Ενδιαφέροντα θέματα για ειδικούς και μη ειδικούς: 
Ασθενής με συγκοπή

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Guidelines on syncope and pacing, by ESC, ACC/AHA

ACC/AHA/HRS 2008 Guidelines for Device-Based Therapy of Cardiac Rhythm Abnormalities
A Report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (Writing Committee to Revise the ACC/AHA/NASPE 2002 Guideline Update for Implantation of Cardiac Pacemakers and Antiarrhythmia Devices)

Developed in Collaboration With the American Association for Thoracic Surgery and Society of Thoracic Surgeons

Guidelines for the diagnosis and management of syncope (version 2009)
The Task Force for the Diagnosis and Management of Syncope of the European Society of Cardiology (ESC)

2013 ESC Guidelines on cardiac pacing and cardiac resynchronization therapy
The Task Force on cardiac pacing and resynchronization therapy of the European Society of Cardiology (ESC). Developed in collaboration with the European Heart Rhythm Association (EHRA).

2017 ACC/AHA/HRS Guideline for the Evaluation and Management of Patients With Syncope
A Report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines and the Heart Rhythm Society
Loss of consciousness: a common clinical problem
Significance of Syncope

“The only difference between syncope and sudden death is that in one you wake up”. 
A lot of terminology causing confusion in everyday clinical practice...
Clarification of Definitions

**Loss of Consciousness**
A cognitive state in which one lacks awareness of oneself and one’s situation, with an inability to respond to stimuli

**Transient LOC**
Self-limited loss of consciousness that can be divided into syncope and nonsyncope conditions

**Nonsyncope conditions:** not caused by cerebral hypoperfusion

**SYNCOPE:** a T-LOC due to transient global cerebral hypoperfusion
Syncope: Definition

Guidelines for the diagnosis and management of syncope (version 2009)

The Task Force for the Diagnosis and Management of Syncope of the European Society of Cardiology (ESC)

Syncope is a **SYMPTOM** of T-LOC (transient loss of consciousness) due to transient global cerebral hypoperfusion characterized by rapid onset, short duration, and spontaneous complete recovery.
Clarification of Definitions

Guidelines for the diagnosis and management of syncope (version 2009)

The Task Force for the Diagnosis and Management of Syncope of the European Society of Cardiology (ESC)

1.1 Definitions

**Syncope** is a T-LOC due to transient global cerebral hypoperfusion characterized by rapid onset, short duration, and spontaneous complete recovery.

This definition of syncope differs from others by including the cause of unconsciousness, i.e. transient global cerebral hypoperfusion. Without that addition, the definition of syncope becomes wide enough to include disorders such as epileptic seizures and concussion. In fact, the definition then becomes that of *T-LOC*, a
# Clarification of Definitions

<table>
<thead>
<tr>
<th>Term</th>
<th>Definition/Comments and References</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Syncope</strong></td>
<td>A symptom that presents with an abrupt, transient, complete loss of consciousness, associated with inability to maintain postural tone, with rapid and spontaneous recovery. The presumed mechanism is cerebral hypoperfusion (24,30). There should not be clinical features of other nonsyncope causes of loss of consciousness, such as seizure, antecedent head trauma, or apparent loss of consciousness (i.e., pseudosyncope) (24,30).</td>
</tr>
<tr>
<td><strong>Loss of consciousness</strong></td>
<td>A cognitive state in which one lacks awareness of oneself and one’s situation, with an inability to respond to stimuli.</td>
</tr>
<tr>
<td><strong>Transient loss of consciousness</strong></td>
<td>Self-limited loss of consciousness (30) can be divided into syncope and nonsyncope conditions. Nonsyncope conditions include but are not limited to seizures, hypoglycemia, metabolic conditions, drug or alcohol intoxication, and concussion due to head trauma. The underlying mechanism of syncope is presumed to be cerebral hypoperfusion, whereas nonsyncope conditions are attributed to different mechanisms.</td>
</tr>
<tr>
<td><strong>Presyncope</strong> (near-syncope)</td>
<td></td>
</tr>
</tbody>
</table>
## Classification of syncope

### Reflex (neurally-mediated) syncope
- **Vasovagal:**
  - Mediated by emotional distress: fear, pain, instrumentation, blood phobia.
  - Mediated by orthostatic stress.

- **Situational:**
  - Cough, sneeze.
  - Gastrointestinal stimulation (swallow, defaecation, visceral pain).
  - Micturition (post-micturition).
  - Post-exercise.
  - Post-prandial.
  - Others (e.g., laugh, brass instrument playing, weightlifting).

- **Carotid sinus syncope**

- **Atypical forms** (without apparent triggers and/or atypical presentation).

### Syncope due to orthostatic hypotension
- **Primary autonomic failure:**
  - Pure autonomic failure, multiple system atrophy, Parkinson’s disease with autonomic failure, Lewy body dementia.

- **Secondary autonomic failure:**
  - Diabetes, amyloidosis, uraemia, spinal cord injuries.

- **Drug-induced orthostatic hypotension:**
  - Alcohol, vasodilators, diuretics, phenothiazines, antidepressants.

- **Volume depletion:**
  - Haemorrhage, diarrhoea, vomiting, etc.

### Cardiac syncope (cardiovascular)
- **Arrhythmia as primary cause:**
  - Bradycardia:
    - Sinus node dysfunction (including brady-cardia/tachycardia syndrome).
    - Atrioventricular conduction system disease.
    - Implanted device malfunction.

- **Tachycardia:**
  - Supraventricular.
  - Ventricular (idiopathic, secondary to structural heart disease or to channelopathies).

- **Drug induced bradycardia and tachyarrhythmias**

- **Structural disease:**
  - Cardiac: cardiac valvular disease, acute myocardial infarction/ischaemia, hypertrophic cardiomyopathy, cardiac masses (atrial myxoma, tumors, etc), pericardial disease/tamponade, congenital anomalies of coronary arteries, prosthetic valves dysfunction.
  - Others: pulmonary embolus, acute aortic dissection, pulmonary hypertension.
Causes of Syncope

- Unknown: 36.6%
- Vasovagal: 21.2%
- Cardiac: 9.5%
- Stroke or transient ischemic attack: 4.1%
- Orthostatic: 9.4%
- Medication: 6.8%
- Other: 7.5%
<table>
<thead>
<tr>
<th>Age</th>
<th>Source</th>
<th>Reflex %</th>
<th>OH %</th>
<th>CV %</th>
<th>Non-Sync. %</th>
<th>Unexplained %</th>
<th>Setting</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt; 40 yrs</td>
<td>†</td>
<td>51</td>
<td>2.5</td>
<td>1.1</td>
<td>18</td>
<td>27</td>
<td>ED &amp; CPU</td>
</tr>
<tr>
<td>40-60 yrs</td>
<td>†</td>
<td>37</td>
<td>6</td>
<td>3</td>
<td>19</td>
<td>34</td>
<td>ED &amp; CPU</td>
</tr>
<tr>
<td>&lt; 65 yrs</td>
<td>‡</td>
<td>68.5</td>
<td>0.5</td>
<td>12</td>
<td></td>
<td>19</td>
<td>CD</td>
</tr>
<tr>
<td>60/65 yrs</td>
<td>‡</td>
<td>52</td>
<td>3</td>
<td>34</td>
<td></td>
<td>11</td>
<td>CD</td>
</tr>
<tr>
<td></td>
<td>§</td>
<td>62</td>
<td>8</td>
<td>11</td>
<td></td>
<td>14</td>
<td>GD</td>
</tr>
<tr>
<td></td>
<td>†</td>
<td>25</td>
<td>8.5</td>
<td>13</td>
<td>12.5</td>
<td>41</td>
<td>ED &amp; CPU</td>
</tr>
<tr>
<td>&gt; 75 yrs</td>
<td>§</td>
<td>36</td>
<td>30</td>
<td>16</td>
<td></td>
<td>9</td>
<td>GD</td>
</tr>
</tbody>
</table>

† = Olde Norkamp  
‡ = Del Rosso  
§ = Ungar  
ED = emergency department  
CPU = chest pain unit  
CD = cardiology department  
GD = geriatric department
Syncope: an important clinical entity
Why?
Syncope: the impact

- ~40% of the population will have at least one syncopal event in their lifetime

- 10% of falls by elderly are believed due to syncope

- **Major morbidity** reported in 6\(^{\text{1}}\)
  (e.g., fractures, motor vehicle accident)

- **Minor injury** reported in 29\(^{\text{1}}\)
  (e.g., lacerations, bruises)

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Syncope: High Incidence and Likely to Increase

- 7814 participants followed for an average of 17 years, 822 reported syncope

- Estimated 10-year cumulative incidence of syncope was 6%

- The incidence rates increased with age, with a sharp rise at 70 years

- 22% of the study participants with syncope had a recurrence

Soteriades et al. NEJM 2002; 347: 878
Epidemiology

Schematic presentation of the distribution of age and cumulative incidence of first episode of syncope in the general population from subjects up to 80 years is shown.

Syncope: QOL Impact

- Anxiety/Depression: 73%¹
- Alter Daily Activities: 71%²
- Restricted Driving: 60%²
- Change Employment: 37%²

Syncope

• In one-third of participants, a cause for syncope could not be assigned.
• Risk of death was increased by 31% among all participants with syncope.
• Risk of death was doubled among participants with cardiac syncope.
• Neurologic T-LOC (CVA, TIA, seizure) also associated with three-fold risk of stroke.

Soteriades et al. NEJM 2002; 347: 878
A pt with Syncope: how should I approach?
Initial evaluation

The initial evaluation should answer the key questions:

1. Syncope: is it cardiac or not?
2. Has the underlying aetiological diagnosis been determined?
3. Are there data on the presence of a high risk of cardiovascular events or death?
Guidelines for the diagnosis and management of syncope (version 2009)

The Task Force for the Diagnosis and Management of Syncope of the European Society of Cardiology (ESC)

Conditions incorrectly diagnosed as syncope

- Disorders with partial or complete (LOC) but without cerebral hypoperfusion:
  - Epilepsy,
  - Metabolic disorders including hypoglycemia, hypoxia, hyperventilation with hypocapnia,
  - Intoxication,
  - Vertebrobasilar TIA (Transient Ischemic Attack).

