Screening for Sudden Death in Athletes

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Background

• Sudden death in an apparently healthy athlete is a tragic event
• High publicized and generate significant attention which then may lead to an increase in resources to prevent another event

• Issues:
  • How many athletes are affected by sudden cardiac death?
  • What should screening consistent of?
  • What are some of the causes of SCD in this population?
Scope of Problem

• True incidence is difficult to estimate
  # Athletes who have experienced sudden death
  # Athletes at Risk

• Data accumulation
  • Media reports
  • Registries
  • Insurance claims
## Previous Estimates of Incidences

<table>
<thead>
<tr>
<th>First Author (Ref. #)</th>
<th>Year</th>
<th>Incidence (per Athlete-Person Yrs)</th>
<th>Total Number of Cases</th>
<th>Definition(s)</th>
<th>Time Frame of Events</th>
<th>Population</th>
<th>Collection Method(s)</th>
<th>Age Range (yrs)</th>
<th>Study Period</th>
</tr>
</thead>
<tbody>
<tr>
<td>Roberts and Stovitz (5)</td>
<td>2013</td>
<td>1/417,000</td>
<td>4</td>
<td>SCD</td>
<td>C/T</td>
<td>MN State High School League</td>
<td>Catastrophic Insurance Records</td>
<td>12-19</td>
<td>1993-2012</td>
</tr>
<tr>
<td>Drezner et al. (11)</td>
<td>2014</td>
<td>1/71,000</td>
<td>13</td>
<td>SCA+D</td>
<td>All</td>
<td>MN high school athletes</td>
<td>Public Media Reports (Parent Heart Watch)</td>
<td>14-18</td>
<td>2003-2012</td>
</tr>
<tr>
<td>Maron et al. (6)</td>
<td>2014</td>
<td>1/63,000</td>
<td>64</td>
<td>SCD</td>
<td>All</td>
<td>NCAA athletes</td>
<td>U.S. National Registry of Sudden Death in Athletes; NCAA Memorial Resolutions List</td>
<td>17-26</td>
<td>2002-2011</td>
</tr>
<tr>
<td>Harmon et al. (7)</td>
<td>2015</td>
<td>1/54,000</td>
<td>79</td>
<td>SCD</td>
<td>All</td>
<td>NCAA athletes</td>
<td>1) NCAA Resolutions List; 2) Parent Heart Watch database; and 3) NCAA insurance claims.</td>
<td>18-26</td>
<td>2003-2013</td>
</tr>
<tr>
<td>Harmon et al. (12)</td>
<td>2016</td>
<td>1/101,000 SCD</td>
<td>69 SCD</td>
<td>SCD</td>
<td>All</td>
<td>High school athletes from 7 states (CA, FL, MN, NJ, OH, TN, and TX)</td>
<td>Parent Heart Watch database</td>
<td>14-18</td>
<td>2007-2013</td>
</tr>
<tr>
<td></td>
<td></td>
<td>1/67,000 SCD+SCA</td>
<td>104 SCA+SCD</td>
<td></td>
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</table>

### Infrequent Event

### Variation in Databases
Demographics

• Males have a 3-5 times higher incidence of SCD compared to female athletes
• Data from NCAA
  • Black athletes have a 3.2 times higher rate of SCD compared to white athletes
  • Division I black basketball players
• Sporting activity increased risk of sudden death 2-4 times
• Rate of non-sporting SCD much higher
• Oregon Sudden Unexpected Death Study
  • 1,1184 nonsport-associated SCD
  • 63 sport-associated SCD
<table>
<thead>
<tr>
<th>AHA Recommendations</th>
<th>Pre-Participation Physical Evaluation</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Medical History</strong></td>
<td><strong>Heart Health Questions About You</strong></td>
</tr>
<tr>
<td>1. Chest pain/discomfort/tightness/pressure related to exertion</td>
<td>6. Have you ever had discomfort, pain, tightness, or pressure in your chest during exercise?</td>
</tr>
<tr>
<td>2. Unexplained syncope/near syncope†</td>
<td>5. Have you ever passed out or nearly passed out DURING or AFTER exercise?</td>
</tr>
<tr>
<td>3. Excessive and unexplained dyspnea/fatigue or palpitations, associated with exercise</td>
<td>12. Do you get more tired or short of breath more quickly than your friends during exercise?</td>
</tr>
<tr>
<td>4. Prior recognition of a heart murmur</td>
<td>7. Does your heart ever race or skip beats (irregular beats) during exercise?</td>
</tr>
<tr>
<td>5. Elevated systemic blood pressure</td>
<td>8. Has a doctor ever told you that you have any heart problems? If so, check all that apply:</td>
</tr>
<tr>
<td>6. Prior restriction from sports</td>
<td>- High blood pressure   - A heart murmur</td>
</tr>
<tr>
<td>7. Prior testing for heart disease, ordered by a physician</td>
<td>- High cholesterol   - A heart infection</td>
</tr>
<tr>
<td></td>
<td>- Kawasaki disease   - Other: __________</td>
</tr>
</tbody>
</table>

