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Key Concepts in the Evaluation of Screening Approaches for Heart Disease in Children and Adolescents

A Science Advisory From the American Heart Association

William T. Mahle, MD, FAHA; Craig A. Sable, MD, FAHA; Paul G. Matherne, MD, FAHA; J. William Gaynor, MD; Michael H. Gewitz, MD, FAHA; on behalf of the American Heart Association Congenital Heart Defects Committee of the Council on Cardiovascular Disease in the Young
The aforementioned document provided a clear roadmap to assess and develop enhanced screening strategies. In the interim, however, many communities in the United States continue to explore the role of supplementary screening techniques. These enhanced screening programs are often modeled on previous strategies carried out at the regional or national level in other countries. A seminal study offered some evidence for ECG screening to prevent sudden death in young athletes in the Veneto region of Italy.5,6 This mandatory program is limited to athletes. Thus, it is not clear that communities in the United States would see the same benefit. The postscreen sudden death rate in Veneto region is similar to the sudden death rate in a similar-sized population in Minnesota in whom screening was performed with history and physical examination but without routine ECG acquisition.7 Another national screening protocol was instituted in Israel that included not only ECGs but also exercise stress tests. A recent review of this program suggested that the sudden death rate has not been affected.8 An additional concern is that focusing only on competitive athletes is discriminatory. Children and adolescents often engage in vigorous physical activity outside structured athletic programs. Moreover, sudden cardiac death is not limited to physical exertion.9 Hence, screening programs focused only on athletic participation have too narrow a scope.

Local or Regional Strategies Used in United States for Screening School-Age Children

Currently, there are no standardized strategies in the United States for screening the school-age child, and there are few published studies assessing the performance of pilot screening protocols. A 1997 study from Nevada screened 5615 high school athletes with ECGs at 30 schools. That study reported a sensitivity of 70% for detecting cardiac disease with ECG compared with 6% for history and physical examination alone.10 However, most of the positives from this study were minor rhythm abnormalities with no cases of either cardiomyopathy or anomalous coronary detected. Another study among university students demonstrated enhanced detection of silent cardiac disease with the addition of the ECG, but the false-positive rate reached 17%.11 Vetter and colleagues12 reported that office-based screening of a general pediatric population (aged 5–19 years), which included ECG and echocardiography, was feasible. Previously undetected heart defects were found in 23 of 400 children (5.8%), 10 of which were considered to be serious. The largest study in the United States screened >32 000 high school students; however, comprehensive follow-up data were not available, so false-positive and false-negative rates are not known.13

In addition to the small number of peer-reviewed reports, numerous groups have conducted local screening of student-athletes for heart defects using a combination of ECG and echocardiography. Often, these programs are in response to a recent sudden death in the community or in a family member. The screening programs may be sponsored by local physicians, sometimes in collaboration with vendors or nonprofit organizations. These efforts are often praised by local parent groups and media but generally have not been used to generate data that can be used to support more rigorous screening protocols.

Some for-profit agencies offer reduced-cost echocardiograms or ECGs that are marketed directly to athletic programs or individuals. These entities have used social media and direct advertising to reach target audiences. Not uncommonly, these programs include references to recent sudden death events to promote the need for enhanced screening. It is entirely possible that for-profit entities may prove to provide a flexible cost-effective means to screen the pediatric population at risk for sudden death. However, for the most part, these for-profit agencies have not reported the findings of their screening programs. Therefore, it is difficult to evaluate the efficacy of such initiatives.

Because of these limitations, the 2007 AHA statement on athletic preparticipation did not endorse mandatory screening with ECG or other noninvasive tests.3 This recommendation is sound and remains relevant to the current approach to the school-age child.

