Redefining Sudden Cardiac Death: Insights from the San Francisco POST SCD Study

10 September 2016
California Heart Rhythm Symposium
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Disclosures

• Major
  – Research grant: R01 HL102090 (NIH / NHLBI)
  – Research grant: R01 HL126555 (NIH / NHLBI)
  – Research grant: DP14-1403 (CDC)
  – Research grant: R24 A1067039 (NIH)

• Minor
  – Honorarium: Biotronik

Etiology of Sudden Cardiac Death

Magnitude of Sudden Cardiac Death in the U.S.

# deaths/year

0 100,000 200,000 300,000 400,000 500,000

AIDS Breast Cancer Lung Cancer Stroke SCD

References:
Sudden Cardiac Death: Definitions

ACC/AHA/HRS, 2006:

“SCA is the sudden cessation of cardiac activity so that the victim becomes unresponsive, with no normal breathing and no signs of circulation. If corrective measures are not taken rapidly, this condition progresses to sudden cardiac death.”

Methodological Issues in Population Studies of SCD

- Estimates in the US range from 184,000-450,000 annually due to subjective/inconsistent methods of data collection
  - Most data predates modern era of PPCI, statins, etc
  - Derived from homogenous populations
- Where does the data come from?
  - Death record review of listed COD
  - Retrospective review of paramedic/ER narratives
  - Incomplete medical records
- Which definition should we use for SCD?
  - WHO (Hinkle-Thaler) criteria?
  - Documented VF?
Comprehensive Surveillance of SCD

- Oregon SUDS (Chugh, JACC, 2004)
- WHO criteria
- Portland, OR: population 1,000,000
- Track dozens of ambulance companies and area hospitals
- Review of all available records
- SCA+SCD: 53/100,000

Sudden Cardiac Arrest vs. Sudden Cardiac Death

SCA
SCD

Sudden “Cardiac” Death

SCA
CAD
Tamponade
Valvular
Neurologic
DCM
HCM
Ao Dissection
Hemorrhage
1st electrical disease
Sudden Arrhythmic Death

SCA
CAD
Tamponade
Valvular
Neurologic
DCM
HCM
Hemorrhage
Ao Dissection
1st electrical disease

Study Design

1. Complete capture of all OOH SCDs for accurate population incidence
   - Single surveillance source, County ME, to which all OOH deaths are reported by law
   - SF DPH death certificate cross-check to confirm complete capture
2. Comprehensive autopsy of all SCDs to refine to arrhythmic deaths
   - Cranial vault, cardiac mass, LV measurements, Coronary vessels sectioned every 5mm, histology
3. Prediction model to help refine external registry SCDs to arrhythmic SDs
   - Future precision genotype-phenotype correlations within POST SCD cases
4. Identify pathologic correlates and predictors of arrhythmic SD

Case Adjudication

IRBs with all county hospitals
All outside medical records obtainable via medicolegal authority
- PMH (active problems, prescriptions, recent visits)
- Medications (e.g., QT-prolonging, methadone)
- Paramedic run sheets and rhythms
- Autopsy findings (including toxicology and histology)
- CIED interrogations if present

Adjudication panel

Dr. Phil Ursell
Chief Cardiac Pathologist, UCSF

Dr. Ellen Moffatt
Medical Examiner, City and County of San Francisco

Dr. Zian H. Tseng
Study PI, Cardiac Electrophysiologist, UCSF

Dr. Jeff Olgin
Chief of Cardiology, UCSF

Dr. Anthony Kim
Neurologist, Director of UCSF Stroke Center
Table 1: Non-Sudden Deaths

