To Screen of Not to Screen
The Italian/European and American Point of View

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Venice Arrhythmia
Consiglio Room 12:30-14:00
Friday October 16, 2015

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American Reaction To the Italian/European
No Conflicts of Interest
To Screen or Not to Screen
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- Background
- Evidence Based Medicine
- U.S. Screening Strategy
- Knowledge Gaps
- NHLBI Working Group Recommendations
- Economic/Legal/Ethical
- AEDs
- Conclusions
CV screening is widely recommended by professional societies.

In the USA, current AHA recommendations-H &P.

Limitations of the H &P are acknowledged, the AHA cites overwhelming support for the principle of this public health initiative as part of the rationale.

AHA also acknowledges that efficacy of the various athlete screening strategies is not easily resolved in the context of evidence-based medicine.
Cardiac evaluation of athletes before participation is intuitively attractive to identify athletes at risk for SCD

Screening to detect CV disease in athletes supported by the AHA and by the Sports Cardiology Study Group of the ESC

Both guidelines recommend a personal and family history and physical examination, but the European guidelines recommend obtaining routine electrocardiograms (ECGs)

AHA supports individual quality controlled local, community or student related ECG initiatives are supported if they are conducted properly with adequate resources
Incidence of sudden death stratified by athletic or general population and the years of the study population

<table>
<thead>
<tr>
<th>Country</th>
<th>Author</th>
<th>Population</th>
<th>Years</th>
<th>Incidence / 100,000/year</th>
</tr>
</thead>
<tbody>
<tr>
<td>Italy</td>
<td>Corrado</td>
<td>Athletes</td>
<td>1980-1981</td>
<td>3.6</td>
</tr>
<tr>
<td>Italy</td>
<td>Corrado</td>
<td>Athletes</td>
<td>2007-2008</td>
<td>0.40</td>
</tr>
<tr>
<td>US</td>
<td>Maron</td>
<td>Athletes</td>
<td>1985-2006</td>
<td>0.44</td>
</tr>
<tr>
<td>Israel</td>
<td>Steinvil</td>
<td>Athletes</td>
<td>1985-1997</td>
<td>2.54</td>
</tr>
<tr>
<td>Israel</td>
<td>Steinvil</td>
<td>Athletes</td>
<td>1998-2009</td>
<td>2.66</td>
</tr>
<tr>
<td>US</td>
<td>Van Camp</td>
<td>Athletes</td>
<td>1983-1993</td>
<td>0.33</td>
</tr>
<tr>
<td>Denmark</td>
<td>Holst</td>
<td>Athletes</td>
<td>2000-2006</td>
<td>1.21</td>
</tr>
<tr>
<td>Denmark</td>
<td>Holst</td>
<td>All children</td>
<td>2000-2006</td>
<td>3.76</td>
</tr>
<tr>
<td>Japan</td>
<td>Tanaka</td>
<td>All children</td>
<td>1989-1996</td>
<td>1.32</td>
</tr>
<tr>
<td>Canada</td>
<td>Atkins</td>
<td>Children 1-11</td>
<td>2005-2007</td>
<td>3.73</td>
</tr>
</tbody>
</table>

Annual Causes of Death in U.S. Population Age 1-21 (CDC)

79,000,000

(http://webappa.cdc.gov/sasweb/ncipc/leadcaus10.html)
Causes of Death in U.S. Population Age 1-25 (CDC) 
90,000,000

(http://webappa.cdc.gov/sasweb/ncipc/leadcaus10.html)
The 14-Element AHA Recommendations for Pre-participation Cardiovascular Screening of Competitive Athletes

**Medical history & Personal history**
- 1. Chest pain/discomfort/tightness/pressure related to exertion
- 2. Unexplained syncope/near-syncope†
- 3. Excessive and unexplained dyspnea/fatigue or palpitations, associated with exercise
- 4. Prior recognition of a heart murmur
- 5. Elevated systemic blood pressure
- 6. Prior restriction from participation in sports
- 7. Prior testing for the heart, ordered by a physician

