The number needed to screen to prevent 1 death per million per year can be calculated by multiplying the sensitivity of ECG for the condition ***X*** prevalence of disease **X** risk of death (overall and during sport).

The usually accepted prevalence of HCM is 1:500. However, it may be as high as approximately 1:200 in the general population and in various studies in athletes as high as 1 in 113 and as low as 1:1861 to 1:2618 in athlete populations.[1,2,48,49] The annual mortality from HCM is approximately 0.5% in an HCM registry, which represents an enriched population;[48,50] in an unselected population, the incidence of SCD is estimated at 0.2% to 0.3% per year.[51] ARVC has a prevalence of 1 in 5000 with an annual mortality of 0.8%.[52,53] In 1 million athletes screened, 2000 would be expected with HCM and 200 with ARVC, with 4 to 10 deaths caused by HCM and 1.6 due to ARVC. It is important to note that many of these HCM-related deaths would occur at rest or during light activity.[20,29]

The prevalence of LQTS and WPW is approximately 1 per 2000. The annual mortality rate for LQTS and WPW is estimated at 0.5 to 2.0 per 1000 and 0.14 to 0.36 per 1000 patient-years, respectively.[54,55] For every 1 million athletes screened, it would be expected that 500 would have LQTS with 0.25 to 1 athlete deaths annually. For WPW, 500 athletes per million would have the condition with 0.07 to 0.18 anticipated deaths due to the condition. The overall combined

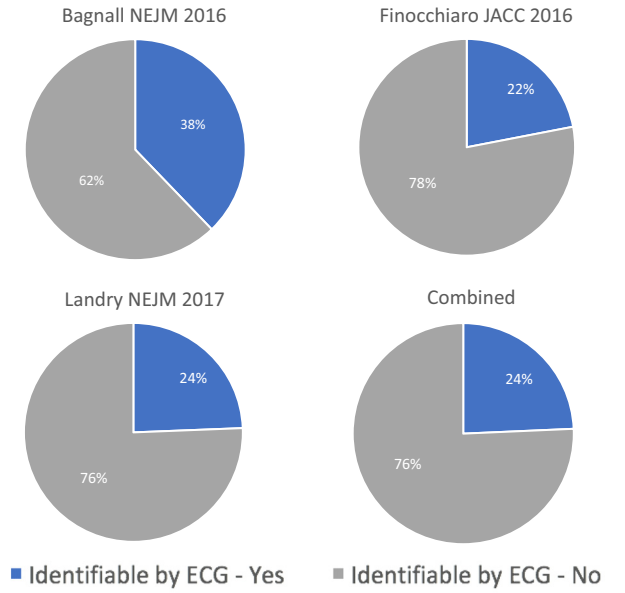

Figure 3. The expected percent of cases of sports-related SCD identifiable by ECG based on cause of death and the ECG's ability to detect those conditions. ECG, electrocardiogram.

Table 3. Number of potential deaths on a per disease basis and number needed to screen to identify one SCD per year

Condition	Prevalence of disease	No. with disease per million screened	Percent mortality per year	No. of deaths per million	No. of deaths per million during exercise	No. identified who are expected to survive	No. needed to screen to identify 1 fatality per year*
HCM	1/500	2000	0.2%-0.5%	4-10	2.26-5.65	1993	111,111-277,777
ARVC	1/5000	200	0.5%-0.8%	1-1.6	0.92-1.47	199.5	1,250,000-2,000,000
LQTS	1/2000	500	0.05%-0.2%	0.25-1	0.05-0.2	499.5	1,333,333-5,333,333
WPW	1/2000	500	0.014%-0.125%	0.07-0.625	0.01-0.1	499.5	1,600,000-14,285,714
Total		3200		5.32-13.22	3.23-7.42	3191.5	

ARVC, arrhythmogenic right ventricular cardiomyopathy; HCM, hypertrophic cardiomyopathy; LQTS, long QT syndrome; SCD, sudden cardiac death; WPW, Wolff–Parkinson–White.