- Disorders without impairment of consciousness:
  - Cataplexy,
  - Drop attacks,
  - Falls,
  - Functional (psychogenic pseudosyncope),
  - TIA of carotid origin.
Syncope initial evaluation

History, Physical Examination, ECG

Transient loss of consciousness

Suspected syncope

Evaluation as clinically indicated

Yes

Initial evaluation: history, physical examination, and ECG (Class I)

Cause of syncope certain

Risk assessment

Cause of syncope uncertain

Treatment

Further evaluation

2017 ACC/AHA/HRS Guideline for the Evaluation and Management of Patients With Syncope
Causes of True Syncope

**Neurally-Mediated**
- VVS
- CSS
- Situational
  - Cough
  - Post-Micturition

**Orthostatic**
- Drug-Induced
- Volume depletion
- ANS Failure
  - Primary
  - Secondary

**Cardiac Arrhythmia**
- Brady
  - SN Dysfunction
  - AV Block
- Tachy
  - VT
  - SVT
- Channelopathy

**Structural Cardio-Pulmonary**
- Myocardial Ischemia
- DCM
- Aortic Stenosis
- HCM
- PH
- ARVC
- Aortic Dissection

Unexplained Causes = Approximately 1/3

DG Benditt, MD. U of M Cardiac Arrhythmia Center
## Clarification of Definitions

<table>
<thead>
<tr>
<th>Cardiac (cardiovascular) syncope</th>
<th>Syncope caused by bradycardia, tachycardia, or hypotension due to low cardiac index, blood flow obstruction, vasodilatation, or acute vascular dissection (35,36).</th>
</tr>
</thead>
<tbody>
<tr>
<td>Noncardiac syncope</td>
<td>Syncope due to noncardiac causes which include reflex syncope, OH, volume depletion, dehydration, and blood loss (35).</td>
</tr>
</tbody>
</table>

### Reflex (neurally mediated) syncope

- **Vasovagal syncope (VVS)**
  - The most common form of reflex syncope mediated by the vasovagal reflex. VVS: 1) may occur with upright posture (standing or seated or with exposure to emotional stress, pain, or medical settings; 2) typically is characterized by diaphoresis, warmth, nausea, and pallor; 3) is associated with vasodepressor hypotension and inappropriate bradycardia; and 4) is often followed by fatigue. Typical features may be absent in older patients (24). VVS is often preceded by identifiable triggers and/or by a characteristic prodrome. The diagnosis is made primarily on the basis of a thorough history, physical examination, and eyewitness observation, if available.

- **Carotid sinus syndrome**
  - Reflex syncope associated with carotid sinus hypersensitivity (30). Carotid sinus hypersensitivity is present when a pause $\geq 3$ s and/or a decrease of systolic pressure $\geq 50$ mm Hg occurs upon stimulation of the carotid sinus. It occurs more frequently in older patients. Carotid sinus hypersensitivity can be associated with varying degrees of symptoms. Carotid sinus syndrome is defined when syncope occurs in the presence of carotid sinus hypersensitivity.

- **Situational syncope**
  - Reflex syncope associated with a specific action, such as coughing, laughing, swallowing, micturition, or defecation. These syncope events are closely associated with specific physical functions.
### Clarification of Definitions

<table>
<thead>
<tr>
<th>Definition</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Orthostatic hypotension (OH)</strong></td>
<td>A drop in systolic BP of ≥20 mm Hg or diastolic BP of ≥10 mm Hg with assumption of an upright posture (31).</td>
</tr>
<tr>
<td><strong>Initial (immediate) OH</strong></td>
<td>A transient BP decrease within 15 s after standing, with presyncope or syncope (31,32).</td>
</tr>
<tr>
<td><strong>Classic OH</strong></td>
<td>A sustained reduction of systolic BP of ≥20 mm Hg or diastolic BP of ≥10 mm Hg within 3 min of assuming upright posture (31).</td>
</tr>
<tr>
<td><strong>Delayed OH</strong></td>
<td>A sustained reduction of systolic BP of ≥20 mm Hg (or 30 mm Hg in patients with supine hypertension) or diastolic BP of ≥10 mm Hg that takes &gt;3 min of upright posture to develop. The fall in BP is usually gradual until reaching the threshold (31).</td>
</tr>
<tr>
<td><strong>Neurogenic OH</strong></td>
<td>A subtype of OH that is due to dysfunction of the autonomic nervous system and not solely due to environmental triggers (e.g., dehydration or drugs) (33,34). Neurogenic OH is due to lesions involving the central or peripheral autonomic nerves.</td>
</tr>
<tr>
<td><strong>Psychogenic pseudosyncope</strong></td>
<td>A syndrome of apparent but not true loss of consciousness that may occur in the absence of identifiable cardiac, reflex, neurological, or metabolic causes (30).</td>
</tr>
<tr>
<td><strong>Unexplained syncope (syncope of undetermined etiology)</strong></td>
<td>Syncope for which a cause is undetermined after an initial evaluation that is deemed appropriate by the experienced healthcare provider. The initial evaluation includes but is not limited to a thorough history, physical examination, and ECG.</td>
</tr>
</tbody>
</table>
Clarification of Definitions

Orthostatic intolerance: A syndrome consisting of a constellation of symptoms that include frequent, recurrent, or persistent lightheadedness, palpitations, tremulousness, generalized weakness, blurred vision, exercise intolerance, and fatigue upon standing. These symptoms can occur with or without orthostatic tachycardia. OH, or syncope (24). Individuals with orthostatic intolerance have ≥1 of these symptoms associated with reduced ability to maintain upright posture.

Orthostatic tachycardia: A sustained increase in heart rate of ≥30 bpm within 10 min of moving from a recumbent to a quiet (nonexertional) standing position (or ≥40 bpm in individuals 12-19 y of age) (24,30,31).

Postural (orthostatic) tachycardia syndrome (POTS): A clinical syndrome usually characterized by all of the following: 1) frequent symptoms that occur with standing (e.g., lightheadedness, palpitations, tremulousness, generalized weakness, blurred vision, exercise intolerance, and fatigue); and 2) an increase in heart rate of ≥30 bpm during a positional change from supine to standing (or ≥40 bpm in those 12-19 y of age); and 3) the absence of OH (>20 mm Hg reduction in systolic BP). Symptoms associated with POTS include those that occur with standing (e.g., lightheadedness, palpitations); those not associated with particular postures (e.g., bloating, nausea, diarrhea, abdominal pain); and those that are systemic (e.g., fatigue, sleep disturbance, migraine headaches) (37). The standing heart rate is often >120 bpm (31,38-42).
Orthostatic hypotension

POTS (postural tachycardia syndrome)

Neurogenic orthostatic hypotension

Pronounced fall in blood pressure with a blunted heart rate response

BP responses in different types of syncope

Exaggerated heart rate response without syncope
### Characteristics associated with cardiac causes of syncope

**More Often Associated With Cardiac Causes of Syncope**

- Older age (>60 y)
- Male sex
- Presence of known ischemic heart disease, structural heart disease, previous arrhythmias, or reduced ventricular function
- Brief prodrome, such as palpitations, or sudden loss of consciousness without prodrome
- Syncope during exertion
- Syncope in the supine position
- Low number of syncope episodes (1 or 2)
- Abnormal cardiac examination
- Family history of inheritable conditions or premature SCD (<50 y of age)
- Presence of known congenital heart disease

*2017 ACC/AHA/HRS Guideline for the Evaluation and Management of Patients With Syncope*
Characteristics associated with non cardiac causes of syncope

<table>
<thead>
<tr>
<th>More Often Associated With Noncardiac Causes of Syncope</th>
</tr>
</thead>
<tbody>
<tr>
<td>Younger age</td>
</tr>
<tr>
<td>No known cardiac disease</td>
</tr>
<tr>
<td>Syncope only in the standing position</td>
</tr>
<tr>
<td>Positional change from supine or sitting to standing</td>
</tr>
<tr>
<td>Presence of prodrome: nausea, vomiting, feeling warmth</td>
</tr>
<tr>
<td>Presence of specific triggers: dehydration, pain, distressful stimulus, medical environment</td>
</tr>
<tr>
<td>Situational triggers: cough, laugh, micturition, defecation, deglutition</td>
</tr>
<tr>
<td>Frequent recurrence and prolonged history of syncope with similar characteristics</td>
</tr>
</tbody>
</table>
Recommendations
Carotid sinus massage (CSM)

- **Indications:**
  - CSM is indicated in patients > 40 years with syncope of unknown aetiology after initial evaluation.
  - CSM should be avoided in patients with previous TIA or stroke within the past 3 months and in patients with carotid murmurs (except if carotid Doppler studies exclude significant stenosis).

- **Diagnostic criteria:**
  - CSM is diagnostic if syncope is reproduced in presence of asystole longer than 3 s and/or fall in SBP > 50 mmHg.
ECG

Guidelines for the diagnosis and management of syncope (version 2009)
The Task Force for the Diagnosis and Management of Syncope of the European Society of Cardiology (ESC)

- Abnormal in 50% of patients. Identifies potential cause in 2-11%
  - Pre-excitation
  - Conduction Delays
  - MI
  - LVH/RVH (Hypertrophic CM, Aortic Stenosis, Pulmonary HTN)
  - QT Interval (QTc=460) should raise suspicion
  - Brugada Abnormalities
  - Epsilon Waves (ARVC)
ECG changes in the Brugada syndrome

Strickberger, S. A. et al. Circulation 2006;113:316-327
Different patterns of QT prolongation in LQTS

LQT3

Chromosome 3

II

aVF

V5

Long ST segment
Peaked T wave

LQT2

Chromosome 7

Notched T wave

LQT1

Chromosome 11

Broad based T wave

Strickberger, S. A. et al. Circulation 2006;113:316-327
Twelve-lead ECG in normal sinus rhythm with epsilon wave

Kenigsberg, D. N. et al. Circulation 2007;115:e538-e539
“Syncope may be an acute result of major hemodynamic abnormalities or a manifestation of serious underlying disease”
Diagnostic flowchart in patients with suspected T-LOC
T-LOC – suspected syncope

Initial evaluation

Syncope

Certain diagnosis
Treatment

Uncertain diagnosis

Risk stratification

High risk**
Early evaluation & treatment

Low risk recurrent syncopes
Cardiac or neurally-mediated tests as appropriate
Delayed treatment guided by ECG documentation

Low risk Single or rare
No further evaluation

T-LOC non syncopal
Confirm with specific test or specific consultation
Treatment

www.escardio.org/guidelines
European Heart Journal 2009;30:2631-2671
Conditions that may impose hospital admission

