Sudden Cardiac Death and Asians

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Disclosures
None

Sudden Cardiac Death: Definitions

- WHO definition of SCD:
  - Unexpected death within 1 h of symptom onset if witnessed
  - Unexpected death within 24 h of having been observed alive and symptom-free if unwitnessed

- Cardiac arrest due to VT/VF, usually in the setting of underlying structural heart disease

- SCA survivors: SCA with resuscitation or spontaneous reversion

Magnitude of Sudden Cardiac Death in the U.S.

3. 2000 Heart and Stroke Statistical Update, American Heart Association
SCD Rates by Gender and Country

US SCD Rates in Men 1989-98

US SCD Rates in Women 1989-98

2007 SCD Rates in San Francisco County by Ethnicity
SCD Risk in Asian-Americans

- SCD rates for Asians overall are lower than for other ethnic groups
- SCD and cardiovascular disease still the leading cause of death in Asians
- Little data exist on specific risk in Asian subgroups
- Extrapolating from coronary disease risk, Asian Indians and Filipino subgroups likely to be at higher risk for SCD
Primary Electrical Diseases: "Normal Heart"

- Long QT syndromes (9 so far)
  - Normal QTc <440ms (men) or < 460ms (women)
  - Due to K channel mutations causing longer repolarization interval
  - SCD can present with exertion (LQT1), emotion (LQT2), or sleep (LQT3)
  - Risk can be affected by ethnicity: SNP (G643S) in KCNQ1 has 11% prevalence in Japanese population
- Short QT syndromes
  - QTc < 340ms
- Polymorphic ventricular tachycardia
  - RyR mutations
- Wolff-Parkinson-White syndrome
  - Ventricular pre-excitation (delta wave)

Brugada/Sudden Unexpected Nocturnal Death Syndrome

- Young, apparently healthy males from SE Asia
- "lai tai (death during sleep)" in Thailand
- "bangungut (rise and moan in sleep followed by death)" in the Philippines
- "pokkuri (unexpected SCD at night)" in Japan
- Majority of affected individuals are Asian
  - Prevalence 2x higher in Japan vs. Finland and U.S.
  - Men up to 9x higher incidence than women
- Sodium channel mutation (SCN5A)
- Typical ECG pattern of pseudo RBBB, ST elevation in V1-V3
- SCD may be the first and only clinical event, in up to 1/3
  - Typically ages 22 - 65
  - Fever is an important trigger
  - More common at night/sleep than in day/awake, not usually associated with exercise

Typical Brugada ECG Patterns

Brugada/SUNDs

- Diagnostic criteria:
  - Type 1 ECG, or conversion of type 2/3 to type 1 plus at least 1 of
  - Documented VF, polymorphic VT
  - Family hx SCD < 45y
  - Type 1 ECG in family members
  - EPS + for VT
  - Unexplained syncope
  - Nocturnal agonal respiration
- EP challenge with procainamide
- Rx: ICD
  - quinidine

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Primary Electrical Diseases: “Normal Heart”

- SCD can often be the first catastrophic manifestation of disease
- Syncope is an important risk factor
  - Suspect arrhythmic cause when:
    - Sudden collapse without prodrome
    - Palpitations
    - During exertion
- Risk stratification with:
  - Echocardiography to evaluate for structural heart disease
  - ECG
    - QT interval
    - Brugada pattern
    - WPW/delta wave
  - Family history of SCD
- Screening of family members: hx, ECG
- Referral to electrophysiologist

Sarcomeric and Cytoskeletal Protein Mutations Cause Genetic Cardiomyopathies and SCD

Etiology of Sudden Cardiac Death


Structural Cardiac Diseases Predisposing to SCD

- Hypertrophic cardiomyopathy
- Dilated cardiomyopathy
- Arrhythmogenic right ventricular dysplasia
- Alcoholic cardiomyopathy
- Myocarditis
- Mitral valve prolapse
- Congenital coronary anomalies
Etiology of Sudden Cardiac Death


Risk Factors for SCD in Coronary Artery Disease

- Previous MI
  - Common CV risk factors (smoking, HTN, hyperlipidemia) primarily identify underlying risk of CAD, rather than risk for SCD itself
- Diabetes mellitus
- Left ventricular dysfunction (low EF)
- CHF (NYHA class)
  - CHF patients experience SCD at 6-9x the rate of the general population
- Previous SCD event
- Prior episode of VT/VF

LVEF as a Predictor of SCD Risk

<table>
<thead>
<tr>
<th>LVEF</th>
<th>Rate of SCD at 1 year (Study)</th>
</tr>
</thead>
<tbody>
<tr>
<td>&gt; 40%</td>
<td>1.4% (GISSI)</td>
</tr>
<tr>
<td>≤ 35%</td>
<td>8% (TRACE)</td>
</tr>
<tr>
<td>≤ 30%</td>
<td>9.4% (MADIT II)</td>
</tr>
</tbody>
</table>