<table>
<thead>
<tr>
<th>Sub-Category</th>
<th>Total (%)</th>
<th>US 2011 Population 2011</th>
</tr>
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<tbody>
<tr>
<td>Age, mean ± SD</td>
<td>62.8 ± 14.5</td>
<td>73.1 ± 11.6</td>
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<tr>
<td>Male, n (%)</td>
<td>74 (70%)</td>
<td>350,179 (51%)</td>
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<tr>
<td>White</td>
<td>44 (42%)</td>
<td>290,089 (42%)</td>
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<td>Black</td>
<td>8 (8%)</td>
<td>40,751 (6%)</td>
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<td>Hispanic</td>
<td>8 (8%)</td>
<td>102,913 (15%)</td>
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<tr>
<td>Asian</td>
<td>37 (35%)</td>
<td>232,762 (34%)</td>
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<tr>
<td>Other</td>
<td>8 (8%)</td>
<td>24,174 (3%)</td>
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Table 2: Cause of Sudden Deaths without Autopsy

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Table 3: Excluded Natural Deaths

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SCD Case Study #1

- 74 yo Filipino gentleman
  - 4 V CABG 2002
  - EF 22%, fixed defect anterior, inferior walls
  - Diabetes
- Admitted for fever and bronchitis, receiving IV antibiotics
- Troponin negative, slightly fluid overloaded
- Called to consult on several asymptomatic runs of NSVT (5-7 beats) and to consider primary prevention ICD

SCD Case Study #1

- Recommended uptitration of β blocker, ICD implant as an outpatient after completing antibiotic treatment
- ICD scheduled for 1 month after discharge
- 2 weeks later patient found dead in the morning by wife
- Pt had returned to usual state of health, no complaints the night before

“Non-Cardiac SCD”

- Referring MD
- At autopsy, 2.5 L fresh blood in stomach and duodenum
- Heart: no acute coronary lesions
- Cause of death: exsanguination
- ICD would not have prevented SCD, pt may not have survived procedure
SCD Case Study #2

- 78 yo Caucasian man
  - Dilated cardiomyopathy, stable EF 25%
  - Paroxysmal AF
  - Primary prevention ICD implanted 3 years ago, no shocks
- In usual state of health when wife went shopping
- 3 hours later wife found him unresponsive
- Paramedics called, asystole on arrival, no resuscitation attempted

ICD Interrogation

VF ≠ Sudden Arrhythmic Death

- At autopsy
  - Massive subarachnoid hemorrhage (requires perfusing rhythm)
  - Heart 760 g
- Neurocardiogenic injury
  - VF due to acute adrenergic surge
- Despite rhythm documentation of VF, cause of death was neurologic
Sudden Neurologic Death
13% of Non-Cardiac Causes

- Chemical Overdose (N=65) 34%
- Other Non-Cardiac (N=25) 13%
- Infection (N=23) 12%
- Pulmonary Embolism (n=18) 9%
- Aortic Aneurysm/Dissection (N=18) 9%
- Intracranial Hemorrhage (N=15) 6%
- Sepsis (N=14) 5%
- Other Cardiogenic (N=11) 1%
- Other Pulmonary (N=10) 2%
- Other Trauma (N=10) 1%
- Other GI (N=8) 1%

13% of non-cardiac SCDs (5% overall)

