ECG Screening for Sudden Cardiac Death in Children and Adolescents

Is it Money Well Spent? Is There an Optimal Age for Screening?

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Sudden cardiac death (SCD) in otherwise healthy children is tragic. Increasing attention has been paid to preventing these untimely events, particularly with regard to cardiac causes, because these are the most common causes, though not the exclusive ones. Interest has centered on sports participation, as about 25% of such events occur at this time, and the use of attention deficit hyperactivity disorder (ADHD) medication, which may or may not precipitate SCD in susceptible individuals. A recent National Heart, Lung and Blood Institute panel evaluated the evidence base for addressing the prevention of SCD and found too many gaps in evidence to formulate general recommendations for SCD prevention in the young. Particular concerns surround: lack of knowledge of the true incidence of SCD; absence of a pilot ECG screening program to test the effectiveness of various screening methodologies; identification of the most effective screening strategy (the most useful screening method, and selective screening in high-risk individuals versus universal screening at a specific age); and limited knowledge of the impact of a screening program on the both the quality of life and clinical outcomes of the asymptomatic individuals and families screened. The report states “before a significant public health investment is made in large scale ECG screening, it would be ideal to empirically demonstrate a link between screening and improved health outcomes.”

To fill a critical gap in the evidence, Leslie and colleagues have performed a detailed analysis of the cost and benefits of combined history, physical and ECG screening for the more common causes of SCD in children age 8, who are initiating stimulant therapy for ADHD, and adolescents age 14, who are participating in high school sports. Although their analyses and algorithms are necessarily complex, they have attempted to focus the problem by limiting screening to the two time points and populations described above, and prevention of SCD from 3 conditions: hypertrophic cardiomyopathy (HCM), Wolff-Parkinson-White syndrome, and the long QT syndrome (LQTS). These restrictions were used not only to simplify the analysis and interpretation, but also because they are the most common causes of SCD in childhood. The data available to parameterize the model are much more robust than for other rarer conditions. In contrast to some previous analyses in overlapping populations, the investigators found that the incremental cost-effectiveness of screening was high at between $91,000 (age 14 screening) and $204,000 (age 8 screening) per life-year saved. The estimates were most sensitive to the following parameters: disease prevalence, baseline mortality, and the relative risk of mortality attributable to stimulant medication use and sports participation.

The authors are to be lauded for addressing the many complexities of screening in their model. One strength of the study is the use of ranges of estimates for many of the model parameters. This overcomes the problem of picking a single, potentially incorrect, value and provides a range that can offer guidance in the absence of complete outcomes data. The authors have been reasonably conservative in estimating the parameters for their model. However, they have not included estimates of increased noncardiac causes of mortality in untreated ADHD patients. If included, the true cost of screening might be considerably higher than the estimates that Leslie et al derived. For instance, the results for the ADHD stimulant population are highly dependent on the presumption that mortality is increased by stimulant therapy (relative risk >1.0); however, the literature suggests that this may not be true.

For LQTS, the authors have used a low prevalence rate for LQTS of 7/100,000 as the central parameter for their model in patients 14 years of age, significantly below what may be the best data from Schwartz et al, who estimated a prevalence in neonates at about 1/2500 (40/100,000). The important point here is that the estimate in children 8 and 14 years of age may be appropriately low, because by the age of 8, many, if not most, LQTS patients who will present in childhood have either presented with disease or died as a consequence of it.

Screening for LQTS in Neonates

An alternative age to screen for LQTS is infancy. Based on molecular autopsy data, 10% to 15% of sudden infant death syndrome deaths are attributable to LQTS. The rates of sudden infant death syndrome are carefully tracked by almost all developed countries and vary from about 0.7 to 1.0/1000. The rate of unexplained SCD secondary to LQTS alone in the infant population would thus be about 0.1/1000 (10/100,000), which is between 2 and 12 times the total SCD rate estimates for children 1 to 18 years of age in the United States.
States (0.8–6/100 000),3 about 5 times the rate in National Collegiate Athletic Association (NCAA) athletes (2.3/100 000), and comparable to the highest risk NCAA group of basketball players (8.8/100 000).12 These infant data also suggest that almost as many infants have SCD from LQTS alone each year (about 400) as all school age children from all other causes (500–1000).

