Screening for Sudden Cardiac Death in Children: Useful Tool or Wishful Thinking?

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The potential for screening young individuals for increased risk of sudden cardiac death has been actively debated within the medical community, as well as in the public. Different views from both sides of the Atlantic on the feasibility and rationality of such an approach are enriching the debate. Data from a Japanese nationwide electrocardiographic screening program on school children provided further valuable insights into this topic. In the following article, evidence on the utility of mass screening, with the inclusion of electrocardiography, is critically discussed.

Keywords: sudden cardiac death, children, screening, electrocardiogram

Introduction

Sudden cardiac death (SCD) in a healthy young individual is a highly tragic and emotional event. Especially when happening in a social environment, like during a competition or school sport, broad publicity is highly likely to happen. Public reporting may lead to the impression of a high incidence of SCD in the young and often triggers a debate on the possibility of preventing such tragic cause of death. In particular, those involved in the organization of competitive sport activities are highly motivated to require screening programs that would eliminate this risk.

Epidemiology

SCD in the young is a rare event with a low epidemiologic impact. A nationwide study performed in Denmark on patients 1–35 years of age found an annual incidence rate of 2.8 per 100,000 person-years, if the non-autopsied cases were included, and 1.9 per 100,000 person-years, if only the autopsied SCD cases were included. Most cases of sudden death occurred during sleep (41%) or normal daily activities (41%) and only 16% occurred during moderate and vigorous exercise. Maron et al. pointed out that among high school and college students who had SCD, only 28% were competitive athletes and the remaining 72% were non-athletes. Such data have posed questions on the strategy of focusing only on pre-participation screening in athletes. The incidence of out-of-hospital cardiac arrest in children was highest in infants (72.71 per 100,000), with sudden infant death syndrome as the most common cause, and was much lower in children (3.73 per 100,000) and adolescents (6.37 per 100,000). Therefore, strategies that focus on infants may have a much bigger yield than those applied for older children. The frequency of death from various causes was compared among individuals <25 years of age by Maron et al. Motor vehicular accidents (11,015 per year), homicides (5,717 per year), and suicides (4,189 per year) far outnumbered the cases of death from all causes in athletes (120 per year) and death detectable by electrocardiographic (ECG) screening in National Collegiate Athletic Association athletes (2 per year). These results further questioned the epidemio-
logic impact of SCD that is specifically associated with competitive sports.

**Screening Strategies**

Cardiovascular screening to detect conditions that predispose to SCD in the young includes an accepted, yet unproven, standard consisting of history and physical examination. In the United States, this strategy remains to be a mainstream during pre-participation screening at the least. The other strategies that were suggested and partially evaluated include the 12-lead ECG, echocardiography, and, potentially, genetics. In Europe, based on a single Italian study, electrocardiography has been increasingly used, specifically in pre-participation evaluation, and is sometimes included in the guidelines imposed by national regulators. The Seattle criteria on electrocardiography to specifically detect pathologies in persons aged 14–35 years who are involved in competitive sports have been published and revised several times. Although with improvement over time, the degree of disagreement among over-reading physicians has been significant and reached up to one third of the tracings if both cardiologists and sports physicians were combined in the evaluation group. Pediatricians and pediatric electrophysiologists did not do better on the correct ECG interpretation of different pathologic conditions, which ranged between 70 and 90%. False-positive results triggered them to prescribe a number of unnecessary diagnostic tests and false-negative results might have led to missed tests. The data derived from these studies casted doubt on the utility of the 12-lead ECG as a universal screening tool with acceptable accuracy for detecting the risk for a very rare condition.

**Results from Larger Screening Studies**

The widely cited Italian study was based on history, physical examination, and resting ECG; derived its data on SCD from a prospective registry; and revealed a significant decrease in the incidence of SCD in athletes after including ECG screening. The study was criticized for its short pre-screening period, which may have missed seasonal variations and the associated immortality bias from an accidental peak in the SCD incidence. Other studies could not show similar results. Specifically, the Israel Sport Law study did not reveal any impact of screening by history, physical examination, and resting and exercise ECG on SCD incidence. The Italian study included 42,386 subjects and generated a positive screening result in 9%, of which 2% had cardiovascular disease and 0.2% had conditions that were potentially lethal to preclude participation in sports. Therefore, in terms of the screening objective, 8.8% had a false-positive result, and the implication was additional costs for evaluation. Other authors have shown that false positivity may be decreased to 2.5% by refinements in the ECG criteria and by training.

**General Theory Behind Screening**

The United States National Heart, Lung and Blood Institute working group published in 2011 a Report on Screening for SCD in the Young. The authors have summarized the following general prerequisites for a successful screening program for a given disease condition:

1. The number of persons at risk is epidemiologically relevant;
2. An appropriate screening test is available and does not carry significant adverse effects;
3. Early detection of a target condition leads to appropriate intervention;
4. Treatment is available, effective, and has an acceptable cost-benefit ratio in term of adverse effects;
5. Disease treatment is associated with reduction of morbidity and/or mortality;
6. Better results are achieved with early disease detection through screening than with a later establishment of a diagnosis during clinical disease manifestation; and, in general,
7. The screening program reduces the morbidity/mortality of the target condition.

