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GLOBAL EXPERTS, LOCAL LEARNING
Special
Syncope Guidelines: What’s New?

Samuel Asirvatham, MD & Miguel A. Gonzalez, MD
Saturday, June 24, 2017
10:25 to 11:10 a.m.
Conclusions

• **Risk stratification is critical**
  
  History, physical examination and simple screening tests for structural heart disease

• **Medical therapy for vasovagal syncope is largely empiric**
  
  Beta antagonists, alpha agonists, volume expansion
  
  Role of pacing unclear

• **Tilt-testing is useful if it reproduces clinical symptoms**
  
  Premature use of tilt test in syncope algorithm is misleading

• **Neurological testing is of little value unless suggested by history and examination**
Syncope at Mayo Clinic

- 600-1,000 ER patients/year
- 2,000-2,500 outpatient clinic evaluation/year
- 400 hospital admissions/year
- 30% of electrophysiology practice
  - 500 arrhythmia consults/year
  - 250 EP studies/year
  - 300 tilt table testing/year
Syncope and Mortality

Kapoor: Medicine, 1990
Causes of Syncope

- Reflex-mediated
- Orthostatic hypotension
- Psychiatric
- Neurologic
- Cardiac
- Humorally mediated
Causes of Syncope

Mayo Clinic: 1996-1998 (n=1,291)

<65 years
n=607

- Cardiogenic: 43%
- Vasovagal: 24%
- CHS: 17%
- Undetermined: 13%
- Other: 10%

≥65 years
n=684

- Cardiogenic: 30%
- Vasovagal: 23%
- CHS: 19%
- Undetermined: 18%
- Other: 19%
# Value of the History and Physical Examination

<table>
<thead>
<tr>
<th>Study</th>
<th>N</th>
<th>Dx by Hx &amp; PE (%)</th>
<th>Dx by ECG (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Kapoor 1990</td>
<td>433</td>
<td>32</td>
<td>7</td>
</tr>
<tr>
<td>Ben-Chetrit 1995</td>
<td>101</td>
<td>33</td>
<td>11</td>
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<tr>
<td>Martin 1984</td>
<td>170</td>
<td>53</td>
<td>1</td>
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<tr>
<td>Eagle 1983</td>
<td>100</td>
<td>52</td>
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<tr>
<td>Silverstein 1982</td>
<td>108</td>
<td>38</td>
<td></td>
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<tr>
<td>Day 1982</td>
<td>198</td>
<td>74</td>
<td>2</td>
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<tr>
<td>All studies</td>
<td>1100</td>
<td>45</td>
<td>5</td>
</tr>
</tbody>
</table>
Key Features of History

- **Prodromal symptoms**
  - Nausea, diaphoresis, claustrophobia, palpitations
- **Abruptness of onset, offset**
  - Spaghetti vs. celery syncope
- **Associated incontinence, seizure activity**
  - Post-ictal confusion, prostration
Key Features of Examination

• **Arterial pressure**
  Supine, seated, upright, upright after 1-2 mins
  Right and left arms

• **Precordium**
  LV aneurysm
  RV lift, palpable P2

• **Cardiac murmur**
  Effects of valsalva maneuver, standing, squatting
  Left decubitus position
Algorithm for Evaluation of Syncope

History, Physical Exam, ECG

Diagnostic (vasovagal, situational, orthostatic hypotension)
- Treat

Suggestive (AS, PE, seizure familial SCD)
- Specific tests
  - Treat

Unexplained syncope
Algorithm for Evaluation of Syncope

Unexplained Syncope

Organic heart disease (abnormal ECG, exertional symptoms, abrupt syncope)

- Evaluate OHD
  - Arrhythmia Screen
    - +
      - CSM
        - Evaluate OHD
  - -

Age > 60 y

- CSM
  - Evaluate OHD
  - -

No suspected heart disease

First episode

- Infrequent
  - Loop monitor, tilt test, psych eval
  - Frequent
    - Observe
      - Tilt test, psych eval
  - +
    - +
      - -
Screening for Arrhythmias

• Ambulatory ECG
• Loop recorder
  Continuous (King of Hearts)
  Heart Card
  Implantable recorder
• Electrophysiologic testing
24 Hour Ambulatory ECG Yield

1,512 patients

Syncope/presyncope during monitoring (17%)

Arrhythmia without symptoms (15%)

Documented arrhythmia (2.1%)

Gibson: AJC 53, 1984
External Loop Recorder Yield

526 patients

Palpitations/syncope/presyncope

Transmission (49%)  No transmission (51%)

Arrhythmias (35%)  No arrhythmias (14%)

Shen: Mayo Clinic Proc, 1987
Implantable Loop Recorder
Implantable Loop Recorder
ILR: Rhythm at time of symptoms

