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EXPERT OPINION

ECG screening to prevent sudden cardiac death on the sports field: Is there now evidence supporting such practice?

Roy J. Shephard¹

Abstract

Objectives: Occasional incidents of sudden death on the sports field have provoked conflicting views on risk reduction through pre-participation screening. Some sports physicians call simply for a thorough clinical examination, but others insist that this must be coupled with a resting ECG examination. Debate has been particularly vigorous in the past ten years; the present article briefly recapitulates earlier arguments and seeks an appropriate, evidence-based current recommendation. *Methods:* Ovid/Medline, PubMed, Google Scholar and personal files were searched for articles related to ECG screening and sudden, exercise-related cardiac death, with particular reference to publications appearing in the past 10 years. *Results:* The introduction of mandatory ECG screening in Italy in 1982 was justified after the fact by a drop in sudden deaths from an unusually high level in the year before the law was enacted to a level typical of North American during the subsequent decade. The criteria used in screening were not athlete-specific, and false positives excluded many potential competitors from play. Moreover, compulsory screening that began in Israel in 1979 had no effect upon the incidence of sudden death. Attempts to develop athlete-specific ECG norms have developed at least 4 options, all rated against clinical judgments rather than their success in identifying those later succumbing to sudden, exercise-related death. The low incidence of such events militates against the setting of criteria that will not have an excessive false positive rate; indeed, some recent authors query whether sudden death is indeed more common in athletes than in the sedentary population. *Conclusions:* Randomized trials examining the consequences of ECG screening and subsequent restriction of physical activity are needed, and the merits of this approach must be compared with a stronger emphasis upon secondary prevention and emergency preparedness. But at present ECG screening still lacks the sensitivity and specificity to be an effective tool in reducing the risk of SERCD. **Health & Fitness Journal of Canada 2015;8(3):14-22.**

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From ¹Faculty of Kinesiology & Physical Education, University of Toronto, Toronto, ON.

E-mail: royjshep@shaw.ca

Introduction

A sudden exercise-related cardiac death (SERCD) is a tragic event that casts a long shadow not only over those immediately affected, but also over all who are seeking to encourage a greater involvement of the population in physically active pursuits. Some authors have suggested that is also a disturbingly common occurrence. One recent analysis of NCAA athletes in the United States found that SERCD was the commonest medical cause of death among this population, accounting for a greater mortality than suicide and homicide combined (Harmon et al., 2015). SERCD was particularly prevalent among basketball players, causing the death of 1 in 9,000 participants; moreover, other basketball enthusiasts were living only because they had undergone early and effective cardiac resuscitation. Even at the high-school level, one report found male athletes had a relative risk of SERCD 4.95 times greater than that of non-athletes (Torsdal et al., 2014), although the risk was not increased for female competitors.

Could the risk of such incidents be reduced by a more thorough pre-participation screening of athletes? In particular, would the recording of a resting ECG add to the effectiveness of such screening by identifying individuals with dangerous arrhythmogenic and structural cardiac abnormalities (Price et al., 2014)? The value of the resting ECG as a means of reducing the incidence of SERCD has long been a matter of controversy (Chaitman, 2007; Myerburg and Vetter, 2007; Shephard, 2005, 2008), with Italy and Israel now making such screening a mandatory component of pre-participation examination, and at least one U.S. report suggesting that preliminary ECG screening is feasible even for high-school athletes (Marek et al., 2011).

We will recapitulate here the traditional positions of North American and European sports cardiologists regarding such initiatives, and will then examine whether a flurry of recent papers warrants a change in recommended policies for the screening of Canadian competitors.

Traditional approaches to pre-participation screening of young athletes

The traditional view of many sports physicians in North America has been that while pre-participation screening should include a thorough clinical history and physical examination, universal ECG screening was unwarranted (Maron, Thompson, Ackerman et al., 2007; Shephard, 2008), and had no solid objective evidence base. In terms of identifying those vulnerable to SERCD, the sensitivity and specificity of the ECG data were demonstrably relatively poor. There was an excessive proportion of

false positive diagnoses, sometimes as high as 40%, and this caused much anxiety for the athletes concerned, often leading to massive costs for additional investigations such as echocardiography and/or a needless prohibition of sport participation. Moreover, National statistics provided no evidence that the clinical screening of athletes without recourse to a resting ECG led to any higher incidence of sudden death than that observed in European countries such as Italy, where annual ECG screening of athletes is now required by law (Shephard, 2008, 2011).

