Syncope
What’s the Issue?

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Syncope

• I have no disclosures relevant to this talk
1. Incidence and prevalence
2. Broad differential
3. Risk Stratification
4. Work up and treatment for vasovagal syncope
5. Conclusions
Syncope:
Partial or complete loss of consciousness with interruption of awareness of oneself and one’s surroundings
SYNCOPE – Background

- Syncope is common in the general population\(^1\)
- Syncope accounts for 3-5% of Emergency Department (ED) visits and 1-3% of all hospital admissions\(^2,3\)
- Not created equal
- Cardiac syncope doubled the risk of death from any cause with a 6 mo mortality rate >10\(^%\)\(^4\)

Syncope: Pathophysiology

- Common final pathway is decreased cerebral perfusion
- Cessation of cerebral perfusion for as little as 3-5 seconds can result in syncope
- Decreased cerebral perfusion may occur as a result of decreased cardiac output or decreased systemic vascular resistance.
RISK STRATIFICATION

• Etiology can be benign…
  or deadly…
  that’s the rub…

• HISTORY alone identifies the cause  up to 85% of the time

• POINTS to CONSIDER
  – Previous episodes
  – Character of the events, witnesses
  – Events preceding the syncope
  – Events during and after the episode
Syncope: Etiology

- **Neurally-Mediated**
  - Vasovagal
  - Carotid Sinus
  - Situational
    - Cough
    - Post-micturition
    - Defecation
    - Swallow
  - 66%

- **Orthostatic**
  - Drug Induced
  - Volume Depletion
  - ANS Failure
    - Primary
    - Secondary
  - 10%

- **Cardiac Arrhythmia**
  - Brady
    - Sick sinus
    - AV block
  - Tachy
    - VT
    - SVT
  - Inherited
  - 11%

- **Structural Cardio-Pulmonary**
  - Aortic Stenosis
  - HOCM
  - Pulmonary Hypertension
  - 5%

- **Non-Syncopal**
  - Psychogenic
  - Metabolic
  - Epilepsy
  - Intoxications
  - TIA
  - Falls
  - 6%

**Unknown Cause = 2%**

Brigole et al. Heart 2007;93:130-136
Short-Term High Risk Criteria

- Severe structural or CAD (CHF, low EF, prior MI)
- Clinical or EKG -> Arrhythmia
  - During exertion or supine
  - Palpitations
  - NSVT
  - Bifascicular block
  - Bradycardia
  - Pre-excited QRS complex
  - RBBB with ST elevation in V1-V3 (Brugada pattern)
  - Long or short QT
  - Negative T waves in right precordial leads, epsilon waves or ventricular late potentials suggestive of ARVC
- Severe anemia
- Electrolyte disturbance
**Syncope Algorithm**

1. **History, Physical Exam, ECG**
   - Diagnosis? Yes, certain or suspected: Treat
   - Diagnosis? No, unexplained

2. **Abnormal ECG or SHD?**
   - No: Frequent Symptoms?
     - Yes: Options: CSM, 24-Hour Holter, 30-Day Event Recorder, ICM*
     - No: Cardiac Evaluation Options: Echo, EPS, Enzymes, Exercise Test

3. **Diagnosis?**
   - Yes: Treat
   - No: ICM*

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SHD = Structural Heart Disease  
CSM = Carotid Sinus Massage  
EPS = Electrophysologic Study  
ICM* = *Provides up to 36 months of continuous monitoring

This is a general protocol to assist with the management of patients. This is not designed to replace clinical judgment or individual patient needs.
NEURALLY MEDIATED SYNCOPE

- Vasovagal, carotid sinus, situational
- Represents 66% of patients with syncope
- No increased risk for cardiovascular morbidity or mortality associated with reflex mediated syncope.
Features suggestive of Neurally-Mediated causes?