**Family history**
- 8. Premature death (sudden and unexpected, or otherwise) before 50 y of age attributable to heart disease in ≥1 relative
- 9. Disability from heart disease in close relative <50 y of age
- 10. Hypertrophic or dilated cardiomyopathy, long-QT syndrome, or other, or clinically significant arrhythmias;

**Physical examination**
- 11. Heart murmur
- 12. Femoral pulses to exclude aortic coarctation
- 13. Physical stigmata of Marfan syndrome
- 14. Brachial artery blood pressure (sitting position)§

Maron et al *Circulation*. 2014;130:1303-1334.)
Italian/European Screening Strategy

young competitive athletes

family and personal history, physical examination, 12-lead ECG

negative findings

eligible for competition

no evidence of cardiovascular disease

further examinations (echo, stress test, 24-h Holter, cardiac MRI, angio/EMB, EPS)

diagnosis of cardiovascular disease

management according to established protocols
Pre-participation athletic screening and athletic restriction in Italy, the United States and Israel

<table>
<thead>
<tr>
<th>Country</th>
<th>Years</th>
<th>Screening</th>
<th>Initial</th>
<th>Examiner</th>
<th>Death</th>
</tr>
</thead>
<tbody>
<tr>
<td>Italy</td>
<td>1981-2008</td>
<td>Mandatory</td>
<td>History, PE, ECG, ETT, Echo</td>
<td>Sports Medicine MD</td>
<td>Decreased</td>
</tr>
<tr>
<td>United States</td>
<td>1985-2006</td>
<td>Recommended</td>
<td>History, PE</td>
<td>MD Non-MD</td>
<td>No decrease</td>
</tr>
<tr>
<td>Israel</td>
<td>1985-2009</td>
<td>Mandatory</td>
<td>History, PE, ECG, ETT, Echo</td>
<td>Certified MD</td>
<td>No decrease</td>
</tr>
</tbody>
</table>
ESC Sports Cardiology Study Group recommend systematic pre-participation screening for young competitive athletes with personal and family history, physical exam, and 12 lead ECG in the Italian mode.

This strategy has not been translated on a national basis to other countries other than Israel.

A recent NIH/NHLBI position paper did not support mass screening of young athletes (<40 year old) with ECGs concluding that insufficient evidence was currently available.

The group recommended pilot screening studies in target populations.

Screening tests in young athletes

Currently in use
Cheap
Nondiagnostic
Poor sensitivity
Poor specificity

Useful for electrical diseases
Suggestive for some CVD
Relatively cheap
Moderate sensitivity
Moderate to high specificity
Low PPV

Useful for structural CVD
Misses electrical disease
Expensive
Poor sensitivity
High specificity

Slide courtesy of: Kaltman J, MD Chief, Heart Development and Structural Diseases Branch National Heart, Lung, and Blood Institute
Kaltman J et al. Screening for Sudden Cardiac Death in the Young: Report From a National Heart, Lung Circulation. 2011;123:1911-1918
U.S. Preventive Services Task Force’s Analytic Framework

Screening

(1) Evidence - screening reduces morbidity and/or mortality?
(2) Disease prevalence?
(3) Sensitivity and specificity of the test?
   Is there significant variation between examiners in how the test is performed?
(4) Does treatment reduce the incidence of the intermediate outcome?
   How do the efficacy and effectiveness of treatments compare in community settings?
(5) Does treatment improve health outcomes for people diagnosed clinically?
   Do people diagnosed by screening to have even better outcomes than those diagnosed clinically?
(6) Is the intermediate outcome reliably associated with reduced morbidity and/or mortality?
(7) Does screening result in adverse effects? Is the test acceptable to patients?
   What are the potential harms, and how often do they occur?
(8) Does treatment result in adverse effects?