For their part, Italian investigators pointed to 3 pieces of evidence, gathered after rather than before enactment of the mandatory screening policy that apparently supported the need for a universal ECG screening of athletes. Firstly, they claimed that in the Veneto region of Italy, sudden cardiovascular deaths among athletes dropped from 3.6/100,000 in 1979-1980 to 0.4/100,000 in 2003-2004, and they linked this observation to the introduction of mandatory ECG screening for athletes in the year 1982 (Corrado et al., 2006). However, the total number of deaths involved in this comparison was very small (4.7/year in 1979-1981, and 2.6/year from 1982 to 1992). Critics further noted that Italian incidents were not necessarily exercise-related, and that there was no comparison of screened versus non-screened athletes. Rather, the effect of screening upon the incidence of fatal events was imputed from a comparison of unusually high rates in 1979-1980 (3.5-4.0 per 100,000) with subsequent findings for the same population, which were similar to those seen in North America (Maron et al., 2009) and in Denmark (Holst et al., 2010)

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where ECG screening of athletes was not a routine practice. Furthermore, in Israel, where compulsory ECG screening was introduced in 1979, a comparison of sudden deaths among competitive athletes found rates of 2.54/100,000 athlete-years for the ten years before and 2.66/100,000 for the 10 years following enactment of screening legislation (Steinvil et al., 2011); the authors of this report noted that if they had focused on a shorter time interval than 10 years, as in the Italian report, they might also have reached the conclusion that screening was beneficial.

A second plank in the Italian reasoning was a subsequent U.S. study that compared clinical examination vs. clinical plus ECG evaluation in a sample of 510 athletes (Baggish et al., 2010). This report claimed that inclusion of a resting ECG increased screening sensitivity from 45.5% to 90.9% and increased the negative predictive value from 98.7% to 99.8%. In fact, 11 individuals were said to have "dangerous" abnormalities after ECG testing, as against only five athletes that were identified by history and physical examination alone. However, the ECG records were analyzed using the unsatisfactory older European College of Cardiology standards of normality, based on healthy members of the general population rather than on the ECG profile of highly-trained athletes, and the "gold standard" adopted to compare the two diagnostic approaches was not the subsequent incidence of SERCD, but rather a comparison of findings with clinicians' reports suggestive of cardiac abnormalities which had been seen during "limited" echocardiographic imaging. It seems inherently improbable and difficult to accept that 11 of 510

unselected college athletes were at imminent risk of SERCD.

The third piece of evidence was a cost-effectiveness analysis (Wheeler et al., 2010). This analysis claimed that adding an ECG to the screening process saved 2.1 life-years for every 1,000 athletes that were screened, at a cost of U.S. \$42,000 per life-year saved. If the calculation were correct, health economists would accept this as a reasonable use of medical resources. Nevertheless, the estimates of benefit were based simply on the apparent decrease of sudden deaths in Italy following the introduction of mandatory screening, a finding negated by Israeli investigations. Moreover, the costs of such screening were based on 2004 American figures for a single ECG evaluation, as drawn from the U.S. National Center for Health Statistics, although the Italian experience is based upon an annual screening of athletes throughout their competitive careers. A further important fallacy in the cost-effectiveness analysis is that no allowance was made for the loss of life-years associated with advocacy of a sedentary lifestyle; this expense would be incurred not only by true positive cases, but also by the 40% of athletes who were tested and received a false-positive diagnosis.

Having reviewed available evidence, I previously concluded (Shephard, 2011) that even if the apparently weak claims of a reduction in sudden cardiac deaths, diagnostic efficacy and an acceptable cost-benefit ratio were to be substantiated by further research, the fundamental barriers to effective screening as set out in Bayes' theorem (Andermann et al., 2008) were not addressed. The disease prevalence was extremely low, and the ECG evaluation lacked an appropriate level of sensitivity

and specificity to detect the small number of athletes who were really vulnerable.

Does recent research require a reconsideration of traditional views?

Debate on the need for the ECG screening of athletes continues, raising the question whether recent research requires a change of traditional views (Drezner, 2015). New developments have included a detailed meta-analysis comparing the merits of clinical vs. clinical plus ECG testing, the development of athlete-specific criteria for analysis of the resting ECG, and further evidence on the incidence of SERCD and its pathology.