The authors stated that none of the prerequisites has been unequivocally proven for screening for SCD in the young. Should the effect of screening be evaluated by a prospective randomized study, the number of individuals to include would be nearly 8 million, assuming an 80% chance of detecting a change in the end point.

**Cost of Screening**

Several studies calculated the cost of screening according to the United States reimbursement conditions. In the report by Leslie et al., the expenses of screening before sports participation at 14 years of age depended on the relative risk of the condition (3.8–1.0 per 100,000 person-years) and ranged between USD 67,495 and
USD 574,711 per life-year saved. The generally accepted societal threshold in the United States was set at USD 50,000 to USD 100,000 per life-year.

Recommendations

Based on available data, a scientific statement by the American Heart Association and the American College of Cardiology, endorsed by the Pediatric and Congenital Electrophysiology Society and the American College of Sports Medicine, on the Assessment of the 12-Lead Electrocardiogram as a Screening Test for Detection of Cardiovascular Disease in Healthy General Populations of Young People (12–25 Years of Age)\textsuperscript{15} was formulated and included the following:

1. Mandatory and universal mass screening with 12-lead ECG of large general populations of young healthy individuals aged 12–25 years to identify genetic, congenital, and other cardiovascular abnormalities is not recommended for athletes and non-athletes alike (Class III, no evidence of benefit; Level of Evidence C).

2. Screening with 12-lead ECG or echocardiogram in association with comprehensive history taking and physical examination to identify or raise a suspicion for genetic, congenital, and other cardiovascular abnormalities may be considered for relatively small cohorts of young healthy individuals aged 12–25 years (e.g., in high schools, colleges/universities, or local communities) and is not necessarily limited to athletes, provided that close physician involvement and sufficient quality control can be achieved. If undertaken, such initiatives should recognize the known and anticipated limitations of the 12-lead ECG as a population screening test, including the expected frequency of false-positive and false-negative test results, as well as the cost required to support these initiatives over time (Class IIb; Level of Evidence C).

The recently published European position paper from the EHRA and the EACPR, which are branches of the ESC, on pre-participation cardiovascular evaluation of athletic participants to prevent sudden death\textsuperscript{16} stated that

1. The protocol of pre-participation evaluation (PPE), including clinical history, physical examination, and 12-lead ECG, was demonstrated to have superior diagnostic capability than clinical history and physical examination alone. There is compelling scientific evidence that the 12-lead ECG substantially improves the diagnostic power of PPE, mostly due the capability to identify potentially arrhythmogenic conditions, such as cardiomyopathies and channelopathies.

2. Available data suggested that routine echocardiography or other imaging modalities did not add substantial diagnostic power to the PPE as a mass screening technique and did not appear to be cost-effective. Therefore, at the moment, the ECG-based PPE is the most effective protocol (i.e., best clinical practice) to evaluate athletes, although several limitations should be acknowledged.

3. Relevant to the diagnostic capability of the ECG screening protocol is the issue of false-positive ECGs and the challenge of appropriate interpretation of the ECG in trained athletes. The updated recommendations for interpretation of an athlete’s ECG based on the Seattle criteria represent a useful document.

4. This panel believes that PPE should be considered and advised for individuals performing regular and intense exercise after proper information on both its benefits and limitations. In addition, sport organizations, such as the international Olympic committee, as well as national and international federations, share the responsibility to properly inform elite and professional athletes on the benefits and limitations of the PPE and to advise PPE for professional athletes on the basis of perceived responsibility and public scrutiny.

5. Suggestions on global national PPE programs go far beyond the scope of this document.

Summary

Available studies did not unequivocally support mass ECG screening to decrease the rate of SCD in the young for the following reasons:

1. Existing variability in ECG interpretation;
2. The burden of false-positive findings;
3. Psychological and financial consequences;
4. High cost per one life-year saved; and
5. Lack of studies confirming its utility.

The other strategies that may be more effective and cost efficient include:

1. Family screening in probands with SCD or detected malignant arrhythmias;
2. Rational placement and availability of automatic external defibrillators; and
3. Screening of specific populations at highest risk (e.g., children < 1 year of age).

Future directions include:

1. Identification of the goals of screening, such as detection of those with silent disease vs. those who will die;
2. Refinement of the ECG criteria with optimal trade-off between sensitivity and specificity;
3. Training on the interpretation of screening ECGs and development of automated ECG analysis;
4. Decision on screening of athletes or the entire population;
5. Honest communication of the possibility of false-positive results before screening;
6. Assessment of compliance with screening; and
7. Evaluation of the harms of screening, including cost, exclusion from participation in the sports activities, and psychological issues.

Well-controlled studies on defined populations or areas, such as the ECG school screening program in Japan, will provide invaluable data to establish rational screening strategies in the future.

Conflict of Interest

The authors have no conflicts of interest to declare.

References

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