| 1. Has a doctor ever denied or restricted your participation in sports for any reason? |
| 9. Has a doctor ever ordered a test for your heart? (For example, ECG/EKG, echocardiogram) |
| 11. Have you ever had an unexplained seizure? |
## Family History

8. Premature death (sudden and unexpected or otherwise) before 50 yrs of age attributable to heart disease ≥1 relative

9. Disability from heart disease in a close relative <50 yrs of age

10. Hypertrophic or dilated cardiomyopathy, long QT syndrome or other ion channelopathies, Marfan syndrome, or clinically significant arrhythmias; specific knowledge of genetic cardiac condition in family member

## Heart Health Questions About Your Family

13. Has any family member or relative died of heart problems or had an unexpected death before age 50 (including drowning, unexplained car accident, or sudden infant death syndrome)?

14. Does anyone in your family have hypertrophic cardiomyopathy, Marfan syndrome, arrhythmogenic right ventricular cardiomyopathy, long QT syndrome, short QT syndrome, Brugada syndrome, or catecholaminergic polymorphic ventricular tachycardia?

15. Does anyone in your family have a heart problem, pacemaker, or implanted defibrillator?

16. Has anyone in your family had unexplained fainting, unexplained seizures, or near drowning?
American Heart Association and Pre-Participation Evaluation Monograph

<table>
<thead>
<tr>
<th>Physical examination</th>
<th>Physical examination</th>
</tr>
</thead>
<tbody>
<tr>
<td>11. Heart murmur‡</td>
<td>a. Heart</td>
</tr>
<tr>
<td></td>
<td>■ Murmurs (auscultation standing, supine, with or without Valsalva)</td>
</tr>
<tr>
<td></td>
<td>■ Location of point of maximal impulse</td>
</tr>
<tr>
<td>12. Femoral pulses to exclude coarctation</td>
<td>b. Pules</td>
</tr>
<tr>
<td></td>
<td>■ Simultaneous femoral and radial pulses</td>
</tr>
<tr>
<td>13. Physical stigmata of Marfan syndrome</td>
<td>c. Appearance</td>
</tr>
<tr>
<td></td>
<td>■ Marfan stigmata (kyphoscoliosis, high-arched palate, pectus excavatum, arachnodactyly, arm span &gt;height, hyperlaxity, myopia, MVP, aortic insufficiency)</td>
</tr>
<tr>
<td>14. Brachial artery blood pressure (sitting position)§</td>
<td>d. Blood pressure</td>
</tr>
</tbody>
</table>

- General lack of awareness across many school districts
- No prospective studies to evaluate
- Meta-analysis showed History sensitivity/specificity of 20%/95%, Physical Exam 9%/97%
Electrocardiography

- Already mandated in Israel and Italy
- Recommended by European Society of Cardiology and International Olympic Committee
- May improve sensitivity for screening for possible etiologies of potential sudden death
- No mandate in the United States
- Logistics of financial cost and number of participants
Conclusions:
• Decrease in SCD after Italian Sports Law may ignore significant variation before law imposed
• Israel incidences with significant variation
• No difference between Minnesota (No screening) and Israel lines
• Immortality bias: Some patients died suddenly and never made it to screening which would make screening look more favorable