Recent authors have suggested that a clinical history and a physical examination alone have a poor sensitivity and a high false-positive rate when seeking to identify athletes at risk of sudden, exercise-induced cardiac death (Fudge et al., 2013). The gold standard for the evaluation of screening has remained a clinical judgment concerning reported abnormalities rather than the actual occurrence of SERCD. Harmon et al., (2015) carried out a meta-analysis based upon 15 articles and studies of 47,137 athletes. Unfortunately, 9 of the 15 articles that were included in this analysis used dated ECG criteria that were not athlete-specific. The analysis calculated an average sensitivity and specificity of 20%/94% for case histories, and of 9%/97% for physical examination, compared with 94%/93% for ECGs. The proportion of false positive findings ranged widely for both clinical history (1-31%) and ECG analysis (1-19%), but the main objection to both clinical history and physical examination was the low sensitivity of the examination (detection of anomalies 7-44% and 3-24% respectively). Potentially lethal ECG

findings were noted in as many as 0.3% of the total sample, including the Wolf-Parkinson-White syndrome (67 cases, 42% of anomalies), long QT syndrome (18, 11%), hypertrophic cardiomyopathy (18, 11%), dilated cardiomyopathy (11, 7%), myocardial ischaemia (9, 6%), and arrhythmogenic right ventricular cardiomyopathy (4, 3%).

The development of athlete-specific norms for ECG parameters (Corrado et al., 2009) has been suggested as a potential game-changer, offering sports cardiologists the hope of distinguishing the effects of physiological cardiac hypertrophy from the abnormal signals associated with hypertrophic cardiomyopathy, suggested by some investigators as one of the common causes of sudden cardiac death. The European Society of Cardiology (ESC) convened an international panel of experts who published new recommendations for interpretation of the resting ECG in athletes in 2005; further revisions to these norms were made in 2009. Pelliccia et al., (2000) had originally screened 1,005 high-performance athletes, concluding that as many as 40% presented dangerous ECG abnormalities meriting exclusion from sport. However, they used the revised, athletic-specific norms of 2009 to reanalyze the same tracings (Corrado et al., 2009), and found that the proportion of ECGs classed as abnormal was reduced from 40% to 11%. Uberoi et al. (2011) likewise initially found 40% of abnormal records in U.S. athletes, with at least 10% regarded as indications for further laboratory evaluation, but using revised Seattle norms of 2013 (Drezner et al., 2013), only 4% of ECGs were regarded as sufficiently abnormal to require further testing. The changes of ECG interpretation

introduced by U.S. investigators in 2013 (Drezner et al., 2013) altered the cut-off value for a long QT segment, and excluded criteria of right atrial enlargement, leaving T-wave inversion as one of the primary indicators of abnormality. Applying the Seattle criteria to a sample of 330 competitive rowers, Wasfy et al. (2015) reduced the reported proportion of abnormalities from the 47% indicated by the ESC criteria to just 4%. Likewise, Pickham et al., (2014) noted that the percentages of abnormalities reported in a sample of 1417 athletes reported according to ESC and Seattle criteria were 26% and 6% respectively, and a study of the youth division of 2 soccer clubs found ECG abnormalities dropping to just 3% with application of the Seattle criteria (Bessem et al., 2015). Exeter and colleagues (2015) estimated that the proportion of false positive diagnoses could be reduced by a further 36% if physicians were provided with standard diagnostic criteria, rather than relying upon impressions and personal judgment. Plainly, the revisions of diagnostic criteria introduced over the past several years have greatly reduced the proportion of positive ECG diagnoses; however, it has yet to be shown by prolonged studies of mortality trends whether the new criteria are the most appropriate in identifying individuals who are indeed at a high risk of SERCD (Zorzi et al., 2015).