<table>
<thead>
<tr>
<th>Cardiac Arrhythmic Conditions</th>
<th>Cardiac or Vascular Nonarrhythmic Conditions</th>
<th>Noncardiac Conditions</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sustained or symptomatic VT</td>
<td>Cardiac ischemia</td>
<td>Severe anemia/gastrointestinal bleeding</td>
</tr>
<tr>
<td>Symptomatic conduction system disease or Mobitz II or third-degree heart block</td>
<td>Severe aortic stenosis</td>
<td>Major traumatic injury due to syncope</td>
</tr>
<tr>
<td>Symptomatic bradycardia or sinus pauses not related to neurally mediated syncope</td>
<td>Cardiac tamponade</td>
<td>Persistent vital sign abnormalities</td>
</tr>
<tr>
<td>Symptomatic SVT</td>
<td>HCM</td>
<td></td>
</tr>
<tr>
<td>Pacemaker/ICD malfunction</td>
<td>Severe prosthetic valve dysfunction</td>
<td></td>
</tr>
<tr>
<td>Inheritable cardiovascular conditions predisposing to arrhythmias</td>
<td>Pulmonary embolism</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Aortic dissection</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Acute HF</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Moderate-to-severe LV dysfunction</td>
<td></td>
</tr>
</tbody>
</table>

HCM indicates hypertrophic cardiomyopathy; HF, heart failure; ICD, implantable cardioverter-defibrillator; LV, left ventricular; SVT, supraventricular tachycardia; and VT, ventricular tachycardia.
## Short and long term morbidity and mortality risk of syncope

<table>
<thead>
<tr>
<th>Short-Term Risk Factors (≤30 d)</th>
<th>Long-Term Risk Factors (&gt;30 d)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>History: Outpatient Clinic or ED Evaluation</strong></td>
<td></td>
</tr>
<tr>
<td>Male sex (74,85,101,102)</td>
<td>Male sex (68,90)</td>
</tr>
<tr>
<td>Older age (&gt;60 y) (88)</td>
<td>Older age (67,74,75,90)</td>
</tr>
<tr>
<td>No prodrome (68)</td>
<td>Absence of nausea/vomiting preceding syncopeal event (93)</td>
</tr>
<tr>
<td>Palpitations preceding loss of consciousness (83)</td>
<td>VA (68,90)</td>
</tr>
<tr>
<td>Exertional syncope (83)</td>
<td>Cancer (68)</td>
</tr>
<tr>
<td>Structural heart disease (70,83,88,101,103)</td>
<td>Structural heart disease (68,103)</td>
</tr>
<tr>
<td>HF (74,83,85,88)</td>
<td>HF (90)</td>
</tr>
<tr>
<td>Cerebrovascular disease (70)</td>
<td>Cerebrovascular disease (68)</td>
</tr>
<tr>
<td>Family history of SCD (70)</td>
<td>Diabetes mellitus (104)</td>
</tr>
<tr>
<td>Trauma (68,101)</td>
<td>High CHADS-2 score (95)</td>
</tr>
<tr>
<td><strong>Physical Examination or Laboratory Investigation</strong></td>
<td></td>
</tr>
<tr>
<td>Evidence of bleeding (83)</td>
<td>Abnormal ECG (84,90,93)</td>
</tr>
<tr>
<td>Persistent abnormal vital signs (70)</td>
<td>Lower GFR</td>
</tr>
<tr>
<td>Abnormal ECG (68,72,74,75,105)</td>
<td></td>
</tr>
<tr>
<td>Positive troponin (75)</td>
<td></td>
</tr>
</tbody>
</table>

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2017 ACC/AHA/HRS Guideline for the Evaluation and Management of Patients With Syncope
### TABLE 6  Examples of Syncope Risk Scores

<table>
<thead>
<tr>
<th>Study/Reference</th>
<th>Year</th>
<th>Sample N</th>
<th>Events N (%)</th>
<th>Outcome Definition</th>
<th>ED Events*</th>
<th>Predictors</th>
<th>NPV (%)†</th>
</tr>
</thead>
<tbody>
<tr>
<td>Martin (90)</td>
<td>1997</td>
<td>252</td>
<td>104 (41%)</td>
<td>1-y death/arrhythmia</td>
<td>Yes</td>
<td>Abnormal ECG; &gt;45 y of age; VA; HF</td>
<td>93</td>
</tr>
<tr>
<td>Sarasin (74)</td>
<td>2003</td>
<td>175</td>
<td>30 (17%)</td>
<td>Inpatient arrhythmia</td>
<td>Yes</td>
<td>Abnormal ECG; &gt;65 y of age; HF</td>
<td>98</td>
</tr>
<tr>
<td>OESIL (67)</td>
<td>2003</td>
<td>270</td>
<td>31 (11%)</td>
<td>1-y death</td>
<td>N/A</td>
<td>Abnormal ECG; &gt;65 y of age; no prodrome; cardiac history</td>
<td>100</td>
</tr>
<tr>
<td>SFSPR (72)</td>
<td>2004</td>
<td>684</td>
<td>79 (12%)</td>
<td>7-d serious events§</td>
<td>Yes</td>
<td>Abnormal ECG; dyspnea; hematocrit; systolic BP &lt; 90 mm Hg; HF</td>
<td>99</td>
</tr>
<tr>
<td>Boston Syncope Rule (70)</td>
<td>2007</td>
<td>293</td>
<td>68 (23%)</td>
<td>30-d serious events</td>
<td></td>
<td>Yes</td>
<td>Symptoms of acute coronary syndrome; worrisome cardiac history; family history of SCD; VHD; signs of conduction disease; volume depletion; persistent abnormal vital signs; primary central nervous event</td>
</tr>
<tr>
<td>Del Rosso (69)</td>
<td>2008</td>
<td>260</td>
<td>44 (17%)</td>
<td>Cardiac etiology</td>
<td>N/A</td>
<td>Abnormal ECG/cardiac history; palpitations; exertional; supine; precipitant (a low-risk factor); autonomic prodrome (low-risk factors)</td>
<td>99</td>
</tr>
<tr>
<td>STEPS (68)</td>
<td>2008</td>
<td>676</td>
<td>41 (6%)</td>
<td>10-d serious events¶</td>
<td>Yes</td>
<td>Abnormal ECG; trauma; no prodrome; male sex</td>
<td>—</td>
</tr>
<tr>
<td>Syncope Risk Score (75)</td>
<td>2009</td>
<td>2,584</td>
<td>173 (7%)</td>
<td>30-d serious events¶</td>
<td>No</td>
<td>Abnormal ECG; &gt;90 y of age; male sex; positive troponin; history of arrhythmia; systolic BP &gt; 160 mm Hg; near-syncope (a low-risk factor)</td>
<td>97</td>
</tr>
<tr>
<td>ROSE (73)</td>
<td>2010</td>
<td>550</td>
<td>40 (7%)</td>
<td>30-d serious events¶</td>
<td>Yes</td>
<td>Abnormal ECG; B-natriuretic peptide; hemoglobin; O₂Sat; fecal occult blood</td>
<td>98</td>
</tr>
</tbody>
</table>

Use of risk stratification scores may be reasonable in the management of patients with syncope (67, 68, 72, 73, 75, 87, 89, 100, 101).
Syncope initial evaluation

Serious medical conditions present? (Table 7)

Yes
- Inpatient evaluation (Class I)

No
- Manage presumptive reflex-mediated syncope in outpatient setting (Class IIa)
- Structured ED observation protocol for intermediate-risk pts (Class IIa)
- Manage selected pts with suspected cardiac syncope in outpatient setting (Class IIb)

Colors correspond to Class of Recommendation in Table 1.
ED indicates emergency department; pts, patients.
Further evaluation
Additional Evaluation and Diagnosis

Initial evaluation: history, physical exam, ECG (Class I)

- Initial evaluation clear
  - No additional evaluation needed*
  - Targeted blood testing (Class IIa)†

- Initial evaluation unclear
  - Initial evaluation suggests reflex syncope
    - Referral for autonomic evaluation (Class IIa)†
  - Initial evaluation suggests neurogenic OH
    - Tilt-table testing (Class IIa)†
  - Initial evaluation suggests CV abnormalities
    - Cardiac monitor selected based on frequency and nature (Class I)

Options
- Stress testing (Class IIa)†
- TTE (Class IIa)†
- EPS (Class IIa)†
- MRI or CT (Class IIb)†
- Implantable cardiac monitor (Class IIa)†
- Ambulatory external cardiac monitor (Class IIa)†

Colors correspond to Class of Recommendation in Table 1.

*Applies to patients after a normal initial evaluation without significant injury or cardiovascular morbidities; patients followed up by primary care physician as needed.

†In selected patients (see Section 1.4).

CT indicates computed tomography; CV, cardiovascular; ECG, electrocardiogram; EPS, electrophysiological study; MRI, magnetic resonance imaging; OH, orthostatic hypotension; and TTE, transthoracic echocardiography.
## Diagnostic Assessment: Yields

<table>
<thead>
<tr>
<th>Procedure</th>
<th>Yield (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Initial Evaluation</strong></td>
<td></td>
</tr>
<tr>
<td>History, Physical Exam, ECG, Cardiac Massage</td>
<td>38-40</td>
</tr>
<tr>
<td><strong>Other Tests/Procedures</strong></td>
<td></td>
</tr>
<tr>
<td>Head-Up Tilt</td>
<td>27</td>
</tr>
<tr>
<td>External Cardiac Monitoring</td>
<td>5-13</td>
</tr>
<tr>
<td>Insertable Loop Recorder (ILR)</td>
<td>43-88(^{3-5})</td>
</tr>
<tr>
<td>EP Study</td>
<td>&lt;2-5</td>
</tr>
<tr>
<td>Exercise Test</td>
<td>0.5</td>
</tr>
<tr>
<td>EEG</td>
<td>0.3-0.5</td>
</tr>
<tr>
<td>MRI</td>
<td>No data available(^6)</td>
</tr>
</tbody>
</table>
Transthoracic echocardiography can be useful in selected patients presenting with syncope if structural heart disease is suspected.

CT or MRI may be useful in selected patients presenting with syncope of suspected cardiac etiology.

Routine cardiac imaging is not useful in the evaluation of patients with syncope unless cardiac etiology is suspected on the basis of an initial evaluation, including history, physical examination, or ECG.
Heart Monitoring Options

- **12-Lead**
  - 10 Seconds

- **Holter Monitor**
  - 2 Days

- **Event Recorders** (non-lead and loop)
  - 7-30 Days

- **ILR**
  - Up to 14 Months

Cardiac Monitoring

Guidelines for the diagnosis and management of syncope (version 2009)

The Task Force for the Diagnosis and Management of Syncope of the European Society of Cardiology (ESC)

- ECG monitoring is indicated in patients with clinical or ECG features suggesting arrhythmic syncope.
- Immediate in-hospital monitoring (in bed or telemetric) is indicated in high risk patients.
- Holter monitoring is indicated in patients with frequent syncope or presyncope (≥ 1 per week).
- ILR is indicated in:
  - An early phase of evaluation in patients with recurrent syncope of uncertain origin, absence of high-risk criteria and high likelihood of recurrence within battery longevity of the device.
  - High-risk patients in whom a comprehensive evaluation did not demonstrate a cause of syncope or lead to a specific treatment.
- ILR should be considered to assess the contribution of bradycardia before to consider cardiac pacing in patients with suspected or certain reflex syncope presenting with frequent or traumatic syncopal episodes.
- External loop recorders should be considered in patients who have inter-symptom intervals ≤ 4 weeks.

