Syncope in Specific Populations: Elderly, Athletes, Channelopathies

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Syncope: A Symptom, Not a Diagnosis

- Self-limited loss of consciousness and postural tone
- Relatively rapid onset
- Variable warning symptoms
  - May be absent in older persons with amnesia for event
- Spontaneous, complete, and usually prompt recovery without medical or surgical intervention

Underlying mechanism: transient global cerebral hypoperfusion.

Scope of the Problem

- Cumulative lifetime incidence in general population up to 35%
- 1% of all hospital admissions
- 3% of all ER visits; up to 65% are vasovagal
- 6% incidence in institutionalized elderly
- 6% annual mortality if no cause established
- 12 - 25% recurrence rate
Causes of Syncope

Neurally-Mediated Reflex
- VVS
- CSS
- Situational
  - Cough
  - Post-micturition

Orthostatic
- Drug-induced
- ANS Failure
  - Primary
  - Secondary

Cardiac Arrhythmia
- Bradycardia
  - Sinus pause/ arrest
  - AV block
- Tachycardia
  - VT, SVT
  - LQTS, Brugada, etc.

Structural Cardio-Pulmonary
- Aortic stenosis
- HCM
- Pulmonary hypertension
- Pulmonary embolism
- Aortic dissection

Cardiovascular Causes

General Comments

- History, history, history
- High risk if structural heart disease
- High risk if associated with exertion
- Minimum evaluation
  - ECG
  - Echo
  - ± stress test

Unexplained Causes ≈10%

**Vasovagal/Neurocardiogenic Syncope**

- Occurs at all ages, may occur in families
- Associated with depression and somatic disorders, and ↑ed frequency near menses
- Often has specific triggers (situational), usually occurs in upright position and rare during exercise
- 3 phases: prodrome, LOC, post-syncopal period
- Peri-event amnesia common
- 17 - 35% suffer significant injury
- 5 - 7% have fractures
- Up to 4% with VVS may have cardiac syncope

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**Younger Adults**

- OH, situational, seizures, drugs
- 1° arrhythmia
- 15%
- 30%
- 40%
- 15%

**Elderly**

- OH, CSS, situational, seizures, drugs
- 1° arrhythmia, LV obstruction
- 30%
- 25%
- 15%
- 30%

Features of Unexplained Syncope in Older Adults

- High incidence of comorbid conditions
- 24% recurrence rate
- Concurrent BP and HF Rx increases susceptibility to + HUT
- Only 9% had an etiology established during follow-up
- Lower diagnostic yield of history and tests compared in younger patients

Roussanov et al. *Am J Geriatric Cardiol* 2007;16:249 N=304 (VA patients)

Drug-Induced QT Prolongation Principal Offenders

- Anti-arrhythmic Agents
  - Class IA...Quinidine, procainamide, disopyramide,
  - Class III...Sotalol, dofetilide
  - Amiodarone, dronedarone
- Anti-anginal Agents
  - Ranalozine
- Psychoactive Agents
  - Phenothiazines, amitriptyline, imipramine, ziprasidone
- Antibiotics
  - Erythromycin, azithromycin
  - Pentamidine, fluconazole,
  - Ciprofloxacin and its relatives
- Antihistamines
  - (Terfenadine), astemizole
- Others
  - (Cisapride)
  - Droperidol, haloperidol
  - Methadone
Methadone: Cardiac Arrest

Survival in Patients with Syncope

**Clues to Cause of Syncope from PE**

- Left ventricular impulse abnormalities suggest past myocardial infarction/CM
- Ventricular hypertrophy (need for AV synchrony)
- S3 gallop
- Murmurs (aortic stenosis, HCM)
- Pulmonary hypertension
- Mitral valve prolapse (PSVT, VT, autonomic dysfunction)
- Carotid sinus massage indicating CSH

**Natural History of Aortic Stenosis**

Percentage Survival over Years with and without AVR for onset of CHF, Syncope, Angina.

