Neurocardiogenic Syncope

Christopher Bonnet, M.D.
Director, Clinical Electrophysiology

Definition of Syncope

- Abrupt and transient loss of consciousness
- Loss of postural tone
- Spontaneous and rapid recovery

Transient loss of consciousness with prompt spontaneous recovery
Presyncope, Syncope and SCD

SCD vs. Syncope

<table>
<thead>
<tr>
<th>SYNCOPE</th>
<th>SCD</th>
</tr>
</thead>
<tbody>
<tr>
<td>No CPR</td>
<td>CPR</td>
</tr>
<tr>
<td>Spontaneous recovery</td>
<td>Electric or</td>
</tr>
<tr>
<td></td>
<td>Pharmacologic</td>
</tr>
<tr>
<td></td>
<td>cardioversion</td>
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Epidemiology of Syncope

- 3.0% in men and 3.5% in women according to Framingham study
- accounts for 6% of hospital admissions and 3% of emergency room visits annually
- incidence increases with age with a sharp rise at age 70
Recurrence rate
- Review of 433 patients, the cumulative incidence of syncope at three years was:
  - 31% for patients with cardiovascular etiology
  - 36% for those with noncardiovascular causes
  - 43% for those with syncope of unknown etiology

Clinical Significance of Syncope
- Injuries - occur in 35% of syncopal attacks
  - Psychological impact
  - Prognosis dependent on underlying disease

General Classification of Syncope
- Cardiac
- Noncardiac
- Undetermined cause
Syncope

**Types**
- Orthostatic
- Neurogenic
- Cardiogenic
- Neurocardiogenic
- Unknown

<table>
<thead>
<tr>
<th>Type</th>
<th>Percentage</th>
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<tbody>
<tr>
<td>Migraines, TIA, Seizures</td>
<td>10%</td>
</tr>
<tr>
<td>Vasovagal Syncope (VVS)</td>
<td>18%</td>
</tr>
<tr>
<td>Carotid Sinus Hypersensitivity (CSH)</td>
<td>1%</td>
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</table>


**History**: syncope triggered by emotional stress, painful or noxious stimuli, fear, prolonged standing, associated with prodromal symptoms (dizzy, lightheaded, pale, diaphoretic, nauseated...)

**Uncommon causes of Syncope**

**CVD**
- Arrhythmia causes: SVT
- Nonarrhythmic causes: PE, Pulmonary HTN, Dissecting aortic aneurysm, subclavian steal, atrial myxoma, cardiac tamponade

**Noncardiovascular diseases**
- Hyperventilation
- Migraine
- Carcinoid syndrome
- Metabolic: Hypoglycemia and hypoxia
- Multivessel obstructive cerebrovascular disease
Characteristics of Syncopal Symptoms

<table>
<thead>
<tr>
<th>Etiology</th>
<th>Symptoms Before Syncope</th>
<th>Symptoms During Syncope</th>
<th>Symptoms After Syncope</th>
</tr>
</thead>
<tbody>
<tr>
<td>Orthostatic Hypotension</td>
<td>Patient was sitting or lying down</td>
<td>Rising from sitting or lying position; begins feeling lightheaded</td>
<td>No residual effects</td>
</tr>
<tr>
<td>Neurogenic Syncope</td>
<td>Headache; visual disturbances</td>
<td>Convulsions; vertigo; urinary &amp; fecal incontinence</td>
<td>Residual effects; patient is disoriented after event</td>
</tr>
<tr>
<td>Cardiogenic Syncope</td>
<td>No prodromal symptoms</td>
<td>Patient had sudden loss of consciousness</td>
<td>No residual effects</td>
</tr>
<tr>
<td>Neurocardiogenic Syncope</td>
<td>Prodrome with feelings of warmth, nausea; situational vagus present</td>
<td>Loss of consciousness usually with prodrome</td>
<td>Residual feelings of nausea and warmth</td>
</tr>
</tbody>
</table>