2017 ACC/AHA/HRS Guideline for the Evaluation and Management of Patients With Syncope

<table>
<thead>
<tr>
<th>Level</th>
<th>Code</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>C</td>
<td>The choice of a specific cardiac monitor should be determined on the basis of the frequency and nature of syncope events.</td>
</tr>
<tr>
<td>I</td>
<td>B</td>
<td>To evaluate selected ambulatory patients with syncope of suspected arrhythmic etiology, the following external cardiac monitoring approaches can be useful:</td>
</tr>
<tr>
<td>I</td>
<td>B</td>
<td>1. Holter monitor</td>
</tr>
<tr>
<td>I</td>
<td>B</td>
<td>2. Transtelephonic monitor</td>
</tr>
<tr>
<td>I</td>
<td>B</td>
<td>3. External loop recorder</td>
</tr>
<tr>
<td>I</td>
<td>B</td>
<td>4. Patch recorder</td>
</tr>
<tr>
<td>IIa</td>
<td>B-NR</td>
<td>5. Mobile cardiac outpatient telemetry</td>
</tr>
<tr>
<td>IIa</td>
<td>B-R</td>
<td>To evaluate selected ambulatory patients with syncope of suspected arrhythmic etiology, an ICM can be useful.</td>
</tr>
</tbody>
</table>
### Guidelines for the diagnosis and management of syncope (version 2009)

The Task Force for the Diagnosis and Management of Syncope of the European Society of Cardiology (ESC)

- Tilt testing is indicated in case of unexplained single syncopal episode in high-risk settings* or recurrent episodes in the absence of organic heart disease, after cardiac causes of syncope have been excluded.
- Tilt testing is indicated when it is needed to demonstrate susceptibility to reflex syncope to the patient.
- Tilt testing should be considered to discriminate between reflex and OH syncope.
- Tilt testing may be considered for differentiating syncope with jerking movements from epilepsy.
- Tilt testing may be indicated for evaluating patients with recurrent unexplained falls.
- Tilt testing may be indicated for evaluating patients with frequent syncope and psychiatric disease.
- Tilt testing is not recommended for assessment of treatment.
- Isoproterenol tilt testing is contraindicated in patients with ischaemic heart disease.

---

### 2017 ACC/AHA/HRS Guideline for the Evaluation and Management of Patients With Syncope

<table>
<thead>
<tr>
<th>Level</th>
<th>Grade</th>
<th>Recommendation</th>
</tr>
</thead>
<tbody>
<tr>
<td>IIa</td>
<td>B-R</td>
<td>If the diagnosis is unclear after initial evaluation, tilt-table testing can be useful for patients with suspected VVS.</td>
</tr>
<tr>
<td>IIa</td>
<td>B-NR</td>
<td>Tilt-table testing can be useful for patients with syncope and suspected delayed OH when initial evaluation is not diagnostic.</td>
</tr>
<tr>
<td>IIb</td>
<td>C</td>
<td>Tilt-table testing is reasonable to distinguish convulsive syncope from epilepsy in selected patients.</td>
</tr>
<tr>
<td>IIa</td>
<td>B-NR</td>
<td>Tilt-table testing is reasonable to establish a diagnosis of pseudosyncope.</td>
</tr>
<tr>
<td>III</td>
<td>B-C</td>
<td>Tilt-table testing is not recommended to predict a response to medical treatments for VVS.</td>
</tr>
</tbody>
</table>
Stress Testing

Guidelines for the diagnosis and management of syncope (version 2009)
The Task Force for the Diagnosis and Management of Syncope of the European Society of Cardiology (ESC)

- **Indications:**
  - Exercise testing is indicated in patients who experience syncope during or shortly after exertion.

- **Diagnostic criteria:**
  - Exercise testing is diagnostic when syncope is reproduced during or immediately after exercise in the presence of ECG abnormalities or severe hypotension.
  - Exercise testing is diagnostic if Mobitz II 2nd degree or 3rd degree AV block develop during exercise even without syncope.
Electrophysiological Testing

Guidelines for the diagnosis and management of syncope (version 2009)
The Task Force for the Diagnosis and Management of Syncope of the European Society of Cardiology (ESC)

- Indications:
  - In patients with ischaemic heart disease, EPS is indicated when initial evaluation suggests an arrhythmic cause of syncope unless there is already an established indication for ICD.
  - In patients with BBB, EPS should be considered when non invasive tests failed to make the diagnosis.
  - In patients with syncope preceded by sudden and brief palpitations non invasive tests failed to make the diagnosis.
  - In patients with Brugada syndrome, ARVC and hypertrophic cardiomyopathy (in selected cases).
  - In patients with high-risk occupations requiring to exclude a CV cause (in selected cases).
  - EPS is not recommended in patients with normal ECG, no heart disease and no palpitations.

<table>
<thead>
<tr>
<th>Level</th>
<th>Grade</th>
<th>Recommendation</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>B</td>
<td>EPS can be useful for evaluation of selected patients with syncope of suspected arrhythmic etiology.</td>
</tr>
<tr>
<td>IIa</td>
<td>B-NR</td>
<td>EPS is not recommended for syncope evaluation in patients with a normal ECG and normal cardiac structure and function, unless an arrhythmic etiology is suspected.</td>
</tr>
<tr>
<td>III: No Benefit</td>
<td>B-NR</td>
<td></td>
</tr>
<tr>
<td>IIb</td>
<td>C</td>
<td></td>
</tr>
<tr>
<td>IIb</td>
<td>C</td>
<td></td>
</tr>
<tr>
<td>III</td>
<td>B</td>
<td></td>
</tr>
</tbody>
</table>
### Neurological Testing

#### Autonomic Evaluation

<table>
<thead>
<tr>
<th>COR</th>
<th>LOE</th>
<th>Recommendation</th>
</tr>
</thead>
<tbody>
<tr>
<td>IIA</td>
<td>C-LD</td>
<td>Referral for autonomic evaluation can be useful to improve diagnostic and prognostic accuracy in selected patients with syncope and known or suspected neurodegenerative disease.</td>
</tr>
</tbody>
</table>

- Determine the underlying cause of neurogenic OH
- Provide prognostic information
- Have therapeutic implications.
### Neurological Testing

<table>
<thead>
<tr>
<th>COR</th>
<th>LOE</th>
<th>Recommendations</th>
</tr>
</thead>
<tbody>
<tr>
<td>IIa</td>
<td>C-LD</td>
<td>Simultaneous monitoring of an EEG and hemodynamic parameters during tilt-table testing can be useful to distinguish among syncope, pseudosyncope, and epilepsy.</td>
</tr>
<tr>
<td>III: No Benefit</td>
<td>B-NR</td>
<td>MRI and CT of the head are not recommended in the routine evaluation of patients with syncope in the absence of focal neurological findings or head injury that support further evaluation.</td>
</tr>
<tr>
<td>III: No Benefit</td>
<td>B-NR</td>
<td>Carotid artery imaging is not recommended in the routine evaluation of patients with syncope in the absence of focal neurological findings that support further evaluation.</td>
</tr>
<tr>
<td>III: No Benefit</td>
<td>B-NR</td>
<td>Routine recording of an EEG is not recommended in the evaluation of patients with syncope in the absence of specific neurological features suggestive of a seizure.</td>
</tr>
</tbody>
</table>
Neurally Mediated Syncope
Vasovagal Syncope: Pace or not?

<table>
<thead>
<tr>
<th>Study or sub-category</th>
<th>Treatment</th>
<th>Control</th>
<th>OR (random) 95% CI</th>
<th>OR (random) 95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>nN</td>
<td>nN</td>
<td></td>
<td></td>
</tr>
<tr>
<td>01 Active pacemaker versus medical/no therapy</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Flammg</td>
<td>0/10</td>
<td>6/10</td>
<td>0.03 [0.00, 0.72]</td>
<td></td>
</tr>
<tr>
<td>SYQMT</td>
<td>2/46</td>
<td>12/47</td>
<td>0.13 [0.03, 0.63]</td>
<td></td>
</tr>
<tr>
<td>VASIS</td>
<td>1/19</td>
<td>14/23</td>
<td>0.04 [0.00, 0.32]</td>
<td></td>
</tr>
<tr>
<td>VPS I</td>
<td>6/27</td>
<td>19/27</td>
<td>0.12 [0.04, 0.41]</td>
<td></td>
</tr>
<tr>
<td>Subtotal (95% CI)</td>
<td>10/2</td>
<td>107</td>
<td>0.09 [0.04, 0.22]</td>
<td></td>
</tr>
<tr>
<td>Total events: 9 (Treatment), 51 (Control)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Test for heterogeneity: $\chi^2 = 1.56, df = 3 (P = 0.67)$, $P = 0%$</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Test for overall effect: $Z = 5.48 (P &lt; 0.00001)$</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>02 Active pacemaker comparison</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ammaradi</td>
<td>0/12</td>
<td>3/8</td>
<td>0.06 [0.00, 1.44]</td>
<td></td>
</tr>
<tr>
<td>Deharo</td>
<td>0/23</td>
<td>4/23</td>
<td>0.09 [0.00, 0.82]</td>
<td></td>
</tr>
<tr>
<td>INVASYS I</td>
<td>0/17</td>
<td>7/9</td>
<td>0.01 [0.00, 0.22]</td>
<td></td>
</tr>
<tr>
<td>Subtotal (95% CI)</td>
<td>52</td>
<td>40</td>
<td>0.04 [0.01, 0.23]</td>
<td></td>
</tr>
<tr>
<td>Total events: 0 (Treatment), 14 (Control)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Test for heterogeneity: $\chi^2 = 1.18, df = 2 (P = 0.55)$, $P = 0%$</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Test for overall effect: $Z = 3.56 (P = 0.0004)$</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>03 Double-blind active pacemaker versus sensing only/pacemaker off</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Synpace</td>
<td>0/16</td>
<td>5/10</td>
<td>1.60 [0.96, 7.67]</td>
<td></td>
</tr>
<tr>
<td>VPS II</td>
<td>16/48</td>
<td>22/82</td>
<td>0.68 [0.30, 1.54]</td>
<td></td>
</tr>
<tr>
<td>Subtotal (95% CI)</td>
<td>64</td>
<td>65</td>
<td>0.83 [0.41, 1.70]</td>
<td></td>
</tr>
<tr>
<td>Total events: 24 (Treatment), 27 (Control)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Test for heterogeneity: $\chi^2 = 0.97, df = 1 (P = 0.32)$, $P = 0%$</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Test for overall effect: $Z = 0.51 (P = 0.61)$</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total (95% CI)</td>
<td>210</td>
<td>212</td>
<td>0.15 [0.05, 0.42]</td>
<td></td>
</tr>
<tr>
<td>Total events: 33 (Treatment), 92 (Control)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Test for heterogeneity: $\chi^2 = 24.08, df = 8 (P = 0.002)$, $P = 68.7%$</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Test for overall effect: $Z = 3.55 (P = 0.0004)$</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Third International Study on Syncope of Uncertain Etiology (ISSUE-3)