Steinvil, JACC, 2011
Primary Electrical abnormalities found in minority of patients
WPW Syndrome

Very low incidence of SCD in WPW (Range 0.001 to 0.003 per patient year)

Risk of SCD may be higher in asymptomatic children compared to adults

Risk factors for sudden death:

History of atrial fibrillation

• Age < 30 yr
• Male gender
• Prior syncope
• Associated congenital or other heart disease
• Familial WPW
Risk Stratification in WPW

- Stress test or external monitor to look for disappearance of delta wave at physiologic heart rates
  - Noise on ECG
- ECG to look for multiple delta wave patterns or atrial fibrillation
- EP Study: loss of pre-excitation < 250 ms
Congenital Long QT Syndrome

Recommendations

• Participation in competitive athletics is a debated issue and may be safe in asymptomatic patients with borderline QT interval and without a FH of sudden death; recommended to be with supervision with AED present

• Non-selective beta blockers (nadolol and propranolol) superior to beta$_1$-selective beta blockers

• High risk patients (exercise induced syncope) should avoid exercise

Competitive Sports Participation in Athletes with Congenital Long QT Syndrome, (Ackerman, JAMA, 2012)

Exercise capacity according to Long QT risk score

<table>
<thead>
<tr>
<th>Static Component, Peak % Maximal Voluntary Left Ventricular Contraction</th>
<th>III High &gt;50</th>
<th>II Moderate 20-50</th>
<th>I Low &lt;20</th>
</tr>
</thead>
<tbody>
<tr>
<td>A Dynamic Component, Peak %</td>
<td>25</td>
<td>4</td>
<td>0</td>
</tr>
<tr>
<td>B Low &lt;40</td>
<td>0</td>
<td>14</td>
<td>34</td>
</tr>
<tr>
<td>C Moderate 40-70</td>
<td>3</td>
<td>22</td>
<td>28</td>
</tr>
<tr>
<td>Dynamic Component, Peak %</td>
<td>C High &gt;70</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

One patient (9 yo, QTc 550 ms) did receive ICD shocks when exercising against medical advice and not taking beta blocker
Increasingly recognized

Structural Cardiac Abnormalities
- Hypertrophic cardiomyopathy
- Arrhythmogenic right ventricular cardiomyopathy
- Congenital coronary artery anomalies
  - Marfan syndrome
  - Mitral valve prolapse/Aortic stenosis

Electrical Cardiac Abnormalities
- Wolff Parkinson White syndrome
- Congenital long QT syndrome
  - Brugada syndrome
- Catecholaminergic polymorphic ventricular tachycardia

Acquired Cardiac Abnormalities
- Infection (myocarditis)
- Trauma (commotio cordis)
- Toxicity (illicit/performance enhancing drugs)
- Environment (hypo/hyperthermia)
Performance Enhancing Drugs

• Anabolic-Androgenic Steroids
  • Impact on heart: atherogenic, thrombotic, vasospastic, direct myocardial injury
  • Risk of myocardial infarction
  • ventricular fibrosis $\rightarrow$ cardiomyopathy and ventricular arrhythmias
  • Development of HTN and left ventricular hypertrophy

• Ephedra
  • Increase BP, HR
  • Marketed for weight loss and performance enhancement
  • Associated with ischemic/hemorragic stroke, cardiac arrhythmias, coronary vasospasm, acute MI, tachycardia induced cardiomyopathy, sudden death

Dhar, Mayo Clin Proc, 2005
Performance Enhancing Drugs

• Creatine
  • Nonstimulant ergogenic aid
  • Increases sustained maximal energy and delays muscle fatigue
  • Aids in regeneration of ATP
  • Fewer adverse effects: weight gain, muscle cramps, severe dehydration with worsening renal function, rhabdomyolysis
  • No known cardiac adverse effects

• Erythropoietin
  • Induces erythrocytosis to increase oxygen carrying capacity
  • High HCT can lead to encephalopathy, pulmonary embolism, MI, peripheral clot formation
Myocarditis