Physical Exam

- Check orthostatic BP’s
- Carotid sinus massage if attached to a monitor
- Cardiac exam (R/O aortic stenosis, HCM and arrhythmia)
- Neurologic exam – if negative, further neurologic eval. is of very low yield (head CT or MRI, carotid dopplers)

ECG Abnormalities Suggesting an Arrhythmic Cause of Syncope

1) Bifascicular block, defined as either LBBB or RBBB combined with left anterior or posterior fascicular block
2) Other intraventricular conduction abnormalities (QRS duration => 0.12 sec.
3) Mobitz Type II 2 degree AV block
4) Asymptomatic sinus bradycardia (<50 bpm) or sinoatrial block
5) Preexcitation complexes (WPW syndrome)
6) Prolonged QT interval
7) ECG typical of Brugada syndrome (RBBB with ST elevation in lead V1 to V3)
8) ECG suggestive of arrhythmogenic right ventricular dysplasia (ARVD) (negative T waves in right precordium, epsilon waves, and ventricular late potentials)
9) Q wave suggestive of myocardial infarction

Data from Brignole, M, Alboni, Benditt, D, et Al, Eur Heart J 2001, 22:1256
Indications for Ambulatory ECG Monitoring to Assess Symptoms Possibly Related to Rhythm Disturbances

Class I
1) Patients with unexplained syncope, near syncope, or episodesic dizziness in whom the cause is not obvious
2) Patients with unexplained recurrent palpitation

Class IIb
1) Patients with episodic shortness of breath, chest pain that is not otherwise explained
2) Patient with neurological events when transient atrial fibrillation or flutter is suspected
3) Patients with symptoms such as syncope, near syncope, episodic dizziness, or palpitation in whom a probable cause other than an arrhythmia has been identified but in whom symptoms persists despite treatment of this other cause

SYNCOPE

- Inpatient versus outpatient evaluation
- Usually dependent on severity (i.e. injury or MVA)
- Structural heart disease suggests a more malignant etiology and usually requires hospitalization

Neurocardiogenic Syncope
Neurocardiogenic Syncope

- Also known as the common faint
- Neurally mediated syndrome (NMS), vasovagal syncope (VVS) or vasodepressor syncope
- Often a diagnosis by exclusion
- Rule out cardiogenic and neurogenic causes first

In a prospective study of 341 patients with syncope, 33 percent had neurocardiogenic syncope.

Reflex response causing vasodilation and bradycardia resulting in systemic hypotension and cerebral hypoperfusion
Presumed Mechanism of Neurocardiogenic Syncope

Pathophysiology

- Both neural (Bezold-Jarisch and carotid sinus reflexes) and endogenous chemical pathways are thought to play a role
- 3 types of autonomic responses seen:
  1) Cardioinhibitory - increased parasympathetic tone manifested as sinus bradycardia, PR prolongation, and advanced atrioventricular block
  2) Vasodepressor response - decreased sympathetic tone which leads to hypotension
  3) Mixed cardioinhibitory and vasodepressor response

Tilt Table Test or Head-Up Tilt (HUT) Testing

Procedure:
Involves tilting patient from supine to 60-80 degrees angle to reproduce syncope

Two Phases:
Passive Phase: without drug
Active phase: isoproterenol infusion
  a) 1 ug/min
  b) 3-5 ug/min

Test Sensitivity: 67-83%
Test Specificity: 75%
Tilt Table Test

- Indications:
  1) Work-up of syncope in patients with structurally normal heart (normal ECG, ECHO, stress test or a non-diagnostic Holter)
  2) Men > 45 y.o. and women > 55 y.o. should undergo stress testing before the test
  3) Women of child bearing age should have a pregnancy test

Upright Tilt Table Test

- Measure HR and BP while tilting them upright
- Attempt to elicit symptoms
- Cannot be used to test efficacy of pharmacologic therapy