**Screening phase**
- 511 met inclusion criteria and received an ILR

**Study phase**
- 89 had ECG documentation of:
  - syncopal recurrence with asystole ≥3 s (#72)
  - or
  - non-syncopal asystole ≥6 s (#17)

**77 randomized**
- 38 assigned and received Pm ON
- 39 assigned and received Pm OFF

**12 refused randomization**
- 3 lost to follow-up
- 9 followed-up (registry):
  - 6 implanted Pm
  - 3 no therapy

**38 analysed**
**39 analysed**

Brignole et al Circulation 2012
Third International Study on Syncope of Uncertain Etiology (ISSUE-3)

First syncope recurrence (intention-to-treat)

NNT=8

NNT=3

AR ↓ 57%

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

Brignole et al Circulation 2012
### Guidelines for the diagnosis and management of syncope (version 2009)

<table>
<thead>
<tr>
<th>Recommendations</th>
<th>Class&lt;sup&gt;a&lt;/sup&gt;</th>
<th>Level&lt;sup&gt;b&lt;/sup&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cardiac pacing should be considered in patients with frequent recurrent reflex syncope, age &gt;40 years, and documented spontaneous cardioinhibitory response during monitoring</td>
<td>IIa</td>
<td>B</td>
</tr>
<tr>
<td>Cardiac pacing may be indicated in patients with tilt-induced cardioinhibitory response with recurrent frequent unpredictable syncope and age &gt;40 after alternative therapy has failed</td>
<td>IIb</td>
<td>C</td>
</tr>
<tr>
<td>Cardiac pacing is not indicated in the absence of a documented cardioinhibitory reflex</td>
<td>III</td>
<td>C</td>
</tr>
</tbody>
</table>

### 2013 ESC Guidelines on cardiac pacing and cardiac resynchronization therapy

<table>
<thead>
<tr>
<th>Recommendations</th>
<th>Class&lt;sup&gt;a&lt;/sup&gt;</th>
<th>Level&lt;sup&gt;b&lt;/sup&gt;</th>
<th>Ref. &lt;sup&gt;c&lt;/sup&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td>3) Reflex asystolic syncope. Pacing should be considered in patients ≥40 years with recurrent, unpredictable reflex syncope and documented symptomatic pause/s due to sinus arrest or AV block or the combination of the two.</td>
<td>IIa</td>
<td>B</td>
<td>5, 18, 19</td>
</tr>
<tr>
<td>4) Asymptomatic pauses (sinus arrest or AV block). Pacing should be considered in patients with history of syncope and documentation of asymptomatic pauses &gt;6 s due to sinus arrest, sinus-atrial block or AV block.</td>
<td>IIa</td>
<td>C</td>
<td>-</td>
</tr>
<tr>
<td>5) Pacing is not indicated in reversible causes of bradycardia.</td>
<td>III</td>
<td>C</td>
<td>-</td>
</tr>
</tbody>
</table>
## Pacemakers in Vasovagal Syncope

<table>
<thead>
<tr>
<th>COR</th>
<th>LOE</th>
<th>Recommendation</th>
</tr>
</thead>
<tbody>
<tr>
<td>IIb</td>
<td>B-R</td>
<td>Dual-chamber pacing might be reasonable in a select population of patients 40 years of age or older with recurrent VVS and prolonged spontaneous pauses.</td>
</tr>
</tbody>
</table>
52 patients (26 TT+ and 26 TT-) with asystolic neurally mediated syncope received a pacemaker.

Syncope recurred in 8 TT+ and in 1 TT- patients in 21 months.
Vasovagal Syncope

VVS

Education on diagnosis and prognosis (Class I)

Counter pressure maneuvers (Class IIa)

Salt and fluid intake (Class IIb)

VVS recurs

Midodrine (Class IIa)

Fludrocortisone (Class IIb)

Beta blocker (in patients >42 y) (Class IIb)

Orthostatic training (Class IIb)

Selected serotonin reuptake inhibitors (Class IIb)

Dual-chamber pacemaker therapy (Class IIb)

Options

Colors correspond to Class of Recommendation in Table 1.

VVS indicates vasovagal syncope.
SAFE PACE study: Kenny et al JACC 2001
Pacing reduced falls 70%, Syncopal events 53%, Injurious events 70%

**2017 ACC/AHA/HRS Guideline for the Evaluation and Management of Patients With Syncope**

**Carotid Sinus Syndrome**

<table>
<thead>
<tr>
<th>COR</th>
<th>LOE</th>
<th>Recommendations</th>
</tr>
</thead>
<tbody>
<tr>
<td>IIa</td>
<td>B-R</td>
<td>Permanent cardiac pacing is reasonable in patients with carotid sinus syndrome that is cardioinhibitory or mixed.</td>
</tr>
<tr>
<td>IIb</td>
<td>B-R</td>
<td>It may be reasonable to implant a dual-chamber pacemaker in patients with carotid sinus syndrome who require permanent pacing.</td>
</tr>
</tbody>
</table>


**Pacing in elderly recurrent fallers with carotid sinus hypersensitivity: a randomised, double-blind, placebo controlled crossover trial.**

Parry SW¹, Steen N, Bexton RS, Tynan M, Kenny RA.
Orthostatic Hypotension

Colors correspond to Class of Recommendation in Table 1. BP indicates blood pressure; OH, orthostatic hypotension.

Midodrine, Droxidopa, Hydrocortisone IIa
Puridostigmine, Octreotide IIb

Therapy options in selected patients

Compression garments (Class IIa)
Counter-pressure maneuvers (Class IIa)
Midodrine (Class IIa)
Droxidopa (Class IIa)
Fludrocortisone (Class IIa)

Increase salt and fluid intake (Class IIb)
Octreotide (Class IIb)
Pyridostigmine (Class IIb)
LBBB and syncope?
<table>
<thead>
<tr>
<th>Study</th>
<th>HV interval after</th>
<th>Progression Rate</th>
</tr>
</thead>
</table>
| Scheinman et al 1983| HV interval       | < 70 $\rightarrow$ 3.5%  
|                     |                   | $\geq 70$ $\rightarrow$ 12%  
|                     |                   | $\geq 100$ $\rightarrow$ 25%  |
| Bergfeldt 1994      | HV interval after Dysopiramide | 47% $\rightarrow$ 75% |
| Petrac 1996         | A – V Block after atrial pacing | 9% $\rightarrow$ 78% |
Mechanism of Syncope in Patients With Bundle Branch Block and Negative Electrophysiological Test

Michele Brignole, MD; Carlo Menozzi, MD; Angel Moya, MD; Roberto Garcia-Civera, MD; Luis Mont, MD; Miguel Alvarez, MD; Francisco Errazquin, MD; Julio Beiras, MD; Nicola Bottoni, MD; Paolo Donato, MD; on behalf of the International Study on Syncope of Uncertain Etiology (ISSUE) Investigators*

(Circulation. 2001;104:2045-2050.)

52 patients

- Syncope
  - 22 (42%)*
  - ILR-detected 19
    - AVB, 12 (63%)
    - SA, 4 (21%)
    - Asystole-undefined, 1 (5%)
    - NSR, 1 (5%)
    - Sinus tachy, 1 (5%)
  - Not detected 3

- Stable AVB
  - 3 (6%)

- ILR-detected pre-syncope
  - 2 (4%)**
- Death
  - 1 (2%)

* 5 of these had also ≥1 presyncope
** drop-out before primary-end point
Mechanism of Syncope in Patients With Bundle Branch Block and Negative Electrophysiological Test

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*(Circulation. 2001;104:2045-2050.)*

<table>
<thead>
<tr>
<th>Event</th>
<th>Count (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Asystole → PMK</td>
<td>22 (42%)</td>
</tr>
<tr>
<td>Non asystolic syncope</td>
<td>5 (9.1%)</td>
</tr>
<tr>
<td>Non syncope recurrences</td>
<td>24 (46%)</td>
</tr>
<tr>
<td>Death during colonoscopy</td>
<td>1 (2%)</td>
</tr>
</tbody>
</table>
Bundle Branch Block and Syncope

Bradycardia detection in Bundle Branch Block (B4) study
Bundle Branch Block and Syncope

Bradycardia detection in Bundle Branch Block (B4) study

Table 2: Diagnosis

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>n</th>
</tr>
</thead>
<tbody>
<tr>
<td>Analysed patients, n = 323</td>
<td></td>
</tr>
<tr>
<td>Initial evaluation</td>
<td></td>
</tr>
<tr>
<td>(Phase I), n = 102</td>
<td></td>
</tr>
<tr>
<td>A-VB</td>
<td>52</td>
</tr>
<tr>
<td>Alt B2</td>
<td>4</td>
</tr>
<tr>
<td>PrB</td>
<td>6</td>
</tr>
<tr>
<td>CSS</td>
<td>13</td>
</tr>
<tr>
<td>Neurology</td>
<td>6</td>
</tr>
<tr>
<td>Others</td>
<td>9</td>
</tr>
<tr>
<td>ILR</td>
<td>70</td>
</tr>
<tr>
<td>Freedom from syncope recurrence</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>n</th>
</tr>
</thead>
<tbody>
<tr>
<td>Analysed patients, n = 323</td>
<td></td>
</tr>
<tr>
<td>Initial evaluation</td>
<td></td>
</tr>
<tr>
<td>(Phase I, II)</td>
<td></td>
</tr>
<tr>
<td>6% diagnosed as syncope</td>
<td></td>
</tr>
<tr>
<td>A-VB</td>
<td>36</td>
</tr>
<tr>
<td>SA</td>
<td>5</td>
</tr>
<tr>
<td>Non-arrhythmic</td>
<td>7</td>
</tr>
<tr>
<td>VT/VF</td>
<td>3</td>
</tr>
<tr>
<td>Brady/tachy</td>
<td>1</td>
</tr>
<tr>
<td>No diagnosis</td>
<td>56</td>
</tr>
</tbody>
</table>

Mortality rate: 6% in Phase I, II vs Phase III: 6.5%

45% of the patients with a negative EPS, an arrhythmia was still documented by ILR.