- Incidence: 42% of sudden death among younger athletes
- Diagnosis: Syndrome of acute heart failure, angina-type chest pain or myopericarditis < 3 months; unexplained troponin elevation, ECG features of cardiac ischemia/arrhythmias; findings on echo and cardiac MRI c/w pericardial effusion and myocarditis

Exercise:
- Murine model, exercise increased myocardial viral levels
- Risk of sudden death does not correlate with amount of inflammation
Myocarditis

Patients should be excluded from competitive and amateur level sporting activity until clinical syndrome resolved

• Reassess patient after resolution of syndrome (3-6 months) with echocardiogram, Holter monitor and exercise ECG, serum markers

Grossly normal heart

Polymorphous inflammatory infiltrate

RT-PCR positive for enterovirus

Basso, Cardiology Clinics, 2007
Inherited Structural Conditions
- Most common cause for sudden death in athletic population
- Hypertrophic Cardiomyopathy
- Arrhythmogenic Right Ventricular Cardiomyopathy
Arrhythmogenic Right Ventricular Dysplasia

- Fibrofatty replacement of the RV myocardium
- Increases risk of sudden death – Exertion related
- Exercise may play a role in disease progression
- James et al. reported that ARVC patients with known desmosomal mutations who were endurance athletes had a higher faster rate of disease progression

James, JACC, 2013
Arrhythmogenic Right Ventricular Dysplasia

Sewant et al. reported that ARVC patients without a family history and without a desmosomal mutation

- likely to do more intense exercise than those with known mutation
- Earlier presentation

Patients with ARVD, possible/borderline ARVD and genotype positive/phenotype negative should not participate in competitive sports or intense recreational exercise

More intense exercise associated with lower VT/VF free survival

1 AHA ACC Task Force 3, 2015
Hypertrophic Cardiomyopathy

- Most common cause for SCD in young competitive athletes
- UK 12% of SCD
- Overall prevalence of SCD due to HCM in athletes estimated at 0.03% to 0.1%

Cardiac Sarcomere mutations

Maron, Lancet, 2013
Hypertrophic Cardiomyopathy

- Phenotype: LVH without chamber dilation without other cardiac or systemic disease capable of producing the magnitude of hypertrophy present
- Sudden Death Risk factor identification in HCM has been useful to identify patients at risk for lethal ventricular tachyarrhythmias
- High intensity sports is an independent risk factor for ventricular arrhythmias regardless of phenotypic expression

Maron, Lancet, 2013
Hypertrophic Cardiomyopathy
AHA/ACC Task Force 3 Recommendations

1. Patients with definite or probable HCM as documented by LVH should not participate in most competitive sports regardless of risk factor or previous intervention

2. Beta blockers and ICD should not be used to facilitate participation in competitive sports in HCM patients

3. Genotype positive, phenotype negative HCM patients is reasonable
   - Cardiac MRI and echo should be used to investigate for HCM expression
Dilated Cardiomyopathy

• May be difficult to distinguish from “athlete’s heart”
• Mildly reduced EF not typical of athlete’s heart
• Athlete’s heart should augment EF or become hyperdynamic with exercise

• Recommendation: Symptomatic athletes with DCM, nonhypertrophied restrictive CM and infiltrative CM should not participate in most competitive sports
Sudden Unexplained Death or Sudden Arrhythmic Death Syndrome

- Morphologically normal heart
- Most common postmortem assessment
- May represent primary electrical disorders/channelopathies
Limitations

• Many recommendations for screening are Class II recommendation with level C of evidence
• Therefore, many recommendations are made based on expert consensus rather with limited data from observational studies
Shared Decision Making
Importance of Emergency Action Plan

- 13,769 out-of-hospital cardiac arrests
- Assessed association between AED and survival to hospital discharge
- Survival 9% with CPR, no AED
- Survival 24% with CPR + AED application
- Survival 38% with CPR + AED shock
- AED associated with greater likelihood of survival (odds ratio 1.75)

Emphasizes importance of training (including coaches), rapid access to AED, communication with local EMS and regular review/rehearsal
Conclusions

• Sudden death in athletes are enormously tragic but fortunately infrequent

• Participation in pre-participation screening may help to detecting possible etiologies for sudden death