Screening for Sudden Cardiac Death in the Young: NIH Study Group. 2011;123:1911-1918
U.S. Screening Gaps in Knowledge

- Precise frequency of SCD in athletes and non-athletes
  Numerator/Denominator
- Pre-participating screening strategies
  Effectiveness, Predictive Accuracy, Cost
- Athletic restriction
  Effectiveness, Predictive Accuracy, Cost
- The ongoing debate related to screening persists because of:
  Knowledge gaps
  Absence of RCTs
2014 Estimated Total U.S. Population: 318,857,056

(Provided by the U.S. Census Bureau through Factfinder.gov)

(http://factfinder.census.gov/faces/tableservices/jsf/pages/productview.xhtml?src=bkmk)
Prevalence of Electrocardiographic Anomalies in Young Individuals—Relevance to Nationwide Cardiac Screening Program

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London, United Kingdom

Objectives
This study sought to investigate the prevalence of potentially abnormal electrocardiographic (ECG) patterns in young individuals to assess the implications for a nationwide screening program for conditions causing sudden cardiac death (SCD).

Background
The Italian experience suggests that pre-participation screening with ECG reduces the incidence of SCD in athletes. However, the majority of SCDs occur in nonathletes. In the United Kingdom, screening for cardiac disorders is confined to symptomatic individuals or those with a family history of inherited cardiac conditions or premature cardiac death.

Methods
Between 2008 and 2012, 7,764 nonathletes ages 14 to 35 years underwent ECG screening. Electrocardiograms were analyzed for group 1 (training-related) and group 2 (potentially pathological) patterns presented in the 2010 European Society of Cardiology position paper, which advocates further evaluation for individuals with group 2 ECG patterns. Results were compared with 4,081 athletes.

Results
Group 1 patterns occurred in 49.1% of nonathletes and 87.4% of athletes (p < 0.001). Group 2 patterns occurred in 21.8% of nonathletes and 33% of athletes (p < 0.001). In nonathletes, QTc interval abnormalities comprised the majority (52%) of group 2 changes, whereas T-wave inversions constituted 11%. Male sex and African/Afro-Caribbean ethnicity demonstrated the strongest association with group 2 ECG patterns.

Conclusions
The study demonstrates that 1 in 5 young people have group 2 ECG patterns. The low incidence of SCD in young people suggests that in most instances such patterns are non-specific. These findings have significant implications on the feasibility and cost-effectiveness of nationwide screening programs for cardiovascular disease in young nonathletes and athletes alike, on the basis of current guidelines. (J Am Coll Cardiol 2014;63:2028–34)
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Prevalence of Electrocardiographic Anomalies in Young Individuals—Relevance to Nationwide Cardiac Screening Program

**Table 1. European Society of Cardiology Classification of Changes of the Athlete's Electrocardiogram**

<table>
<thead>
<tr>
<th>Group 1: Common and Training-Related ECG Changes</th>
<th>Group 2: Uncommon and Training/Unrelated ECG Changes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sinus bradycardia</td>
<td>T-wave inversion</td>
</tr>
<tr>
<td>First-degree AV block</td>
<td>ST-segment depression</td>
</tr>
<tr>
<td>Incomplete RBBB</td>
<td>Pathological Q-waves</td>
</tr>
<tr>
<td>EH</td>
<td>LA enlargement</td>
</tr>
<tr>
<td>Isolated QRS voltage cut-off for LVH</td>
<td>RV enlargement</td>
</tr>
<tr>
<td>ECG</td>
<td>LAD</td>
</tr>
<tr>
<td>Elevator</td>
<td>RVOT</td>
</tr>
<tr>
<td>Ventricular pre-excitation</td>
<td>LBB</td>
</tr>
<tr>
<td>Isolated QRS voltage cut-off for LVH</td>
<td>RBB</td>
</tr>
<tr>
<td>Long-QTC interval (men: &gt;440 ms, women: &gt;400 ms)</td>
<td>Short-QTC interval (men: &lt;300 ms, women: &lt;300 ms)</td>
</tr>
<tr>
<td>Brugada-like EH</td>
<td></td>
</tr>
</tbody>
</table>