7% of patients experienced syncope recurrence after ILR implantation.

33% of patients experienced syncope recurrence without ILR implantation.
2013 ESC Guidelines on cardiac pacing and cardiac resynchronization therapy
LBBB when to pace?

Guidelines for the diagnosis and management of syncope (version 2009)

<table>
<thead>
<tr>
<th>Recommendations</th>
<th>Class</th>
<th>Level</th>
<th>Ref.</th>
</tr>
</thead>
<tbody>
<tr>
<td>1) BBB, unexplained syncope and abnormal EPS. Pacing is indicated in patients with syncope, BBB and positive EPS defined as HV interval of ≥70 ms, or second- or third-degree His-Purkinje block demonstrated during incremental atrial pacing or with pharmacological challenge.</td>
<td>I</td>
<td>B</td>
<td>25, 31</td>
</tr>
<tr>
<td>2) Alternating BBB. Pacing is indicated in patients with alternating BBB with or without symptoms.</td>
<td>I</td>
<td>C</td>
<td>-</td>
</tr>
<tr>
<td>3) BBB, unexplained syncope non diagnostic investigations. Pacing may be considered in selected patients with unexplained syncope and BBB.</td>
<td>IIb</td>
<td>B</td>
<td>32</td>
</tr>
<tr>
<td>4) Asymptomatic BBB. Pacing is not indicated for BBB in asymptomatic patients.</td>
<td>III</td>
<td>B</td>
<td>26, 33, 34</td>
</tr>
</tbody>
</table>

2013 ESC Guidelines on cardiac pacing and cardiac resynchronization therapy
Be aware that...

<table>
<thead>
<tr>
<th>COR</th>
<th>LOE</th>
<th>Recommendations</th>
</tr>
</thead>
<tbody>
<tr>
<td>IIa</td>
<td>B-NR</td>
<td>ICD implantation is reasonable in patients with Brugada ECG pattern and syncope of suspected arrhythmic etiology.</td>
</tr>
<tr>
<td>IIb</td>
<td>B-NR</td>
<td>Invasive EPS may be considered in patients with Brugada ECG pattern and syncope of suspected arrhythmic etiology.</td>
</tr>
<tr>
<td>III: No Benefit</td>
<td>B-NR</td>
<td>ICD implantation is not recommended in patients with Brugada ECG pattern and reflex-mediated syncope in the absence of other risk factors.</td>
</tr>
</tbody>
</table>

Participation in competitive sports is not recommended for athletes with syncope and phenotype-positive HC CPVT, LQTS1, or ARVC before evaluation by a specialist (704,721-724).

In the absence of vagal mechanisms, VA in patients with HCM, CPVT, LQTS1, or ARVC is catecholamine sensitive. Participation in competitive sports in that circumstance in these patients is not recommended (704,715,716).

See Online Data Supplement 42.
Conclusions

• Diagnosis, Aetiology, Risk stratification

• INITIALLY: detailed history, physical examination, a resting 12-lead electrocardiogram (ECG)

• Hospital evaluation and treatment is recommended for patients presenting with syncope who have a serious medical condition relevant to the syncope

• Non cardiac causes of syncope have a better prognosis

• Routine and comprehensive laboratory testing is not useful in the evaluation of patients with syncope.

Towards Targeted Actions!
Οδυσσέας Ελέυθης
Από το Άξιον Εστί:
Τη γλώσσα μου έδωσαν ελληνική

Τη γλώσσα μου έδωσαν ελληνική.
tο σπίτι φτωχικό στις αμμουδιές του Ομήρου...

Μονάχη έγνοια η γλώσσα μου στις αμμουδιές του Ομήρου...

Εκεί σπάροι και πέρκες
ανεμόδαρτα ρήματα
ρεύματα πράσινα μες στα γαλάζια
όσα είδα στα σπτλάχνα μου ν’ ανάβουνε
σφουγγάρια, μέδουσες

με τα πρώτα λόγια των Σειρήνων

όστρακα ρόδινα με τα πρώτα μαύρα ρίγη...

Μονάχη έγνοια η γλώσσα μου, με τα πρώτα μαύρα ρίγη...
Other Key messages:

- 45% of the patients with a negative EPS, an arrhythmia was still documented by ILR.

- No difference in mortality rate between patients diagnosed at Phase I or II, and those who had implanted ILR (6.0 vs. 6.5%).
Vasovagal Syncope: Pace or not?

Sutton et al. Circulation 2000

Ammirati et al. Circulation 2001
Vasovagal Syncope: Pace or not?

Connolly et al JAMA 2003

Raviele et al Eur Heart J 2004
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

Prevalence higher than previously believed

Carotid Sinus Hypersensitivity (CSH)

- No symptoms
- No treatment

CSS
Etiology

- Sensory nerve endings in the carotid sinus walls respond to deformation
- "Deafferentation" of neck muscles may contribute
- Increased afferent signals to brain stem
- Reflex increase in efferent vagal activity and diminution of sympathetic tone results in bradycardia and vasodilatation
Falls: Incidence, Recurrence, CSH*

*Carotid Sinus Hypersensitivity

2 Richardson D. et al. PACE. 1997;20:820.
CSS
Role of Pacing – Syncope Recurrence Rate

- Class I indication for pacing (AHA and BPEG)
- Limit pacing to CSS that is:
  - Cardioinhibitory
  - Mixed
- DDD/DDI superior to VVI
  - Mean follow-up = 6 months

SAFE PACE
Syncope And Falls in the Elderly – Pacing And Carotid Sinus Evaluation

Objective
• Determine whether cardiac pacing reduces falls in older adults with carotid sinus hypersensitivity

Randomized controlled trial (N=175)
• Adults > 50 years, non-accidental fall, positive CSM
• Pacing (n=87) vs. No Pacing (n=88)

Results
• More than 1/3 of adults over 50 years presented to the Emergency Department because of a fall
• With pacing, falls ↓ 70%
• Syncopal events ↓ 53%
• Injurious events ↓ 70%

Conclusions

• Strong association between non-accidental falls and cardioinhibitory CSH

• These patients usually not referred for cardiac assessment

• Cardiac pacing significantly reduced subsequent falls

• CSH should be considered in all older adults who have non-accidental falls

### Table 3. Hazard Ratios for the Outcomes of Interest in Participants with Syncope as Compared with Participants without Syncope.

<table>
<thead>
<tr>
<th>Cause of Syncope</th>
<th>Hazard Ratio (95% Confidence Interval)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Adjusted for Age and Sex</td>
</tr>
<tr>
<td>Any cause</td>
<td></td>
</tr>
<tr>
<td>Death from any cause</td>
<td>1.43 (1.25–1.64)†</td>
</tr>
<tr>
<td>Myocardial infarction or death from coronary heart disease</td>
<td>1.47 (1.15–1.88)‡</td>
</tr>
<tr>
<td>Fatal or nonfatal stroke</td>
<td>1.19 (0.87–1.62)</td>
</tr>
<tr>
<td>Cardiac</td>
<td></td>
</tr>
<tr>
<td>Death from any cause</td>
<td>2.41 (1.78–3.26)†</td>
</tr>
<tr>
<td>Myocardial infarction or death from coronary heart disease</td>
<td>3.56 (2.29–5.55)‡</td>
</tr>
<tr>
<td>Fatal or nonfatal stroke</td>
<td>2.67 (1.43–4.98)‡</td>
</tr>
<tr>
<td>Unknown</td>
<td></td>
</tr>
<tr>
<td>Death from any cause</td>
<td>1.36 (1.13–1.65)‡</td>
</tr>
<tr>
<td>Myocardial infarction or death from coronary heart disease</td>
<td>1.43 (1.00–2.03)$§</td>
</tr>
<tr>
<td>Fatal or nonfatal stroke</td>
<td>0.72 (0.43–1.22)</td>
</tr>
<tr>
<td>Neurologic (including seizure)</td>
<td></td>
</tr>
<tr>
<td>Death from any cause</td>
<td>1.98 (1.45–2.72)†</td>
</tr>
<tr>
<td>Myocardial infarction or death from coronary heart disease</td>
<td>1.02 (0.48–2.17)</td>
</tr>
<tr>
<td>Fatal or nonfatal stroke</td>
<td>3.12 (1.82–5.36)‡</td>
</tr>
<tr>
<td>Vasovagal or other†</td>
<td></td>
</tr>
<tr>
<td>Death from any cause</td>
<td>1.17 (0.95–1.44)</td>
</tr>
<tr>
<td>Myocardial infarction or death from coronary heart disease</td>
<td>1.16 (0.80–1.68)</td>
</tr>
<tr>
<td>Fatal or nonfatal stroke</td>
<td>0.93 (0.57–1.52)</td>
</tr>
</tbody>
</table>

Soteriades et al. *NEJM* 2002; 347: 878
In patients with both syncope and BBB, syncope is suspected to be attributed to atrioventricular AVB, with EPS being able to predict the development of AVB in 87% of patients.

In patients with BBB and negative EPS, the risk of developing a stable AVB was shown to be close to 20% after 4 years, with the risk of syncope recurrence being close to 40% at 3 years.

The positive predictive value is ≥ 80% to identify the patients who will developed AV block.

That show a significant reduction in syncopal recurrences in patients with positive EPS treated with PM, compared with a control group of untreated patients with negative EPS.