Tussive bradycardia

COUGH INDUCED AV BLOCK

POST ATROPINE 600 mcg iv

Right CSM

AF

Sinus arrest
Sudden Cardiac Death in Athletes

- Significance outweighs incidence
  - Events are unusual: 10-25 per year in US
  - Incidence: 1 in 200,000 to 250,000 athletes
- Large number of possible causes, usually related to occult heart disease, often genetically determined and family history valuable
  - Promote electrical instability and VT/VF
  - Often clinically silent until life-threatening event
- Once detected, withdrawal from competition and specific treatment can be life-saving
- Influence of coronary heart disease overwhelming in athletes >35 years of age

Causes of Exertional Syncope

- Neurocardiogenic
- Cerebral/metabolic
- Structural heart disease
- Arrhythmic
Vasovagal Syncope is Common in Endurance Athletes

- Large Venous Capacity
- High Vagal Tone
- Reduced Sympathetic Tone

Be Careful of + Tilt Tables in Athletes

When to Worry?

- History is KEY
- Description of the event/witnesses
  - Was it during exercise?
    - Corrado et al.; 33,000 Italian athletes >15 years old
    - 40/49 sudden deaths occurred during/immediately after exercise
    - 7/40 with prior syncopal episodes
  - Position, prodrome, triggers, time of day, hydration, tonic/clonic or post-ictal, duration
- Previous episodes
- Detailed family history
- An episode where the person was “out” for 3 hours is not cardiac in origin.
SCD in Young Athletes

Most common causes (US)
- HCM (30%)
- Anomalous coronary artery
- ARVC/D
- Commotio cordis

All other causes <5%
- LQTS, WPW, Brugada syndrome

Hypertrophic Cardiomyopathy
- Relatively common (1 in 500 individuals)
- Multiple mutations in cardiac sarcomere proteins
- Autosomal dominant transmission, variable penetrance
- Definition: hypertrophied (>12 mm), non-dilated LV septum in the absence of secondary causes
- Physiologic implications
  - LV outflow tract obstruction
  - Myocardial ischemia
  - Diastolic dysfunction
  - Susceptibility to VT/VF
Syncope in HCM

- Causes
  - SVT (especially AF)
  - VT
  - LV outflow tract gradient
  - Abnormal baroreceptor reflexes
  - Ischemia
- EP studies unreliable
- β-blockers, disopyramide and Ca++ channel blockers do not reduce incidence of SD

ECG in HCM

- HCM may exist without ECG changes
- Athlete’s heart may cause similar changes
Coronary Anomalies

- Most common: anomalous origin of the left main coronary artery from the right sinus of Valsalva
- May cause exercise-induced ischemia and/or VT/VF due to kinking or compression of coronary artery between pulmonary artery and aorta
- Diagnosis should be entertained if history of exertional angina or syncope
- Resting ECG will be normal
- Dx confirmed by CTA or coronary angiography
- Surgical correction

ACCF/AHA HCM Guideline

- Prior cardiac arrest or Sustained VT
- Family history SD in first-degree relative or LV wall thickness >30 mm or Recent unexplained syncope
- Nonsustained VT or Abnormal BP response
- Legend
  - Class I
  - Class IIa
  - Class IIb

Right Ventricular Dysplasia/Cardiomyopathy

- Fibro-fatty replacement of RV myocardium and RV (LBBB) ventricular tachycardia
- Autosomal dominant inheritance; a disease of desmosomes
- Annual mortality 2-3% due to HF or VT/VF
- Initial presentation may be sudden death
- Diagnosis suggested by ECG, echo or MRI
- ICD therapy typically indicated
Sarcoidosis Presenting as “ARVC”

59-year-old male
2 months exertional dyspnea
No dyspnea at rest, chest pain, palpitations, or syncope
Echocardiogram:
   LV normal size and function
   RV diffusely hypokinetic
CT:
   Mediastinal lymphadenopathy

Yared et al. Circulation 2008;118:e113-e115
Pre-participation Screening

• ACC-AHA recommendations: all athletes at onset, follow-up examinations
  
  History: chest pain, syncope, DOE
  PE: murmur (HCM), habitus (Marfans)
  Family history: syncope, sudden death
  ECG not recommended in US

• Compliance with recommendations, even among NCAA division I athletes is poor

Impact of Mandatory Screening: Italy

• 89% reduction in SCD in screened athletes (12-35) with institution of screening including ECG in 1982

Corrado D: JAMA 2006;296:1593-1601
Arguments against screening

- Low incidence of SCD in athletes
- Only 3% of athletes who ultimately die suddenly are identified with screening (Hx and PE)
- Potential impact of ECG
- Overlap with normal adaptation to exercise
- Corrado data reinterpreted: decrease in SCD with screening from 3.6 to 0.4 per 100,000
  - One life saved per 33,000 screened
  - Estimated cost: $1,320,000 per life saved