**Figure 1. Prevalence of ECG Patterns in Nonathletes and Athletes**

<table>
<thead>
<tr>
<th>Group 1</th>
<th>Group 2</th>
<th>Neither</th>
</tr>
</thead>
<tbody>
<tr>
<td>Group 1</td>
<td>Group 2</td>
<td>Neither</td>
</tr>
<tr>
<td></td>
<td>67.4</td>
<td>42.5</td>
</tr>
</tbody>
</table>

**High prevalence Group 2 ECG changes**

<table>
<thead>
<tr>
<th></th>
<th>Black</th>
<th>Non Black</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Non-athlete</td>
<td>29%</td>
<td>21%</td>
<td>&lt;0.003</td>
</tr>
<tr>
<td>Athlete</td>
<td>58%</td>
<td>21%</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

Chandra J Am Coll Cardiol 2014;63:2028–34
2014 NCAA Population: 479,475

(http://web1.ncaa.org/rgdSearch/exec/saSearch)
### American Reaction To the Italian/European Guidelines

<table>
<thead>
<tr>
<th>Author</th>
<th>Year</th>
<th>Population</th>
<th>Cost/Life Year H&amp;P ($)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fuller</td>
<td>1999</td>
<td>Athletes</td>
<td>84,000</td>
</tr>
<tr>
<td>Quaglini</td>
<td>2006</td>
<td>Children</td>
<td>15000</td>
</tr>
<tr>
<td>Wheeler</td>
<td>2010</td>
<td>Athletes</td>
<td>28,000-17,000</td>
</tr>
<tr>
<td>Leslie</td>
<td>2012</td>
<td>Children</td>
<td>91,000-204,000</td>
</tr>
<tr>
<td>Schoen</td>
<td>2013</td>
<td>Athletes</td>
<td>69,000</td>
</tr>
<tr>
<td>Halkin*</td>
<td>2012</td>
<td>Athletes</td>
<td>179,000-240,000</td>
</tr>
</tbody>
</table>

*4,813 lives would be saved over a 20-year span of screening at a cost-per-life-saved of $10.6 to $14.4 million*


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For screening protocol to be appropriate these conditions must be met:

+ The condition being screened should have significant morbidity or mortality

? The disease screened should have treatment that can effect it’s outcome and not merely prematurely identify the inevitable

? Treatment afforded by early detection produces superior results to the early treatment of symptomatic results

+ There must be a sufficiently high prevalence of the condition in the population to merit screening

– Sensitive and specific screening strategies must be identified

– The screening strategy must be cost effective

Screening of athletes fails to meet the criteria necessary for a widespread screening as a public health strategy

Katcher M Risk Profiling and Screening Strategies In Estes N Sudden Cardiac Death in the Athlete Futura 1998
While intuitively appealing, screening programs have not yet been demonstrated to be effective in decreasing the risks inherent in athletics.

The Italian data provides the best evidence to date supporting the pre-participation screening of athletes.

There are many valuable lessons from the Italian experience useful in developing a rigorous, comprehensive registry to study the pre-participation screening process prospectively.

Based on the best available evidence pre-participation screening is effective in Italy but this strategy needs further study.
American Reaction To the Italian/European Guidelines

- Cardiovascular pre-participation screening proposal is highly laudable, has the potential to save young lives, and merits further evaluation.

- The principal US challenges:
  - Scientific
  - Demographic-Population diversity
  - Medical expertise
  - Screening infrastructure
  - Ethical
  - Legal
  - Economic

- Scientific perspective: the best approach is to assess the hypothesis that screening saves lives cost effectively with appropriately designed and while implementing PAD programs with AEDS.
American Reaction To the Italian/European
A fundamental principle of evidence based medicine is that clinical practice should be based on a sound scientific foundation established by clinical studies.

The level of evidence needed for adoption of new strategies should vary according to the clinical situation, and the higher the stakes, the better the evidence should be.

The stakes grow higher in proportion to the size of the affected population, the severity of the illness, the age of the population, and the risks and cost of the intervention.

The stakes are extremely high for pre-participation cardiovascular screening of athletes.

Hlatky, MA, NEJM 2004;350;2126-2128