Am J Cardiol 1999;83:1334-7

Eur Heart J 2011;32:1533-1541
Eur Heart J 2009;30:2631-2671
Pathophysiological Basis of Classification of syncope

Guidelines for the diagnosis and management of syncope (version 2009)

The Task Force for the Diagnosis and Management of Syncope of the European Society of Cardiology (ESC)
## Conditions Uncommonly Associated With Syncope

### Infiltrative

<table>
<thead>
<tr>
<th>Condition</th>
<th>Description</th>
<th>Syncope cause</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fabry disease (544,545)</td>
<td>Lysosomal storage disorder with neuropathic pain, renal failure</td>
<td>Syncope usually due to AV block.</td>
</tr>
<tr>
<td></td>
<td>concentric LVH, and HF.</td>
<td></td>
</tr>
<tr>
<td>Amyloidosis (546,547)</td>
<td>Systemic disease due to amyloid deposition. Light chain amyloidosis affects</td>
<td>Syncope may be due to conduction system disease, arrhythmias, impaired</td>
</tr>
<tr>
<td></td>
<td>the kidneys, heart, and peripheral and autonomic nervous systems.</td>
<td>cardiac output from restrictive cardiomyopathy, or neurological involvement.</td>
</tr>
<tr>
<td>Hemochromatosis (548)</td>
<td>Systemic iron deposition causing liver disease, skin pigmentation, diabetes</td>
<td>Myocardial involvement more common than sick sinus syndrome and AV conduction</td>
</tr>
<tr>
<td></td>
<td>mellitus, arthropathy, impotence, and dilated cardiomyopathy.</td>
<td>disease.</td>
</tr>
</tbody>
</table>

### Endocrine

<table>
<thead>
<tr>
<th>Condition</th>
<th>Description</th>
<th>Syncope cause</th>
</tr>
</thead>
<tbody>
<tr>
<td>Carcinoid syndrome (602)</td>
<td>These tumors can release vasoactive peptides and cause vasodilation,</td>
<td>Syncope is usually due to transient hypotension.</td>
</tr>
<tr>
<td>Pheochromocytoma (602,603)</td>
<td>flushing, pruritus, and gastrointestinal symptoms.</td>
<td></td>
</tr>
<tr>
<td>Mastocytosis (602-609)</td>
<td>Vasoactive intestinal peptide tumor</td>
<td></td>
</tr>
<tr>
<td>Beta thalassemia major (610)</td>
<td>Severe anemia, multiple organ failure, and dilated cardiomyopathy</td>
<td>Syncope may be arrhythmic.</td>
</tr>
<tr>
<td></td>
<td>due to iron overload.</td>
<td></td>
</tr>
</tbody>
</table>

### Hematologic

<table>
<thead>
<tr>
<th>Condition</th>
<th>Description</th>
<th>Syncope cause</th>
</tr>
</thead>
<tbody>
<tr>
<td>Beta thalassemia major (610)</td>
<td>Severe anemia, multiple organ failure, and dilated cardiomyopathy</td>
<td>Syncope may be arrhythmic.</td>
</tr>
<tr>
<td></td>
<td>due to iron overload.</td>
<td></td>
</tr>
</tbody>
</table>
Diagnostic criteria with initial evaluation

- Vasovagal syncope is diagnosed if syncope is precipitated by emotional distress or orthostatic stress and is associated with typical prodrome.
- Situational syncope is diagnosed if syncope occurs during or immediately after specific triggers (cough, sneeze, GI stimulation, micturition, post-exercise, post-prandial).
- Orthostatic syncope is diagnosed when it occurs after standing up and there is documentation of orthostatic hypotension.
- Arrhythmia related syncope is diagnosed by ECG when there is:
  - Persistent sinus bradycardia < 40 bpm in awake or repetitive sinoatrial block or sinus pauses > 3 s.
  - Mobitz II 2nd or 3rd degree atrioventricular block.
  - Alternating left and right BBB.
  - VT or rapid paroxysmal SVT.
  - Non-sustained episodes of polymorphic VT and long or short QT interval.
  - Pacemaker or ICD malfunction with cardiac pauses.
- Cardiac ischaemia related syncope is diagnosed when syncope presents with ECG evidence of acute ischaemia with or without myocardial infarction.
- Cardiovascular syncope is diagnosed when syncope presents in patients with prolapsing atrial myxoma, severe aortic stenosis, pulmonary hypertension, pulmonary embolus or acute aortic dissection.

Class I Level C
### Scoring for prediction of serious events in pts with syncope

<table>
<thead>
<tr>
<th>Study</th>
<th>Risk factors</th>
<th>Score</th>
<th>Endpoints</th>
<th>Results (validation cohort)</th>
</tr>
</thead>
</table>
| **S. Francisco Syncope**<sup>44</sup> | - Abnormal ECG  
- Congestive heart failure  
- Shortness of breath  
- Haematocrit <30%  
- Systolic blood pressure <90 mmHg | No risk = 0 item  
Risk = ≥1 item | Serious events at 7 days | 98% sensitive and 56% specific |
| **Martin et al.**<sup>45</sup> | - Abnormal ECG  
- History of ventricular arrhythmia  
- History of congestive heart failure  
- Age >45 years | 0 to 4 (1 point each item) | 1-year severe arrhythmias or arrhythmic death | 0% score 0  
5% score 1  
16% score 2  
27% score 3 or 4 |
| **OESIL score**<sup>41</sup> | - Abnormal ECG  
- History of cardiovascular disease  
- Lack of prodrome  
- Age >65 years | 0 to 4 (1 point each item) | 1-year total mortality | 0% score 0  
0.6% score 1  
14% score 2  
29% score 3  
53% score 4 |
| **EGSYS score**<sup>42</sup> | - Palpitations before syncope (+4)  
- Abnormal ECG and/or heart disease (+3)  
- Syncope during effort (+3)  
- Syncope while supine (+2)  
- Autonomic prodrome* (-1)  
- Predisposing and/or precipitating factors<sup>b</sup> (-1) | Sum of + and − points | 2-year total mortality | Cardiac syncope probability  
2% score <3  
13% score 3  
33% score 4  
77% score >4 |
Neurally Mediated Syncope: pathophysicsology
Frequency of the causes of syncope according to presence of CVD disease

<table>
<thead>
<tr>
<th>CAUSE</th>
<th>CARDIOVASCULAR DISEASE ABSENT (N=599)</th>
<th>CARDIOVASCULAR DISEASE PRESENT (N=223)</th>
<th>TOTAL SAMPLE (N=822)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>MEN (N=232)</td>
<td>WOMEN (N=367)</td>
<td>MEN (N=116)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>WOMEN (N=107)</td>
</tr>
<tr>
<td></td>
<td>percent of subjects</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cardiac</td>
<td>6.5</td>
<td>3.8</td>
<td>26.7</td>
</tr>
<tr>
<td>Unknown*</td>
<td>31.0</td>
<td>41.7</td>
<td>31.0</td>
</tr>
<tr>
<td>Stroke or transient ischemic attack</td>
<td>1.7</td>
<td>2.5</td>
<td>9.5</td>
</tr>
<tr>
<td>Seizure</td>
<td>7.3</td>
<td>3.3</td>
<td>4.1</td>
</tr>
<tr>
<td><strong>Vasovagal</strong></td>
<td><strong>24.1</strong></td>
<td><strong>24.5</strong></td>
<td><strong>11.2</strong></td>
</tr>
<tr>
<td>Orthostatic</td>
<td>9.5</td>
<td>10.9</td>
<td>6.9</td>
</tr>
<tr>
<td>Medication</td>
<td>7.3</td>
<td>6.5</td>
<td>4.3</td>
</tr>
<tr>
<td>Other†</td>
<td>13.0</td>
<td>6.8</td>
<td>3.5</td>
</tr>
</tbody>
</table>

*When a participant did not seek medical attention for syncope and the history, physical examination, and electrocardiographic findings were not consistent with any of the specific causes, the cause was considered to be unknown.

†Cough syncope, micturition syncope, and situational syncope were included in the category of other causes.
Vasovagal Syncope Classification

Cardioinhibitory
Vasodepressor
Mixed
Unexplained Syncope: ISSUE Classification

**Type 1 Asystole.** RR pause $\geq$ 3 seconds
- Type 1A, Sinus arrest:
  - Progressive sinus bradycardia or initial sinus tachycardia followed by progressive sinus bradycardia until sinus arrest
- Type 1B, Sinus bradycardia plus AV block
  - Progressive sinus bradycardia followed by AV block (and ventricular pause/s) with concomitant decrease in sinus rate
  - Sudden onset AV block (and ventricular pause/s) with concomitant decrease in sinus rate
- Type 1C, AV block
  - Sudden onset AV block (and ventricular pause/s) with concomitant increase in sinus rate

**Type 2, Bradycardia.** Decrease in heart rate $>30\%$ or $<40$ bpm for $>10$ seconds
- Type 2 A. Decrease of heart rate $>30\%$
- Type 2 B. Heart rate to $<40$ bpm for $>10$ seconds

**Type 3, No or slight rhythm variations.** Variations of heart rate $<30\%$ and heart rate $>40$ bpm
- Type 3 A. No variation or $<10\%$ variation in heart rate
- Type 3 B. Increase in heart rate $>10\%$ but $<30\%$ and $<120$ bpm; or, decrease $>10\%$ but $<30\%$ and $>40$ bpm

**Type 4, Tachycardia.** Increase in heart rate $>30\%$ or $>120$ bpm
- Type 4 A. Progressive sinus tachycardia
- Type 4 B. Atrial fibrillation
- Type 4 C. Supraventricular tachycardia (except sinus)
- Type 4 D. Ventricular tachycardia
Orthostatic Hypotension

- Etiology
  - Drug-induced (very common)
    - Diuretics
    - Vasodilators
  - Primary autonomic failure
    - Multiple system atrophy
    - Parkinson’s Disease
    - Postural Orthostatic Tachycardia Syndrome (POTS)

- Secondary autonomic failure
  - Diabetes
  - Alcohol
  - Amyloid

Treatment Strategies for Orthostatic Intolerance

- Patient education, injury avoidance
- Hydration
  - Fluids, salt, diet
  - Minimize caffeine/alcohol
- Sleeping with head of bed elevated
- Tilt training, leg crossing, arm pull
- Support hose
- Drug therapies
  - Fludrocortisone, midodrine, erythropoietin
- Tachy-Pacing (probably not useful)

BP responses in different types of syncope

BP (mmHg)

BP after standing

Time (mins)

OH

VVS

Elderly dysautonomic pattern
Postural Orthostatic Tachycardia Syndrome

- Upright symptoms without hypotension.
- Upright tachycardia—excessive HR response to maintain a low normal BP.
- 500,000 Americans, usually young women
- Partial dysautonomia
- Antecedent infection, surgery, pregnancy
- Treatment—low dose propanolol 10mg tid
Carotid Sinus Syncope

• Syncope related to head turning, shaving, wearing a tight collar

• Pathophysiology
  – Carotid sinus pressure causes a reflex decrease in heart rate and blood pressure
Carotid sinus massage

- **Site**
  - Carotid arterial pulse just below thyroid cartilage

- **Method**
  - Massage, not occlusion.
  - Right followed by left, pause between
  - Duration: 5-10 seconds
  - Posture: supine and erect

- **Risks**
  - 1/5000 massages complicated by TIA

- **Outcome**
  - 3 sec asystole and/or 50mmHg fall in systolic blood pressure with reproduction of symptoms

- **Contraindications**
  - Carotid bruit, known but significant carotid arterial disease, previous CVA, MI last 3 months.
Situational Syncope

• Related to micturition, defecation, swallowing or coughing
• Induced by baroreceptor and mechanoreceptors causing vagal stimulation
• Circumstances of the event are typically diagnostic
Orthostatic syncope