Kim AS, Tseng ZH. Neurology 2016 in press

Presenting Rhythms at EMS Arrival:
Witnessed and Unwitnessed SCDs

- Witnessed N=120
- Unwitnessed N=405

Time from Arrest to Initial Rhythm
Collapsed and Trimmed *witnessed cases only

COD by Initial Rhythm
Witnessed cases only

<table>
<thead>
<tr>
<th>Initial Rhythm</th>
<th>Arrhythmic COD N=78</th>
<th>Non-Arrhythmic COD N=42</th>
<th>Fisher’s Exact</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Agonal/Idioventricular</td>
<td>3 (60%)</td>
<td>2 (40%)</td>
<td>1.0</td>
<td>5</td>
</tr>
<tr>
<td>Asystole</td>
<td>26 (63%)</td>
<td>15 (37%)</td>
<td>0.84</td>
<td>41</td>
</tr>
<tr>
<td>NSR</td>
<td>3 (60%)</td>
<td>2 (40%)</td>
<td>1.0</td>
<td>5</td>
</tr>
<tr>
<td>PEA</td>
<td>2 (13%)</td>
<td>13 (87%)</td>
<td>&lt;0.0001</td>
<td>15</td>
</tr>
<tr>
<td>Sinus Brad</td>
<td>2 (40%)</td>
<td>3 (60%)</td>
<td>0.34</td>
<td>5</td>
</tr>
<tr>
<td>VT/VF</td>
<td>39 (91%)</td>
<td>4 (9%)</td>
<td>&lt;0.0001</td>
<td>43</td>
</tr>
<tr>
<td>Other</td>
<td>2 (67%)</td>
<td>1 (33%)</td>
<td>1.0</td>
<td>3</td>
</tr>
<tr>
<td>Unknown</td>
<td>1 (33%)</td>
<td>2 (67%)</td>
<td>0.61</td>
<td>3</td>
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Sudden Cardiac Death in Patients with Human Immunodeficiency Virus Infection

Zoe H. Tseng, MD, MSc; Sue A. Scoville, MD; David F. Bruno, MD; PhD; SCH; Erin Vanlandingham, RN; MPH; Rosemary Mayers, MD; Joseph K. Wong, MD; Grace V. Hasla, MD; Phyllis Y. Hsu, MD
San Francisco, California, and Baltimore, Maryland

Mortality Rates by Cause and Year

- 230 deaths over 3.7 median years’ follow-up
- 13% SCDs, 86% (30/35) of all cardiac deaths
- Mean HIV SCD rate: 2.6/1,000 PY (95% CI 1.8-3.8), 4.5-fold higher than expected on the basis of the San Francisco population and background SCD rate

Tseng ZH et al. JACC 2012 59(21):1891-6

SCD Case Study #3

- 76-year-old male with mild CAD history of CHB with DDD PPM implanted in 2008
- Underlying rate < 30 bpm
- ERI reached 3 weeks prior
- Without complaint, found dead by his wife the morning before scheduled generator change

SCD Case Study #3

- 74 yo man with CAD, PPM for CHB
- Gen change scheduled for 5 weeks after ERI
- Did not show up to UCSF EP lab: died in sleep
- Autopsy negative (no MI, PE, or bleed)
Sudden Death in Patients with CIEDs

ICD Lead Fracture During Shock Resulting in SCD

- Improved post-market surveillance
- More accurate device failure rates
- Opportunities MD practice improvement: device selection, programming

Autopsy-Proven Sudden Cardiac Death

Magnitude of Sudden Cardiac Death in the U.S.

Etiology of Sudden Cardiac Death


Early and Anticipated Insights

- Incidence and underlying causes vary widely by race, gender
- SCD rates are up to 4-fold higher in HIV+
- CIED problems underestimated
- Sudden neurologic death most common non-cardiac cause after OD
- Precise phenotypes for future genetic association studies
- Evaluation of myocardial fibrosis, cardiac mass, CAD, valvular disease as risk factors
- Precision EMS protocols
- Prediction modeling for true arrhythmic causes in existing SCD cohorts
- Hemorrhage risk with anticoagulants, antiplatelets

Acknowledgements

- SF Medical Examiner’s Office
  - Ellen Moffatt
  - Amy Hart
- UCSF Pathology
  - Phil Ursell
- UCSF EP Section
  - Jeff Ugye
  - Robert Aramendia
  - Brian Moore
  - Nick Clark
  - Ramachandran
- UCSF Epidemiology/Biostatistics
  - Eric Vittinghoff
- SFGH
  - Michelle Kose
  - Dave Hayir
- UCSF Pediatrics
  - Rami Tareen
- SF VAMC
  - Joseph Wong
- UCSF Cardiology
  - Elyse Foster
  - Ian Harris
- UCSF Neurology
  - Anthony Yee
  - Michael Wilson
- SFFD/SFGH Emergency Medicine
  - Karl Sporer
  - Clement Yeh
- UCSF Human Genetics
  - Brad Aouizerat
  - Pui-Yan Kwok
- UCSF Medical Ethics
  - Bernie Lo