A further important issue is the incidence of SERCD in athletes, and whether this is higher than in the general population. A key argument for more extensive exercise clearance than approaches such as the ePARmed-X+ (www.eparmedx.com) and/or clinical examination has been the supposed high risks of elite sport. Italian investigators suggested an annual rate of 2.3/100,000

sudden cardiac deaths in athletes, as compared with 0.9/100,000 in the general population (Corrado et al., 2003). However, other investigators have argued that the majority of sudden cardiac deaths occur in non-athletes, and that the incidence of such deaths in athletes is so low that even if effective screening procedures could be developed, these would have little practical value. A Danish study suggested that the annual incidence of sports-related sudden cardiac death in those aged 12-35 years was 1.2/100,000, and that this was less than the incidence of sudden cardiac death in the general population; moreover, a half of those affected in the Danish sample had warning symptoms (Holst et al., 2010). A second analysis of the Danish population examined all deaths for those aged 12-35 and 36-49 years during the period 2007-2009; the incidence of SERCD for the 2 age groups was even lower, 0.43 and 2.95/100,000 per year in non-competitive athletes, and 0.47 and 6.64/100,000 per year in competitive athletes (Risgaard et al., 2014). Danish figures for sudden cardiac death in the general population from the same 2 age groups were substantially higher (3.2 and 21.7/100,000 per year), implying on grounds of moral equity that if universal screening were to be implemented, it should be applied not only to competitive athletes, but also to non-competitive athletes and to the general population (Maron et al., 2015). An 11-year analysis of NCAA statistics (Harmon et al., 2015) found 79 incidents of sudden cardiac death in 4,242,519 athlete-years, or 1.86 per 100,000 competitors per year. Figures from a 10-year registry of exercise-related cardiac deaths in U.S. college athletes found a somewhat lower incidence of 1.2/100,000 (Maron et al.

2014). Such figures are in reasonable agreement with the Danish data (Holst et al., 2010), although for some unexplained reason the rate for NCAA first-division male basketball players (19.2/100,000) remains anomalously high.

A recent analysis of 36 NCAA autopsies concluded that the majority of cases of SERCD had no obvious pathology at post-mortem (Harmon et al., 2014); previous views that hypertrophic cardiomyopathy was the likely cause of SERCD reflected an inadequate standardization of autopsy procedures. Autopsy reports from the Danish study, likewise, suggested that only a minority of cases of SERCD had even the potential to be detected by combined clinical and resting ECG examinations (Risgaard et al., 2014). Another report underlined that ECG "abnormalities," whether training-related or not, were commonly non-pathologic (Chandra et al., 2014).

Practical conclusions

Although there has been much research on the pre-participation evaluation of athletes during recent years, strong new objective evidence favouring mandatory ECG screening has yet to emerge. SERCD is a rare occurrence, and there is little evidence that victims have been identified by any type of pre-participation screening. Rather, a careful clinical examination meets the demands of both current epidemiology and defensive medical practice (Paterick et al., 2012).

Attempts to introduce athlete-specific schemes for ECG interpretation are welcome, but the recently revised standards have undergone at least 4 revisions over a period of 8 years, with disturbingly large differences in the number of records classified as

pathological according to the protocol that was used (Zorzi et al., 2015). Further, it remains to be demonstrated by long-term follow-up which if any of these schemes has value in detecting the person at risk of SERCD. There remains scope for well-standardized autopsies of those dying during exercise, but existing reports are not encouraging; most incidents have no pathology that could yield an abnormal ECG.

National registries of cardiac deaths that occur during exercise will help future understanding of SERCD. Randomized controlled trials are needed to examine both the positive and the negative consequences of ECG screening and subsequent restriction of physical activity in athletes, with particular attention directed to the adverse effects of prohibiting sport participation in young and symptomless adults (Link and Estes, 2012). There is also a need to compare the relative contributions to community health of screening versus an emphasis upon secondary prevention, with the development of emergency preparedness and effective programmes for cardiac resuscitation (Estes and Link, 2012; Maron et al., 2014).

The problem underlined by Bayes theorem remains for those who advocate ECG screening. Sports cardiologists are searching for a condition with a very low prevalence (Roberts et al., 2015). Possibly, success would be greater if ECG evaluation were to be narrowed to individuals who are symptomatic or have a family history of sudden cardiac death (Chandra et al., 2014), but at present any method of ECG interpretation seems unlikely to achieve the sensitivity and specificity needed to reduce the risk of SERCD, and there is no solid evidence

base for the requirement of universal ECG screening.

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Author's qualifications

The author's qualifications are as follows: Roy J. Shephard, C.M.; Ph.D., M.B.B.S., M.D. [Lond.], D.P.E., LL.D., D.Sc., FACSM, FFIMS.

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