- Sinus rhythm: 29
- Bradycardia: 18
- Failed activation: 8
- Tachycardia: 3
ILR: Etiology of Syncope

- Bradycardia: 18
- Tachycardia: 3
- Neurally mediated: 7
- Nonarrhythmic: 27
Yield of EP study
8 studies, 625 patients with syncope

All patients: OHD+ N = 406
Pts. with VT: OHD+ N = 37
Pts. with bradycardia: OHD+ N = 219
Yield of Neurologic Testing in Syncope

- In patients unselected by history or physical exam for evidence of neurologic disease, yield of EEG, cranial imaging, & neurovascular studies is < 2%
- Carotid disease causes syncope only with high grade stenosis and contralateral carotid occlusion
  - Bruits usually present
- Associated diplopia, paresis, intractable nausea suggest vertebrobasilar insufficiency
## Transient Loss of Consciousness & Cerebral Ischemic Events

**Incidence of Syncope (%)**

<table>
<thead>
<tr>
<th></th>
<th>Stroke</th>
<th>TIA</th>
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<tbody>
<tr>
<td>Ischemic</td>
<td>6.5</td>
<td>Basilar</td>
</tr>
<tr>
<td>Embolic</td>
<td>13.2</td>
<td>Carotid</td>
</tr>
</tbody>
</table>

*Bousser: Ann Med Intern, 1981*
Tilt Testing
Tilt Induced Vasovagal Response

Baseline BP 136/67 mmHg
HR = 115 bpm

BP 54/30 mmHg
HR = 39 bpm

BP 47/29 mmHg
PCL = 700 msec

Baseline Tilt
Vasovagal response
A-V pacing CL = 700 ms
# Tilt Testing in Syncope

## Technical Issues

<table>
<thead>
<tr>
<th></th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Tilt angle</strong></td>
<td>60-80° acceptable</td>
</tr>
<tr>
<td></td>
<td>70° most common</td>
</tr>
<tr>
<td><strong>Tilt duration</strong></td>
<td>30-45 min</td>
</tr>
<tr>
<td></td>
<td>Data support a 45 min protocol</td>
</tr>
<tr>
<td><strong>Drug Provocation</strong></td>
<td>Isoproterenol, NTG, edrophonium</td>
</tr>
</tbody>
</table>

ACC Expert Consensus Conference JACC 1996
# Tilt Testing in Syncope

<table>
<thead>
<tr>
<th></th>
<th>Positive yield (pseudo sensitivity) (%)</th>
<th>Specificity controls (%)</th>
<th>Reproducibility (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Passive tilt</td>
<td>20-75</td>
<td>80-90</td>
<td>60-70</td>
</tr>
<tr>
<td>Isoproterenol</td>
<td>40-85</td>
<td>55-80</td>
<td>65-90</td>
</tr>
</tbody>
</table>
Tilt Testing in Syncope: Caveats

- Negative responses are more reproducible than positive
- Interpretation of positive response relies on similarity of spontaneous and provoked symptoms
- Serial testing for drug efficacy not useful
- Positive response should not halt further evaluation in patients with structural heart disease
Treatment of Vasovagal Syncope

- Mechanisms poorly understood
- Few randomized blinded drug trials
  Small trials with atenolol and paroxetine
- Spontaneous resolution makes many treatments appear effective
- Conflicting data regarding pacing
## Efficacy of Beta-Blockade in VVS

<table>
<thead>
<tr>
<th>Oral drug</th>
<th>(no.)</th>
<th>(%)</th>
<th>Repeat tilt</th>
<th>Continued tilt-proven drug</th>
<th>Discontinued tilt-proven drug</th>
<th>Received empiric Rx</th>
</tr>
</thead>
<tbody>
<tr>
<td>Atenolol</td>
<td>98</td>
<td>91</td>
<td>71</td>
<td>11</td>
<td>10</td>
<td>40</td>
</tr>
<tr>
<td></td>
<td>94</td>
<td></td>
<td>118</td>
<td>10</td>
<td>19</td>
<td>42</td>
</tr>
<tr>
<td>Propranolol</td>
<td>33</td>
<td>100</td>
<td>28</td>
<td>7</td>
<td>5</td>
<td>60</td>
</tr>
<tr>
<td></td>
<td>94</td>
<td></td>
<td>118</td>
<td>10</td>
<td>19</td>
<td>42</td>
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<tr>
<td>Metoprolol</td>
<td>22</td>
<td>100</td>
<td>16</td>
<td>0</td>
<td>4</td>
<td>25</td>
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<tr>
<td></td>
<td>94</td>
<td></td>
<td>118</td>
<td>10</td>
<td>19</td>
<td>42</td>
</tr>
<tr>
<td>Nadalol</td>
<td>4</td>
<td>100</td>
<td>3</td>
<td>67</td>
<td>0</td>
<td>0</td>
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<tr>
<td></td>
<td>94</td>
<td></td>
<td>118</td>
<td>10</td>
<td>19</td>
<td>42</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td>157</td>
<td>94</td>
<td>118</td>
<td>10</td>
<td>19</td>
<td>42</td>
</tr>
</tbody>
</table>