Recommendations for Athletes

- Specific strategies for specific conditions.
- With unequivocal abnormality disqualify from competition.
- Attempting to limit the degree of exertion during participation is not reasonable.
- Accepted guidelines for disqualification as developed by the 26th Bethesda Conference of the American College of Cardiology are available, and very restrictive.
- Remember the “I gotta sleep too” rule (Dr. Paul Thompson)
Long QT syndrome

- QT interval (male >450 ms, female >460 ms)
- Estimated incidence 1 in 5000
- Association with torsades de pointes VT
- Genetic disease of abnormalities in cardiac ion channels (potassium, sodium)
- Risk increases with QTc
- Different genetic abnormalities produce different ECG patterns and sudden death risk

LQTS Risk Factors for Syncope, Cardiac Arrest, and SCD

- Age and Gender
  - ↑ risk for males age 1-12
  - ↑ risk for females age 18-75
- Length of the QTc interval (>500 ms)
- History of recent syncope (past 2 years)
- Torsades de pointes VT and T-wave alternans
- Genetics
26-year-old female with:
Life-long “seizure disorder”
Presents with recurrent syncope 1 week after the birth of her 3rd child

Courtesy of Drs. Arthur Moss and Dan Roden
Risk Stratification

**LQTS Treatment Recommendations**

Asymptomatic < 40 years LQT1,2
- No competitive sports
- No unsupervised swimming
- Avoid hypokalemia
- Avoid QT prolonging drugs
  - [www.qtdrugs.org](http://www.qtdrugs.org), [www.longqt.org](http://www.longqt.org)
- ß-blocker: Propranolol 3mg/kg tid
  - Nadolol 1mg/kg qd or bid

Asymptomatic LQT3
- ß-blocker therapy
- Mexilitine (controversial)

**ICD experience with LQTS**

- 459 patients with genetically confirmed LQTS at Mayo Clinic followed 2000-2010 (average 7.3 year follow-up)
- Shocks
  - Appropriate: 12 patients (24%, 4 LQT1, 8 LQT2, 0 LQT3)
  - Inappropriate: 15 patients (29%, 8 LQT3)
- Risk factors for shocks
  - Secondary prevention indication (p=0.008)
  - Non-LQT3 genotype (p=0.02, no LQT3 received a shock)
  - QTc ≥500 ms (p=0.008)
  - Syncope (p=0.05)
  - TdP (p=0.003)
  - Negative family history (p=0.0001)

Brugada Syndrome

- RBBB and anterior ST elevation
- Risk of SD due to polymorphic VT
- 1/2 have inducible arrhythmia
- Drug therapy, including beta blockers apparently ineffective
- May be unmasked with IV procainamide, flecainide, ajmaline

Brugada et al. Circulation 1998;97:457

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Brugada Syndromes

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<th>Type</th>
<th>Gene</th>
<th>Protein</th>
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<tr>
<td>BrS1</td>
<td>Na(_{\alpha1.5} ) (SCN5A)</td>
<td>(I_{Na\alpha} ) channel (\alpha)-subunit</td>
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<tr>
<td>BrS2</td>
<td>GPD1L</td>
<td>NAD-dependent glycerol-3-phosphate dehydrogenase</td>
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<td>BrS3</td>
<td>Ca(_{\alpha1.2} ) (CACNA1C)</td>
<td>(I_{Ca\alpha} ) channel (\alpha1c)-subunit</td>
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<td>BrS5</td>
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<td>BrS6</td>
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<tr>
<td>BrS7</td>
<td>Na(_{\beta3} ) (SCN3B)</td>
<td>(I_{Na\beta} ) channel (\beta3)-subunit</td>
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Role of Lead Positioning to Record Brugada Pattern


Prognosis of Syncope in Patients with Brugada Syndrome

Antzelevitch et al. *Circulation* 2005; 111:659 N=258 (Registry)
When to Refer Patients with Syncope to an Electrophysiologist

- Arrhythmia or genetic arrhythmia syndrome identified during evaluation:
  - VT due to any cause
  - Bradyarrhythmia caused by Rx that cannot be withheld or changed
  - Supraventricular tachycardia, esp. WPW
- Structural heart disease
- Syncope in athletes or during exercise
- Origin of syncope remains unknown
- Neurocardiogenic syncope, especially if refractory to life-style changes or drug Rx, or associated with prolonged pauses in cardiac rhythm.