Approaches to Screening the Infant or Young Child for Sudden Cardiac Death

Long-QT syndrome or variant channelopathies are cardiac conditions that may be asymptomatic yet lead to sudden death in the very young.14 Accordingly, there has been interest in exploring strategies to identify children with the long-QT syndrome in the general population. Early identification of the long-QT syndrome is particularly attractive because medications, use of automatic implantable defibrillators, and modifications of activities have been associated with significant reduction in risk of sudden death.15,16 Because sudden death events may occur even in infancy, investigators have focused screening strategies in early childhood, especially the neonatal period. A standard 12-lead ECG has been proposed as the most practical screening tool. Many of the data to support this methodology derive from a broad screening program in Italy that focused primarily on reducing the incidence of sudden infant death syndrome.17 Similar screening strategies have been used elsewhere,18 and the concept has been endorsed by a European Cardiology Society task force.19

Despite the promising results from the Italian experience, this strategy has not been widely adopted more than a decade after this approach was first proposed. A number of concerns have been raised about this screening strategy.20 First, interpretation of the neonatal ECG can be challenging, and the overlap of normal variants and the long-QT pattern is significant.21 Even in adults, interpretation of the ECG among observers is varied, and many clinicians, including board-certified cardiologists, may fail to identify critical features of the long-QT syndrome.22 In the United States, most newborn screening strategies are designed to be performed at the time of the delivery hospitalization. Because sensitivity and specificity are very poor for ECG screening in the first few days of life,23 an optimal ECG screening program would require evaluation beyond the first week of life. This would require an extensive screening infrastructure in primary care practices, which may be a considerable challenge in less centralized healthcare systems such as that which exists in the United States. To the best of our knowledge, there are no active clinical ECG-based screening
and to reduce false-positive results.27–29 On the basis of these
upper- and lower-extremity saturations to enhance detection
proposed strategies such as repeated measurements and
into the strengths and weaknesses of this approach and have
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AHA closely monitors the outcomes of local testing screening
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number of additional European studies have provided insights
into the strengths and weaknesses of this approach and have
proposed strategies such as repeated measurements and upper-
and lower-extremity saturations to enhance detection
and to reduce false-positive results.27–29 On the basis of these
studies, there has been ongoing effort and collaborative
discussion among advocacy groups and state and federal
agencies to evaluate and promote pulse oximetry as an enhanced
methodology for screening for critical congenital heart disease in
newborns.30 Recently, the Secretary of Health and Human
Services endorsed the concept of screening newborns for critical
congenital heart disease with pulse oximetry. The AHA formally
supports these recommendations.31 As with any new initiative, it
will be critically important to assess how this screening initiative
performs throughout various healthcare models and across the
population.

Pulse Oximetry for Timely Diagnosis of
Critical Congenital Heart Disease
It is also now well known that late detection or failure to
detect critical congenital heart disease in young infants may
lead to death.24,25 This important topic was addressed in detail
in the 2009 statement entitled “Role of Pulse Oximetry in
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performs throughout various healthcare models and across the
population.

Paradigm for Advancing Cardiovascular
Screening Programs
The Council for Cardiovascular Disease in the Young of the
AHA recognizes the importance of improving the detection of
silent cardiovascular disease in children and the possible incor-
poration of such strategies into routine practice (Table). The
AHA closely monitors the outcomes of local testing screening
strategies and advocates for research to support data collection
and rigorous assessment of these approaches. The following
underlying principles should guide these screening strategies:
1. New screening programs should be based on sound
principles and should not be simply reactive to recent
catastrophic events. A successful screening program
will require extensive planning and will not be able to
eliminate sudden cardiac deaths completely. Estimates of
the prevalence of silent cardiac diseases of interest
are needed to anticipate what benefit might be realized
through enhanced screening.
2. Any broad screening strategy should be widely sup-
ported and available to all children. The AHA does not
support screening strategies that are focused only on
children who have the financial means to pay for such
screening, leaving socioeconomically disadvantaged
youths out of the process. This is especially true
because studies suggest that certain racial groups may
be at a higher risk of sudden death.32
3. Pilot screening programs must track their performance.
At the very least, screening initiatives should record
the proportion of positive screens and what follow-up was
recommended. When possible, the collection of data on
the follow-up of positive screens such as the false-
positive rate and need for additional diagnostic studies
is strongly encouraged.
4. Pediatric cardiovascular specialists need to be included
in strategies that look to identify cardiac disease so that
any enhanced screening strategies are practical in terms
of manpower and integrate well into the current practice
of identifying children thought to be at increased risk
for arrhythmia, ischemia, or sudden death events.
5. Secondary prevention of sudden death with training of
cardiopulmonary resuscitation and deployment of auto-
matic external defibrillators must be emphasized and
supported by local entities such as school boards or state
legislatures.33