Cox: JACC, 1995
Efficacy of Atenolol in VVS

- Randomized, double-blinded, placebo-controlled study
- Inclusion:
  - 50 patients
  - At least 2 episodes VVS in past year
  - Tilt test followed by IV atenolol
- Placebo (N=24) or atenolol 50 mg / day (N=26)
- End-point: time to recurrence of syncope

Madrid: JACC, 2001
Efficacy of Atenolol in VVS

- Tilt test positive in 20 patients
  - IV atenolol prevented another positive tilt-test in 5
- One year follow-up:
  - Median # of syncopal spells 2 (atenolol), 0 (placebo)
  - Median time to recurrence 7 months w/ no difference between groups
- Conclusion:
  - Recurrence rate drops in both groups
  - No effect of atenolol proved

Madrid: JACC, 2001
North American Vasosvagal Pacing Study (VPS)

- Six or more lifetime episodes of syncope
- Tilt test induces syncope/presyncope
  - Relative bradycardia
- Randomized to rate-drop pacemaker
- 54 patients enrolled
- Endpoint: time to first recurrence of syncope

JACC 1999;33:16-20
VPS: Results

- 27 patients randomized to pacer/27 to observation
  - 7% beta-blocker use in both groups
- Time from randomization to syncope
  - No pacer - 54 days
  - Pacer - 112 days
- No effect on presyncope
VPS: Problems

- Non paced group received little medical therapy
- Placebo effect of pacer implant not assessed
- No data regarding frequency of rate-drop pacing and correlation with abortive symptoms
- Possible type II statistical error due to small sample size
Conclusions

• **Risk stratification is critical**
  - History, physical examination and simple screening tests for structural heart disease

• **Medical therapy for vasovagal syncope is largely empiric**
  - Beta antagonists, alpha agonists, volume expansion
  - Role of pacing unclear

• **Tilt-testing is useful if it reproduces clinical symptoms**
  - Premature use of tilt test in syncope algorithm is misleading

• **Neurological testing is of little value unless suggested by history and examination**
Those who suffer from frequent and severe fainting often die suddenly.

Hippocrates 1000 BC
Syncope: Case Study # 1

- 25 year old female
- Flurry of syncopal spells ages 9 and 14
- Restricted from high school sports
- 4 episodes as a high school senior
Syncope: Case Study # 1

• **June 1996**
  - Witnessed syncope
  - Impaired consciousness X 5 minutes
  - No incontinence
  - Possible retrograde amnesia

• **July/ August 1998**
  - Syncope X4 at home
  - No premonitory symptoms/aura
  - Retrograde amnesia
  - No incontinence
Syncope: Case Study # 1

- **Past Medical History**
  - Asthma
  - Closed head injury age 3

- **Family history**
  - Premature CAD
  - No family history of SCD, syncope, seizures

- **Examination**
  - BP 100/78, pulse 64 seated
  - BP 100/54, pulse 72 standing
  - Exam otherwise normal
Syncope: Case Study # 1

- ECG entirely normal
- Echocardiogram entirely normal
Syncope: Case Study # 1

Next Diagnostic Step?

- 1) Head up tilt test
- 2) EP study
- 3) Neurological evaluation
- 4) Loop recorder
Syncope: Case Study # 1

Head up tilt test

- With isoproterenol, 70 degrees, presyncope at 3 min
- Provoked symptoms unlike spontaneous episodes
Syncope: Case Study # 1
Next Diagnostic/Therapeutic Step?

- 1) EP study
- 2) Neurological evaluation
- 3) Loop recorder
- 4) Treat for vasovagal syncope and observe
Syncope: Case Study # 1
Electrophysiologic Study

• Dual retrograde pathways without SVT
Syncope: Case Study # 1

Neurology evaluation

- Examination normal
- EEG sleep and awake-normal
- MRI normal
- Impression-seizure unlikely
Syncope: Case Study # 1
Loop recorder

- Implantable loop recorder placed
- 3 episodes syncope/presyncope
- Device activated by relative after syncopal spell
Syncope: Case Study # 1

R-R Intervals at time of syncope

R-R interval number

R-R interval (msec)

Activation point
Syncope: Case Study # 1
Inpatient observation on epilepsy monitoring unit

- Syncope and presyncope observed
- EEG normal
- Hypotension without bradycardia documented
- Dismissed on fludrocortisone
Syncope: Case Study #2