Carotid Sinus Massage

- Indication:
  a) patients > 40 years old with unknown etiology of syncope after initial evaluation
- Procedure:
  b) Continuous ECG and BP monitoring mandatory
  c) Carotid massage done for 5-10 sec. in both supine and erect positions
- Positive Result:
  a) symptoms are reproduced during or immediately after the massage
  b) asystole longer than 3 sec. and or
  c) a fall in SBP of =>50 mmHg

## Preventive Measures

- Avoid dehydration and severe dieting
- Liberal salt intake if not contraindicated
- Counterpressure support garments from ankles to waist
- Avoid prolonged periods of motionless standing
- Once with prodromal or trigger-assume a recumbent position and cough
- Avoid triggers like heat exposure, painful stimuli

## Treatment

- Reassurance, education, avoidance
- Support stockings, salt liberalization
- Beta blockers
- Midodrine
- Selective Serotonin Reuptake Inhibitors
- Fludrocortisone (Florinef)
- Drug therapy is often not very effective
What are the indications for pacemaker therapy in neurocardiogenic syncope?

- Non-random, observational
- RCTs comparing vs
- RCTs comparing vs

The North American Vasovagal Pacemaker Study (VPS)

Included
- >6 lifetime episodes
- + tilt-table test
  - (relative bradycardia)

Excluded
- Vascular, coronary, myocardial or conduction system disease

54 pts

27 dual-chamber pacemakers with rate-drop response
27 no pacemaker

Primary outcome: first recurrence of syncope

<table>
<thead>
<tr>
<th></th>
<th>Pacemaker</th>
<th>No pacemaker</th>
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<tbody>
<tr>
<td>Recurrence of Syncope</td>
<td>6/27 (22%)</td>
<td>19/27 (70%)</td>
</tr>
<tr>
<td>Time to recurrence</td>
<td>112 days</td>
<td>54 days</td>
</tr>
</tbody>
</table>

54 days
112 days

VPS

Limitations:
- Unblinded
- Small study size
- Time to first occurrence vs total disease burden

J. Am. Coll. Cardiol. 1999;33:16-20
**Vasovagal Syncope International Study (VASIS)**

- >3 episodes in last 2 yrs
- Tilt test cardioinhibition
  - Ventric. Rate <40 for 10 sec
  - Asystole >1 sec
- Repeat tilt testing: no difference
- Pacer arm 10/17 + tests
  - 5 had no bradycardia, 5 pacer did not prevent syncope
  - 1/7 pacer activated in neg test
- 3 episodes in last 2 yrs
- Tilt test cardioinhibition
  - Ventric. Rate <40 for 10 sec
  - Asystole >3 sec

**Permanent cardiac pacing versus medical treatment for the prevention of recurrent vasovagal syncope**

- 93 pts
  - 46 DDD pacemaker + rate drop
  - 47 atenolol 100mg daily
- Unblinded
- Older, highly symptomatic patients with an asystolic response to tilt testing in pacer group

**VPS II**

- >3 episodes in 2 years
- +tilt test
  - HR x BP < 6000/minmHg
- Risk of syncope at 6 months: 40% ODO, 31% DDD
  - RRR 30% (P = 0.14)
- Compared to VPS I
  - Fewer events in non-paced group in VPS II (40% vs 70%)
SYNPACE

- 6 events lifetime
- + tilt test
  - Asystolic: >3 secs
  - Mixed: bradycardic <60 bpm but no asystole
  - Vasodepressor: hypotension only, were excluded
- 29 pts randomized to pacemaker ON (16) or OFF (13)

Syncope recurred 8 (50%) in ON group, 5 (38%) in OFF group
- No significant difference
- Syncopal rates lower postimplantation for both groups
- Non-significant trend of pacing prolonging time to first occurrence

Conclusions

ACC/AHA/HRS 2008 Guidelines for Device based Therapy

Class IIa
Permanent pacing is reasonable for syncope without clear provocative events and with a hypersensitive cardioinhibitory response of 3 seconds or longer.