Role of Local Government to Fund, Initiate,
and Mandate Changes
Governmental authorities have often been involved in the
development and implementation of population-based health
screening programs. Most evident of these, for example, is
the very successful newborn blood-spot screening program
for heritable metabolic disorders. This program was initiated
decades ago at the state level and is maintained primarily by
state budgetary and regulatory authorities. Typically, as with
the blood-spot program, governmental involvement has been
confined to presymptomatic screening for select inherited and
congenital conditions. These programs consider the screening
process to be a part of an essential public health commitment and
require consumer (patient) education, systematic follow-up to
definitive diagnosis, and reliable linkage to long-term treatment
and management to be inherent to any supported screening
program. In this format, the state governments have been
productive in terms of population-based screening.
On the other hand, expansion of screening programs in
response to new medical knowledge, to new technologies, or
to political pressure from specific illness advocacy groups is
often challenged by state funding constraints and by push-
back from a financially stressed provider community. States
have not always been successful in meeting these particular
challenges. In an attempt to affect these issues for the health
of the population at large, the federal government, through
the Newborn Screening Saves Lives Act of 2008, has recently
become involved by providing funding support and by
helping states improve program performance.
The newborn screening programs (blood-spot, hearing assessment, and others) represent an effective professional community, state government, and federal government trilateral relationship that has addressed controversies about both cost and evidence of efficacy. Nevertheless, the role of government in mandatory resource-consuming programs in which costs may not be shared equally among the beneficiaries remains controversial. Recently affected patients, their families, and supporters have taken a more active role in advocating for screening by directly approaching policymakers and legislators. This wave of advocacy at the level of state legislatures for expansion of screening programs of all types involving a widening range of diseases children and young adults will continue to challenge both the professional community and governmental systems. It is imperative that the success of the trilateral paradigm developed as part of the newborn screening programs be preserved and that hastily conceived, politically expedient programmatic changes not be implemented in the absence of comprehensive, science-based preliminary testing of screening hypotheses and methodologies. The very recent decision to expand the newborn screening program with the addition of pulse oximetry screening for critical congenital heart disease fulfills these criteria and thus has appropriately won endorsement at the federal government level after an extended deliberative and evidence-based process.

Parents and Patients as Advocates

The development of screening techniques depends on new medical technologies or, in some cases, applications of existing tools to address important public health concerns. However, in all cases, advocacy groups, driven in large part by patients and their families, play an important role in advancing new screening strategies. Advocacy groups draw attention to the public health importance of the condition, fund preliminary research, and support legislative initiatives. The AHA has relied on patients and their families to support many key initiatives, including cardiovascular screening programs.

Advocates of cardiac screening in children will no doubt play a critical role in shepherding some of the screening strategies described above from concept to practice. It is important for these groups to reach out to the AHA for support. The AHA can provide extensive data on the public health and economic implications of silent cardiac disease in childhood. The AHA can promote well-structured pilot programs or provide scientific statements to inform policymakers. If there are sufficient data, the AHA may provide an endorsement of broad adoption of screening policies, as was the case in newborn pulse oximetry screening. However, if there is insufficient evidence to support screening programs, the AHA may simply advocate for more resources to study the problem.

One must recognize that recommendations that are appropriate in terms of screening in the US pediatric population may or may not apply in other countries. In some cases, data gathered outside the United States can help guide policy decisions in the United States and vice versa. For example, research in Europe on pulse oximetry screening was invaluable in shaping US recommendations. Conversely, health delivery systems vary considerably among countries. Thus, such endorsement of screening strategies will appropriately differ. The AHA seeks to complement the efforts of organizations such as the European Society of Cardiology vis-à-vis screening programs.

Conclusions

Screening for cardiovascular disease that may lead to sudden death in children is of great importance to public health; assessment of screening methodologies for cardiovascular disease in other pediatric populations is critical to the mission of the AHA and the Council for Cardiovascular Disease in the Young. The AHA will strongly support novel approaches to screening in accordance with the principles outlined above. Funding studies to evaluate these strategies is essential to address this problem effectively. However, before the AHA endorses universal screening programs, assembling sound data and the support of other key stakeholders such as governmental agencies and the healthcare community will be necessary.

Disclosures

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*Modest.
Reviewer Disclosures

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