- 78 year old male
- 4 episodes syncope in 4 years
  - 1992- Walking in AM, no bkfst, turned head brief LOC
  - 1993- Standing cooking, rushing in head, brief LOC
  - 1995- Kneeling in church, no bkfst, rushing in head, brief LOC
  - 1996-Standing in kitchen, rushing in head, brief LOC
Syncope: Case Study #2

Medical History

• **PMH**
  Borderline hypertension
  Possible Meniere’s disease

• **Family history**
  No SCD/syncope or CAD

• **Medication**
  Nadolol 10 mg/d
  Meclizine 37.5 mg/d

• **Coronary Risk Factors**
  Gender, hypertension
Syncope: Case Study #2
Examination

- Weight 218 lbs
- BP 160/104 R & L, pulse 70 and regular
- Hear, lung vascular, neurological exams normal
Syncope: Case Study #2

Prior Evaluation

- Chest X ray - LV enlargement
- EKG - Voltage criteria for LVH; one PVC
- Chemistries, CBC, sTSH, UA - normal
- ENT evaluation - no evidence Meniere’s
- Sleep study - suggestive of sleep apnea
Syncope: Case Study #2
Next Diagnostic Step?

- 1) Head up tilt test
- 2) Loop recorder
- 3) Electrophysiologic study
- 4) Neurological evaluation
Syncope: Case Study #2
Head-up tilt test (outside)

- 80 degrees head-up isoproterenol 5 mcg/min
- BP 140 to 90 systolic
- No change in pulse
- Symptoms somewhat similar to spontaneous episodes
Syncope: Case Study #2
Head-up tilt test (Mayo)

- Normal response to CSM
- 70 degrees head-up, isoproterenol 3 mcg/min
- At 20 min BP fell to 70/40, sinus rate fell to 60 bpm
- Symptoms somewhat similar to spontaneous episodes
Syncope: Case Study #2
Next Diagnostic/Therapeutic Step?

- 1) Electrophysiologic study
- 2) Neurological evaluation
- 3) Increase nadolol dose
- 4) Loop recorder
Syncope: Case Study #2

Loop recorder

- Dizzy and lightheaded, but no syncope/presyncope
- Single PVC detected on strip
Syncope: Case Study #2
Next Diagnostic/Therapeutic Step?

- 1) Electrophysiologic study
- 2) Neurological evaluation
- 3) Psychiatric evaluation
- 4) Implantable loop recorder
Syncope: Case Study #2
Electrophysiologic study

- Transthoracic echo prior to EP study
  Inferolateral hypokinesis
  Ejection fraction 45 %
- Ventricular tachycardia reproducibly induced
  2 extrastimuli, drive cycle 400, RVA
  RBBB NAX CL 230
- VT suppressed with sotalol
Syncope: Case Study #3

- 68 year old female
- 7 year history of spells
  - 30-60 min lightheadedness
  - Intermittent syncope
  - Nausea, vomiting, diarrhea, palpitations
- Well between episodes
Syncope: Case Study #3

Medical History

• Cholecystectomy, appendectomy, tonsillectomy

• Family History
  Mother - breast cancer
  Brother - myocardial infarction
  Sister - valvular heart disease

• Medication - estrogen, Ca suppl, ASA 325/d
Syncope: Case Study #3

Examination

- BP 110/60 R & L without orthostatic change
- ENT - nl
- CV - nl
- Skin - no rash
- Abd - nl
Syncope: Case Study #3

Laboratories

- ECG - ventricular paced rhythm
- CXR - normal pacer lead position
- Echocardiogram - normal chamber sizes
Syncope: Case Study #3
Prior Evaluation and Treatment

- 1990 - Coronary angiography normal
- 1993 - EP study and attempted ablation of atrial tachycardia focus “near sinus node”
- 1995 - AV node ablation and pacer implant recurrent spell in hospital after procedure
- Consultations
  - Neurology - ? Seizures
  - Gastroenterology - ? Eating epilepsy
  - Cardiology - ? Postprandial hypotension
Syncope: Case Study #3
Next Diagnostic/Therapeutic Step?

- 1) Psychiatry evaluation
- 2) Urinary metanephrines
- 3) Urinary 5 HIAA
- 4) Bone marrow biopsy
Syncope: Case Study #3

- Bone marrow biopsy - perivascular infiltrates of tryptase positive cells
- Serum tryptase 28 ng/ml
- Diagnosis: systemic mastocytosis
- Treatment: antihistamines and aspirin
Syncope: Case Study #3

• Lessons
  Wacky symptoms in non-wacky patient warrant exhaustive search
  If all the usual suspects are innocent, round up the unusual ones
  Zebras are mostly in other countries and zoos, but only mostly
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