- *Prolonged* standing in a crowded, warm place
- *Preceding* nausea, feeling cold and sweaty
- *After* exertion or post-prandial
- Tonic-clonic movements are short in duration and occur *after* the loss of consciousness
- Long duration of symptoms …>4 years
Tilt-Table Test

• Indications:
  – If a neurocardiogenic cause is suspected
  – Recurrent syncope, no apparent cause, any age
  – Other evaluation unrevealing
  – Treating other potential causes ineffective

• Do not tilt if etiology is clear or if tilt has dangers

# Tilt-Table Findings

<table>
<thead>
<tr>
<th>Neurocardiogenic</th>
<th>Dysautonomic</th>
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</thead>
<tbody>
<tr>
<td>Sudden hypotension with or without bradycardia</td>
<td>Gradual parallel decline in systolic and diastolic blood pressure</td>
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</table>

<table>
<thead>
<tr>
<th>POTS</th>
<th>Psychogenic</th>
</tr>
</thead>
<tbody>
<tr>
<td>An excessive heart rate response to maintain a low normal BP</td>
<td>No change in heart rate, BP, EEG, transcranial blood flow</td>
</tr>
</tbody>
</table>
Heart rate and blood pressure patterns observed in head-up tilt-table testing

A  Classic neurocardiogenic (vasovagal) response

<table>
<thead>
<tr>
<th>HR/BP</th>
<th>Tilt</th>
<th>Head down</th>
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B  Dysautonomic response

<table>
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<tr>
<th>HR/BP</th>
<th>Tilt</th>
<th>Head down</th>
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</tbody>
</table>

C  POTS response

<table>
<thead>
<tr>
<th>HR/BP</th>
<th>Tilt</th>
<th>Head down</th>
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</table>

Shown are the heart rate and blood pressure responses seen during tilt-table testing in patients with various etiologies of syncope including classic neurocardiogenic syncope, pure autonomic failure, or postural orthostatic tachycardia syndrome (POTS).

Implantable Loop Recorder

- Small subcutaneous implantable monitoring device
- 2009 ESC Guidelines recommend for:
  - Early phase evaluation
    - Recurrent syncope with absence of high risk features
    - Suspected or proven reflex syncope before pacing
  - Late evaluation
    - High risk syncope without etiology after exhaustive w/u
Neurocardiogenic Syncope

First line: Treatment Options

• Tilt +, High suspicion (pretest probability despite tilt -)
  – Patient education about pathophysiology of VVS and benign prognosis
  – Increase salt and water intake
  – If prodrome, sit or lie down
  – Tilt-training or counterpressure manuevers
  – Leg compression
• Tilt training: > 90% effective

1. Di Girolamo E Circulation 1999;100:1798
2. Reybrouck T PACE 2000;23:493
Neurocardiogenic Syncope

Drug Therapies: Second Line

• Beta-blockers
• SSRIs
• Midodrine
• Fludrocortisone

• Anticholinergics
  (disopyramide, scopolamine)
• Desmopressin
• Erythropoietin
• Theophylline
Beta Blockers

• Initial observations suggest syncope reduction
  – Rationale is that B-receptor involvement in ventricular baroreceptor reflexes
  – Isuprel (B agonist) can trigger hypotension and bradycardia and BB can prevent the Isuprel effect

• At least 4 randomized trials have failed to show benefit but difficult to demonstrate statistical benefit when placebo effect is so high

• Best data from the POST trial
Prevention of Syncope Trial (POST)

- 208 patients with recurrent syncope and an abnormal tilt table test
- Placebo vs metoprolol (avg dose 122mg daily) with 1 year follow up
- Recurrent syncope occurred in 36 percent of both groups.
- Withdrawal rates were 22 percent in both groups.
- Prespecified analyses according to age (categorized as <42 versus ≥42 years) and tilt table test results did not identify any subgroups that benefited with metoprolol.
Prevention of Syncope Trial (POST)

Sheldon R et al. Circulation 2006;113:1164-1170
FLUDROCORTISONE

• Corticosteroid with primarily mineralocorticoid activity
• Sodium and water retention and potassium excretion
• POST II (multinational, randomized, controlled)
• 211 pts (fludrocortisone vs placebo) for 1yr
• Trend of less events in the fludrocortisone group but NO statistical difference
MIDODRINE