Class IIb
Permanent pacing may be considered for significantly symptomatic neurocardiogenic syncope associated with bradycardia documented spontaneously or at the time of tiltable testing.

Class III
Permanent pacing is not indicated for situational vasovagal syncope in which avoidance behavior is effective and preferred.

65yo F
HPI: LOC while sitting on toilet, no head trauma
PMH: Afib, HTN, HL, recurrent syncope

- Previous syncope: sitting in church, at restaurant, bowel movement
- hx + tilt table test, ILR bradycardic to 40s

88yo F
HPI: Attending to her friends when she falls to floor, +LOC, +loss bladder, +jerking movements of her arms and legs

64yo F
HPI: Walks in the door, finds her friends down, runs to call 911, steps on a banana peel, falls, no LOC

66yo F
HPI: Attending to her friends when she falls to floor, +LOC, +loss bladder, +jerking movements of her arms and legs

59yo F
HPI: Vomiting + diarrhea x3 days, stands up rapidly from supine, falls back onto couch, +LOC

85yo F
HPI: LOC while sitting on toilet, no head trauma
PMH: Afib, HTN, HL, recurrent syncope

- Previous syncope: sitting in church, at restaurant, bowel movement
- hx + tilt table test, ILR bradycardic to 40s

59yo F
HPI: Vomiting + diarrhea x3 days, stands up rapidly from supine, falls back onto couch, +LOC
## Recommendations for Driving in Patients with Syncope

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Disqualifying Criteria</th>
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<tbody>
<tr>
<td><strong>NMS (Neurally mediated syncope)</strong></td>
<td></td>
</tr>
<tr>
<td>VVS and CSH</td>
<td></td>
</tr>
<tr>
<td>- Single episodes, mild symptoms</td>
<td>No restrictions</td>
</tr>
<tr>
<td>- Severe symptoms</td>
<td>Utl symptoms controlled</td>
</tr>
<tr>
<td>- Situational forms</td>
<td>No restrictions</td>
</tr>
<tr>
<td>Syncope of uncertain cause</td>
<td>In case of severe syncope until cause identified, especially in patients with heart disease or at least 6 months without symptoms before (re) - licensing</td>
</tr>
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<tr>
<td>Cardiac Arrhythmias</td>
<td>Any disturbance of cardiac rhythm which is likely to cause syncope</td>
</tr>
<tr>
<td>Pacemaker implant</td>
<td>Within one week</td>
</tr>
<tr>
<td>Successful catheter ablation</td>
<td></td>
</tr>
<tr>
<td>ICD</td>
<td>Within 6 months if no arrhythmia recurrence and no disabling symptoms at time of ICD discharge.</td>
</tr>
</tbody>
</table>

If prophylactic ICD placement one week then no restrictions.
ESC Recommendations for Treatment of Neurocardiogenic Syncope

Class I
1) Explanation of the risk

Conclusions
ACC/AHA/HRS 2008 Guidelines for Device-based Therapy
Class IIa
- Permanent pacing is reasonable for syncope without clear provocative events and with a hypotensive cardioinhibitory response of 3 seconds or longer.

European Society of Cardiology Guidelines on Management of Syncope 2004
Class III
- Cardiac pacing in patients with cardioinhibitory vasovagal syncope with a frequency >5 attacks per year or severe physical injury or accident and age >40.

TTT/HUT (8/30/99)
- Nausea, diaphoresis, & altered gaze
Pacing
- DDD type of pacemaker
- Case to case basis

Rx Neurocardiogenic syncope
- Beta-blockers - most commonly effective therapy
- SSRI: sertraline, flouxetine or paroxetine
- Midodrine (alpha 1 adrenergic agonist)
- Florinef
- Theophylline