• When vertical, blood follows gravity and pools.
• Increased sympathetic tone counteracts this.
• If the response is inadequate, syncope occurs.
• Drop in BP: 20 systolic or 10 diastolic within 3 minutes of standing
• Present in 40% of patients over 70 years old
• May be due to
  – Drugs
  – Volume loss
  – Neurologic damage
More on Orthostatic Hypotension

• Volume loss
  – Assoc. with tachycardia
• Medications
  – Seen in elderly 45% of time
• Situational
  – Micturition, cough, postprandial, carotid sinus sensitivity, defecation, laughing
• Adrenal insufficiency

• Primary autonomic disease
  – Idiopathic, parkinsons disease, multisystem atrophy (Shy-Drager)
• Secondary autonomic disease
  – Neuropathic (dm, amyloid, alcoholism, autoimmune, vitamin deficiency, etc)
  – CNS (cva, MS, tumors, spinal cord)
### Neurogenic Orthostatic Hypotension

**2017 ACC/AHA/HRS Guideline for the Evaluation and Management of Patients With Syncope**

<table>
<thead>
<tr>
<th>Level</th>
<th>Evidence</th>
<th>Recommendation</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>B-R</td>
<td>Acute water ingestion is recommended in patients with syncope caused by neurogenic OH for occasional, temporary relief.</td>
</tr>
<tr>
<td>IIa</td>
<td>C-LD</td>
<td>Physical counter-pressure maneuvers can be beneficial in patients with neurogenic OH with syncope.</td>
</tr>
<tr>
<td>IIa</td>
<td>C-LD</td>
<td>Compression garments can be beneficial in patients with syncope and OH.</td>
</tr>
<tr>
<td>IIa</td>
<td>B-R</td>
<td>Midodrine can be beneficial in patients with syncope due to neurogenic OH.</td>
</tr>
<tr>
<td>IIa</td>
<td>B-R</td>
<td>Droxidopa can be beneficial in patients with syncope due to neurogenic OH.</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Level</th>
<th>Evidence</th>
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</tr>
</thead>
<tbody>
<tr>
<td>IIa</td>
<td>C-LD</td>
<td>Fludrocortisone can be beneficial in patients with syncope due to neurogenic OH.</td>
</tr>
<tr>
<td>IIb</td>
<td>C-LD</td>
<td>Encouraging increased salt and fluid intake may be reasonable in selected patients with neurogenic OH.</td>
</tr>
<tr>
<td>IIb</td>
<td>C-LD</td>
<td>Pyridostigmine may be beneficial in patients with syncope due to neurogenic OH who are refractory to other treatments.</td>
</tr>
<tr>
<td>IIb</td>
<td>C-LD</td>
<td>Octreotide may be beneficial in patients with syncope and refractory recurrent postprandial or neurogenic OH.</td>
</tr>
</tbody>
</table>
**ISSUE**

**Patients with Bundle Branch Block and Negative EP Test**


- 52 Pts with BBB and Insertable Loop Recorder
  - Syncope: 22 Pts (42%)*
  - ILR-Detected: 19
    - AVB: 12 (63%)
    - SA: 4 (21%)
    - Asystole-undefined: 1 (5%)
    - NSR: 1 (5%)
    - Sinus tachy: 1 (5%)
  - Not Detected: 3
    - Stable AVB: 3 Pts (6%)
  - ILR-Detected Pre-Syncope: 2 Pts (4%)**
    - AVB: 2 (4%)
  - Death: 1 Pt (2%)

* 5 of these also had ≥1 presyncope
** Drop-out before primary-end point
Conclusion:

- In patients with BBB and negative EP study, most syncopal recurrences have a homogeneous mechanism that is characterized by prolonged asystolic pauses mainly attributable to sudden-onset paroxysmal AV block.
Frequency of the causes of syncope according to presence of CVD disease

<table>
<thead>
<tr>
<th>CAUSE</th>
<th>CARDIOVASCULAR DISEASE ABSENT (N=599)</th>
<th>CARDIOVASCULAR DISEASE PRESENT (N=223)</th>
<th>TOTAL SAMPLE (N=822)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>MEN (N=232)</td>
<td>WOMEN (N=367)</td>
<td>MEN (N=116)</td>
</tr>
<tr>
<td>Cardiac</td>
<td>6.5</td>
<td>3.8</td>
<td>26.7</td>
</tr>
<tr>
<td>Unknown*</td>
<td>31.0</td>
<td>41.7</td>
<td>31.0</td>
</tr>
<tr>
<td>Stroke or transient ischemic attack</td>
<td>1.7</td>
<td>2.5</td>
<td>9.5</td>
</tr>
<tr>
<td>Seizure</td>
<td>7.3</td>
<td>3.3</td>
<td>6.9</td>
</tr>
<tr>
<td>Vasovagal</td>
<td>24.1</td>
<td>24.5</td>
<td>11.2</td>
</tr>
<tr>
<td>Orthostatic</td>
<td>9.5</td>
<td>10.9</td>
<td>6.9</td>
</tr>
<tr>
<td>Medication</td>
<td>7.3</td>
<td>6.5</td>
<td>4.3</td>
</tr>
<tr>
<td>Other†</td>
<td>13.0</td>
<td>6.8</td>
<td>3.5</td>
</tr>
</tbody>
</table>

*When a participant did not seek medical attention for syncope and the history, physical examination, and electrocardiographic findings were not consistent with any of the specific causes, the cause was considered to be unknown.

†Cough syncope, micturition syncope, and situational syncope were included in the category of other causes.

Soteriades et al NEJM 2002
# Conditions Uncommonly Associated With Syncope

<table>
<thead>
<tr>
<th>Condition</th>
<th>Clinical Characteristics</th>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cardiovascular and Cardiopulmonary</td>
<td>ians</td>
<td></td>
</tr>
<tr>
<td>Cardiac tamponade</td>
<td>Hypotension, tachycardia, cardiogenic shock.</td>
<td>Often tachycardia and hypotension; may be hypotensive and bradycardic acutely.</td>
</tr>
<tr>
<td>Constrictive pericarditis (533–535)</td>
<td>Severe HF symptoms, including edema, exertional dyspnea, orthopnea.</td>
<td>May be associated with cough syncope.</td>
</tr>
<tr>
<td>LV noncompaction (536–539)</td>
<td>Cardiomyopathy characterized by prominent LV trabeculae and deep intertrabecular recesses, due to embryologic perturbation.</td>
<td>Syncope reported in 5%–9% of both adult and pediatric patients. The mechanism may be a tachyarrhythmia.</td>
</tr>
<tr>
<td>Takotsubo cardiomyopathy (540,541)</td>
<td>Apical ballooning and basal hypercontractility, often due to stress.</td>
<td>Syncope is uncommon and may be multifactorial.</td>
</tr>
<tr>
<td>Pulmonary embolus (128,542,543)</td>
<td>Hypoxemia, tachycardia; hypotension and shock leading to pulseless electrical activity cardiac arrest in severe cases.</td>
<td>Syncope due to bradycardia and/or hypotension. One study showed higher prevalence of pulmonary embolus in older patients with first episode of syncope after admission to the hospital. Further confirmation of this finding in the older populations is warranted.</td>
</tr>
<tr>
<td>Pulmonary arterial hypertension</td>
<td>Occurs more often during exertion in younger patients.</td>
<td>Syncope due to inability to augment or sustain cardiac output during exertion, followed by vasodilatation.</td>
</tr>
<tr>
<td>Condition</td>
<td>Description</td>
<td>Syncope-related notes</td>
</tr>
<tr>
<td>-----------------------------------------------</td>
<td>----------------------------------------------------------------------------</td>
<td>---------------------------------------------------------------------------------------</td>
</tr>
<tr>
<td>Cardiac tumors (572)</td>
<td>Triad of obstruction, embolic, and systemic signs and symptoms.</td>
<td>Syncope is often due to obstruction to blood flow.</td>
</tr>
<tr>
<td>Prosthetic valve thrombosis (573-575)</td>
<td>Ranges from asymptomatic to profound HF.</td>
<td>May have similar presentation to a cardiac tumor, with a high risk of embolic phenomenon and obstruction.</td>
</tr>
<tr>
<td>Anomalous coronary artery (576-579)</td>
<td>Common cause of exertional syncope or SCD, classically in young athletes.</td>
<td>Syncope can be due to Bezold Jarisch reflex, hypotension, VT, or AV block.</td>
</tr>
<tr>
<td>Aortic dissection (580-582)</td>
<td>Aortic dissection may manifest with neurological symptoms, myocardial infarction, and HF. Syncope can occur in as many as 13% of aortic dissections.</td>
<td>The risk of in-hospital death, tamponade, and neurological deficits is higher in patients with syncope. Otherwise, syncope alone does not appear to increase the risk of death.</td>
</tr>
<tr>
<td>Subclavian steal (583-587)</td>
<td>The phenomenon of flow reversal in a vertebral artery ipsilateral to a hemodynamically significant stenosis of the subclavian artery. Severe cases resulting in vertebrobasilar ischemia may rarely result in syncope.</td>
<td>Syncope is generally associated with upper-extremity activity.</td>
</tr>
<tr>
<td>Coarctation of the aorta (588)</td>
<td>If severe, it can result in HF or aortic dissection.</td>
<td>Associated bicuspid aortic valve stenosis may be considered with syncope.</td>
</tr>
<tr>
<td>Rheumatoid arthritis (589)</td>
<td>Chronic, autoimmune inflammatory disorder with systemic manifestations.</td>
<td>Rarely associated with complete heart block and syncope.</td>
</tr>
</tbody>
</table>
Risk Stratification

Short-term high-risk criteria requiring prompt hospitalization or intensive evaluation:

- Severe structural or coronary artery disease (HF, low EF or prior MI).
- Clinical or ECG features suggesting arrhythmic syncope:
  - Syncope during exercise or supine.
  - Palpitations at the time of syncope.
  - Family history of Sudden cardiac death (SCD).
  - Non-sustained VT.
  - Bifascicular block (LBBB or RBBB combined with left anterior or left posterior fascicular block or other intraventricular conduction abnormalities with QRS duration ≥ 120 ms).
  - Inadequate sinus bradycardia (< 50 bpm) or sino-atrial block in absence of negative chronotropic medications or physical training.
  - Pre-excited QRS complex.
  - Prolonged or short QT interval.
  - RBBB pattern with ST-elevation in leads V1-V3 (Brugada pattern).
  - Negative T waves in right precordial leads, epsilon waves and ventricular late potentials suggestive of ARVC.
  - Family history of SCD.
- Important co-morbidities (severe anemia, electrolyte disturbance).