- Pro-drug- active metabolite is a peripheral alpha-1 adrenergic receptor
  - Causes venoconstriction and arteriolar constriction
  - Increases cardiac output and increases peripheral resistance
- More effective than Na/volume therapy alone
- Challenge is frequent dosing compliance
- POST 4 (placebo vs midodrine) results due in 2017
SSRIs

- High serotonin levels in the nervous system
- Serotonin modulates the CNS BP and HR
- Di Gerolamo et al conducted a randomized, double-blind, placebo-controlled trial
- Paroxetine (20mg QD) vs placebo over ~25 mo
- Reduction in syncope recurrence
  - 18% with Paxil vs 53% with placebo
- Other studies have found other SSRIs of no benefit
- Can be helpful in psychosocial stressors due to syncope
Pacemakers

• Any role?
• Often a significant bradycardic response in VVS
• But severe vasodepressor reactions often coexist
Study Design:

- 54 patients randomized, prospective, single center
  - 27 DDD pacemaker with rate drop response (RDR)
  - 27 no pacemaker

Patient Inclusion Criteria:

- 6 syncopal events ever
- +HUT
- Relative bradycardia*
Risk of Syncope Recurrence

The VPS I Study

Inclusion: vasodepressor response

Control Group  n = 27
Pacemaker Group n = 27

Connolly SJ. J Am Coll Cardiol 33:16-20, 1999
VPS II Trial – Big Placebo Effect

Time to First Recurrence of Syncope

- Syncope > 5 total or > 2 episodes in 2 years, positive tilt, age > 19
- RR reduction 29%

Connolly S. JAMA 2003:289:2224–2229
**Study design**

**ILR screening phase**
- Neurally-mediated syncopes
  - ILR implantation (Reveal DX/XT)
  - ILR follow-up (max 2 yrs)

**ISSUE 3 study phase**
- ILR eligibility criteria:
  - Asystolic syncope ≥3 s, or
  - Non-syncopal asystole ≥6 s

![Decision tree diagram](image)
ISSUE-3: Intention-to-Treat

Kaplan-Meier survival estimates

log rank: p=0.039
RRR at 2 yrs: 57%

Number at risk

<table>
<thead>
<tr>
<th>Months</th>
<th>Pm OFF</th>
<th>Pm ON</th>
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<tbody>
<tr>
<td>0</td>
<td>39</td>
<td>38</td>
</tr>
<tr>
<td>3</td>
<td>31</td>
<td>32</td>
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<td>6</td>
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<td>24</td>
<td>8</td>
<td>11</td>
</tr>
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</table>
Issue 3 Conclusions

• In patients ≥40 years with severe asystolic NMS:
  • Dual-chamber pacing reduces recurrence of syncope
  • The 32% absolute and 57% relative syncope reduction rate support use of pacing.
• The strategy of using ILR to determine indication for pacing likely explains the positive outcome and difference from prior negative results in pacemaker studies.
Carotid Sinus Syndrome (CSS)

• Syncope clearly associated with carotid sinus stimulation is rare (≤1% of syncope)

• CSS may be an important cause of unexplained syncope / falls in older individuals

CSS - Carotid Sinus Syndrome
Diagnosis

- Carotid Sinus Hypersensitivity (CSH) implies positive response to carotid massage:
  - ≥50 mmHg drop in systolic pressure
  - ≥6 sec asystolic pause
  - CSS = CSH + Reproduction of symptoms

- CSH without symptoms is not treated
- CSS needs a DDD PM

```markdown
<table>
<thead>
<tr>
<th>Heart Rate</th>
<th>ECG波形</th>
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<tbody>
<tr>
<td>120 bpm</td>
<td><img src="image" alt="ECG波形" /></td>
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</tbody>
</table>
```
Conclusions

- Syncope is common
  - Diagnosis can be elusive
  - Treatment elusive
- Risk stratification is important
- Requires good history and physical
- Treatment is education first
- Remember that placebo has been very effective thus education and empowerment should be as effective
- Tilt studies and ILR monitoring can be helpful
- PPMs in select cases
  - >3s asystolic syncope,
  - Asymptomatic >6s pause
  - Carotid Sinus Syndrome
Questions?