Effect of Medical Rx on SCD Risk

- B blockers
  - Powerful effect on SCD risk in CHF
  - 40% reduction in SCD rates in MERIT-HF, CIBIS-II
- ACE-I/ARB
  - Conflicting data on reduction of SCD
  - V-HeFT, TRACE, AIRE: significant reduction in SCD
  - CONSENSUS, SOLVD, SAVE: minimal reduction in SCD
- Aldosterone antagonists
  - Spironolactone and eplerenone significantly reduce SCD
  - EPHESUS: RR 0.79 for SCD, p=0.03
- Statins
  - Associated with lower appropriate ICD shock rates
ICDs Do Save Lives

ICD Therapies for VF/VT

High energy defibrillation shock for VF: 99% effective at DFT + 10J

Secondary Prevention Trials for SCD

• SCD due to VT/VF (not due to reversible cause) [AVID, CASH, CIDS]

• Spontaneous sustained VT, especially in structural heart disease [AVID, CASH, CIDS]

• Unexplained syncope with inducible sustained VT/VF or in presence of advanced structural heart disease

• NNT to prevent one death = 15 pts

Secondary Prevention for SCD

Which SCD survivors are not candidates for ICD?

• VT/VF due to transient or reversible cause (ischemia, electrolytes)

• Polymorphic VT/VF within first 48h after acute MI

• Drug-induced TdeP with normal LV function

• VF due to WPW syndrome

• Pt refusal, severe comorbidities (CA, etc. w/ anticipated survival < 1 y)
ICD Indications

Primary Prevention of SCD

- High-risk, inherited, or acquired conditions (LQTS, HCM, Brugada)
- In advanced structural heart disease (EF ≤ 35%), ischemic or nonischemic etiologies [MADIT II, SCD-HeFT, DEFINITE]
- CAD, EF 36-40%, inducible VT [MUSTT, MADIT I]
- NNT to prevent one death = 18-20 pts

Unwanted Effects of ICDs

- 33-50% inappropriate shock rate [SCD-HeFT, DEFINITE]
  - AF, AFL, T-wave oversensing, sinus tach
  - Agoraphobia, PTSD
- Generator problems, lead malfunction, infection
  - Industry recalls
  - Lead, system extraction for infection: high risk procedure
- Higher HF events and hosp for ICD pts [MADIT II]
  - Frequent RV pacing and dyssynchrony
  - SCDs may be converted to CHF deaths

Shortcomings of Current Treatment Strategies for SCD

- Current method of risk stratification (LVEF) is inadequately sensitive and nonspecific
  - 50% SCD occur in those w/o known cardiac disease
  - Only ~30% 1st prevention pts receive appropriate shocks
- ICD is highly effective but expensive
  - For 1st prevention, $34,000 to $70,200 per QALY gained
- ICD shock ≠ life saved
  - Looking at shock rates overestimates ICD benefit
  - Some VT/VF terminate spontaneously

SCD in Specific Risk Groups

- Patients with high coronary risk profile
- Patients with previous coronary event
- Patients with EF ≥ 35%, congestive heart failure
- Patients with previous out-of-hospital cardiac arrest
- Patients with previous MI, low EF and VT

Selecting Appropriate CHF Patients for ICD Consideration

- Does patient have Class IV symptoms (most patients hospitalized with HF)?
  - No: ICD now
  - Yes: Re-evaluate after 3-6 months

- Does patient have risk profile for heart failure death during next year?
  - Factors to consider: e.g., high blood pressure, diabetes mellitus, angina, heart failure, very high renal sodium, multiple HF hops
  - No: ICD
  - Yes: Re-evaluate after 3-6 months

- Is prognosis for more than one year survival with good overall functional status limited by non-cardiac conditions?
  - No: ICD
  - Yes: Re-evaluate after 3-6 months

- Is patient within 40 days of myocardial infarction?
  - No: ICD
  - Yes: Re-evaluate after 3-6 months

- Are there reversible factors for which treatment may improve LVEF?
  - Yes: Re-evaluate after 3-6 months
  - No: ICD

If all answers “No”: Discuss risks and benefits of ICD in outpatient setting


Is an ICD appropriate for my patient?

- Many Asian patients do not want a “foreign body” implanted
- Often thought of as life or death decision
  - “If we put an ICD in 100 pts with heart disease like yours, over the next 5 years we would expect:
    - 30 pts will die anyway
    - 7-8 pts will be saved by the ICD
    - 10-20 pts will receive unnecessary shocks
    - 5-15 pts will have other complications
    - rest of pts will never use their ICD”

- Removes an opportunity for quick, painless death
  - Some pts will request ICD be turned off to allow for natural death
- Age itself is not a contraindication for consideration of ICD, but less than 20% of pts in trials were > 75 y

SCD in Asians: Take Home Points

- SCD rate in Asians is lower than in other ethnic groups
- SCD and CV mortality is still single the leading cause of death in Asians
- ECG and family history is are important diagnostic tools in the recognition of primary electrical diseases affecting Asians
  - LQTS
  - Brugada/SUNDS
- CAD remains the single most important etiology underpinning SCD in Asians
- Standard medical Rx very effective in decreasing risk of SCD
  - ASA, β blockers, statins, ACE-ARB

SCD in Asians: Take Home Points

- LV ejection fraction remains as the best risk stratifier for risk of SCD, but is insensitive and nonspecific
- ICDs highly effective in the prevention of SCD, but there are important drawbacks and the decision to implant is highly individual
  - Little data specifically in Asians