*Sensitivities for the ECG to detect HCM, ARVC, LQTS, and WPW used were 90%, 50%, 75%, and 100%, respectively.

risk of death from ARVC, HCM, LQTS, and WPW per 1 million athletes annually is 5.32 to 13.23 per million. The risk of death during sport is lower (3.24 to 7.42 per million) (Table 3). It is foreseeable that the 2000 athletes with HCM and 200 athletes with ARVC would be disqualified/restricted from sport.[56] The 500 athletes with WPW and LQTS may be permitted to play depending on treatment and risk stratification.[57] Overall, of the 2200 athletes who would be restricted because of the identification of HCM and ARVC, 99.4% of them would not experience SCD. The PPV of the ECG to predict SCD is very low (0.0016-0.0041). The number needed to screen to prevent a single death in a given year (assuming sport restriction or treatment is 100% effective) is the following: HCM – 100,000 to 250,000; ARVC – 625,000 to 1,000,000; LQTS – 1,000,000 to 4,000,000; and WPW – 1,600,000 to 14,200,000. The aforementioned figures are assuming that the ECG would detect 100% of the cases of HCM, ARVC, LQTS, and WPW. Assuming lower real-world sensitivities, the number needed to screen invariably increases (Table 3).

Limitations

The analyses are limited to examining the impact a preparticipation screening ECG would have on reducing sports-related SCD. Young athletes are more likely to experience SCD during periods of rest, sleep, or light activity, with only 15% experiencing SCD during or immediately after exercise.[20] However, it should be recognized the instantaneous risk of sudden death is highest during and immediately after exercise, when normalized for time spent exercising; athletes are only spending a small fraction of the day engaging in exercise vs leisure activity or sleep. There is no expectation that deaths occurring at rest or during sleep could be prevented by sport restriction.[20] The autopsy series used in this analysis to estimate the prevalence of different cardiac conditions causing SCD originate from jurisdictions where mandatory ECG-inclusive screening does not occur. However, there may be some athletes who underwent screening and were subsequently restricted from sport or underwent treatment to reduce their risk of SCD. Additionally, some of the at-risk athletes may have been identified through case finding (symptoms, abnormal physical examination, family history, or nonscreening ECG) and may have been treated or restricted from sport, potentially transitioning from destined to experience SCA/D to possessing a condition associated with SCA but is now expected to live. The analysis was largely restricted to SCD and not SCA; thus, it is possible that in contemporary autopsy series there is less death from ECG-detectable diseases because of improved automated external defibrillator access and use. This exploratory approach is based on previously published studies, and thus limited by the quality of the existing data. The sensitivities of the ECG to detect the specific conditions used were optimal and favoured the ECG to provide a best-case scenario for ECG detection of conditions associated with SCA/D. It is foreseeable that the real-world sensitivity of the ECG would be considerably less in unselected screening populations and outside of centers of excellence where the ECG sensitivities have been reported.

Conclusion

The ECG is the most effective screening tool at identifying disease associated with SCA/D in young athletes. However, it is important not to blur disease identification with SCA/D prevention. The majority (~75%) of sports-related SCD are caused by conditions that are not readily or poorly identified by ECG. A positive screening ECG has a low PPV to predict true disease. More important, the PPV of the ECG to predict sports-related SCD is extremely low (0.0016-0.0041). The majority of those diagnosed with conditions associated with SCD will never experience sports-related SCD, highlighting the need for improved risk stratification of the individual conditions.

The intent of this analysis is not to suggest that the absolute small number of lives that could be saved with ECG-inclusive cardiovascular screening are inconsequential, nor to imply that the efforts at reducing SCD in athletes are not worthy pursuits, but to critically examine the mass cardiovascular screening ECG's potential ability to reduce sports-related SCD. Cardiovascular screening will never be able to detect all athletes at risk for SCD, irrespective of the screening strategy used. Automated external defibrillators and emergency action plans are proven tools to reduce SCD. As strongly recommended in the "Canadian Cardiovascular Society/Canadian Heart Rhythm Society Joint Position Statement on the Cardiovascular Screening of Competitive Athletes," automated external defibrillator access and emergency action plans are the foundation of ensuring the enhanced safety of our athletes.[5]

Finally, the position statement describes a tiered approach, meaning that once this foundational component is in place, an institution may add additional components of a screening program. If there is a network of experts established to follow up on testing and screening, and to use shared decision making, then it is reasonable to consider screening maneuvers such as history-taking and a physical examination. Adding ECG to the screening process can be considered in this

context only after such supports are in place. Recently, Queen's University tested a novel workflow modification to translate the Canadian Cardiovascular Society Position Statement recommendations into practice.[58] In addition to workflow innovation, it is reasonable to expect that further technologic advances (eg, incorporation of artificial intelligence algorithms, big data methods, accuracy of mobile technology) may alter the calculus toward consideration of ECG as part of screening in the future.

Disclosures

The authors have no conflicts of interest to disclose.

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Supplementary Material

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