The value of ECG screening in the neonatal population has been addressed prospectively as well in 2 different Italian studies.7,13 Taken together, the data from these studies plus the available literature suggest that most of the LQTS cases which lead to sudden infant death syndrome can indeed be identified by ECG screening performed during the neonatal period; however, the best methodology and age (0–2 days versus 14–28 days) for screening remain unclear. Additional questions important for a neonatal ECG screening program are related to effectiveness and cost in preventing SCD during infancy and later in life. A cost-effectiveness analysis using the data from the Italian studies7,13 estimated a relatively low cost per life-year saved at 11 740 Euros (about $16 000) using health care cost estimates from the Italian National Health System.14 Although there are a number of issues in this analysis which have been questioned because of potential cultural and cost differences in the United States compared with Italy and Europe,15 the cost estimate is far below that estimated by Leslie et al,3 and well below the usual cutoff for a screening or therapy to be considered effective.

HCM in Adolescents

HCM in the United States16 and arrhythmogenic right ventricular dysplasia in Italy17 are the most common cardiac findings in adolescents and young adults with SCD. They are rarely a cause of SCD under 12 years of age, and can be identified with ECG screening or clinical findings in these age groups. These observations support the findings of Leslie et al3 that screening at 14 years of age is closer to being considered cost effective. A complicating issue is that the literature suggests that the prevalence of HCM may be as high as 1 in 500,16 and yet the rate of SCD in adolescents from HCM is on the order of 0.3/100 000/yr.16 Thus, for every 600 identified cases of HCM in late adolescence only 1 per year is destined to die from SCD during adolescence. If screening took place at 14 years of age, for every 600 HCM patients identified, a total of 8 will have SCD (1.3%) by 21 years of age (1 per year for 8 years). If case identification is that high, it is critical to determine the financial and personal cost of restricting and treating 77 cases of HCM who will never have an event for every one case that will.

The Health Effects of ADHD Therapy and Sports Participation

A further limitation of the debate relates to the potential health benefits of both ADHD medication and sports participation. The current debate on ADHD medication and potential cardiac complications has not generally accounted for all cause morbidity and mortality related to ADHD in the absence of stimulant medication use. For example, children and adolescents with ADHD are at increased risk for general trauma and being involved in auto accidents, events which are significantly more common than cardiovascular ones, and are known to be substantially reduced with treatment.19–21 Thus, not treating a significant percentage of children who meet indications could lead to significantly increased noncardiac events not only in ADHD patients, but also in the bystanders impacted by the higher rate of serious accidents, perhaps much greater than the lives saved by not prescribing the medication.

A focus on screening sports participants could indirectly limit participation in these activities and deflect from other more prevalent public health issues. Risk of sudden death on the athletic field is a much smaller problem than the current obesity epidemic. A general increase in sports participation or physical activity may have a larger health benefit than the potential rare sudden event related to this participation.22 From a public health standpoint, with a smoking prevalence of 15%, for every 100 000 children screened about 15 000 will become smokers; preventing 10 of these from smoking will add about 70 life-years (http://www.cdc.gov/Features/YouthTobaccoUse). Both tobacco use and obesity are also associated with sudden death in adults.23,24

Other Possible Prevention Strategies

Identification of high risk individuals is an important medical strategy; however, a population-based prevention strategy for sudden death could also be considered. For example, placement of automatic external defibrillators in schools may provide emergency treatment for many affected children and have the added benefit of providing a lifesaving treatment for adults as well. Currently, many more adults are resuscitated in schools with automatic external defibrillators than are children.29 Because many of the conditions under consideration are genetic, cascade screening of families of resuscitated children could also be initiated leading to more efficient case identification.

In summary, Leslie et al1 have filled a critical gap in the evidence for screening to prevent SCD in children and adolescents, particularly by demonstrating the high cost of currently proposed prevention strategies. Preventing a significant portion of SCD in the young might require the following: (1) a neonatal screen for primary arrhythmia conditions like LQTS, as opposed to screening selectively the population who require ADHD medications, and (2) a universal adolescent screen to identify the ECG abnormalities present with structural heart disease, rather than a selective screening of sports participants. Before embarking on such a strategy, further research to fill in evidence gaps identified by the recent National Institutes of Health report is critical.2 We have tried to emphasize the larger context that needs to be considered in approaching this issue, including discussion of the best age to screen, the health benefits of ADHD medication and sports participation, and the potential role of effective treatments at the point of SCD events as alternatives to incurring the high costs of screening.

Disclosures

None.

References


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