

# SYNCOPE

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ΥΓΕΙΟΔΥΝΑΜΙΚΗ, MAVROGENIS

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

## PRACTICE GUIDELINE: FULL TEXT

### 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).

## CLINICAL PRACTICE GUIDELINE

### 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

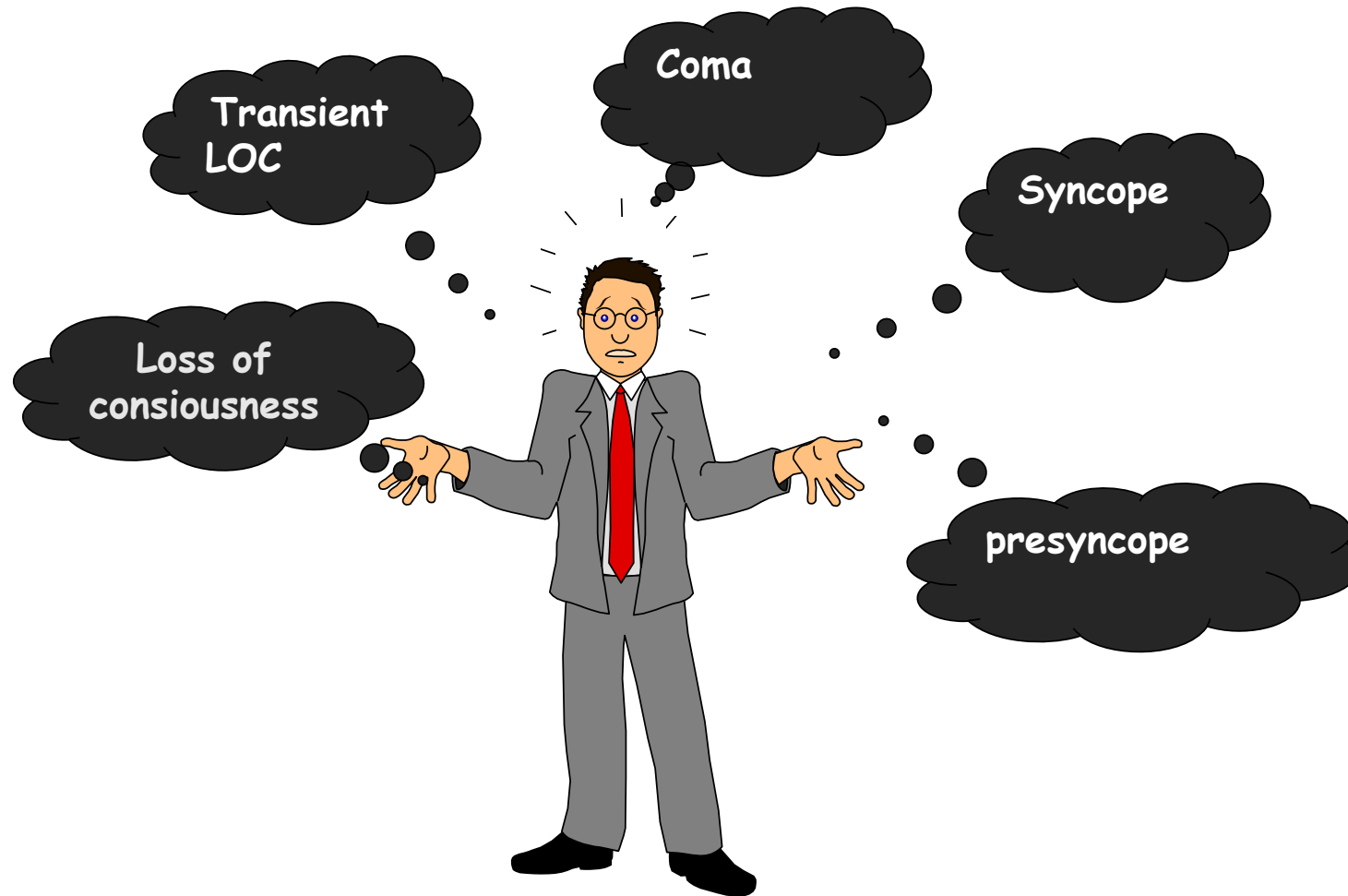


# Significance of Syncope

"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

**Syncope: an important clinical entity  
Why?**



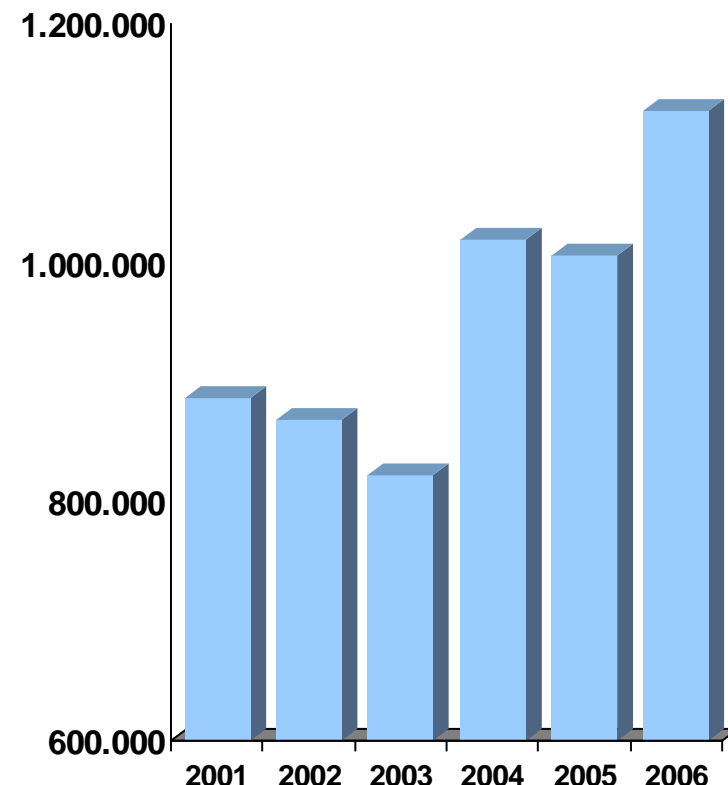
# Syncope: the impact

- ~19% 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%<sup>1</sup>  
(e.g., fractures, motor vehicle accident)
- **Minor injury** reported in 29%<sup>1</sup>  
(e.g., lacerations, bruises)

<sup>1</sup>Kenny RA, et al. eds. *The Evaluation and Treatment of Syncope*. Futura;2003:23-27.

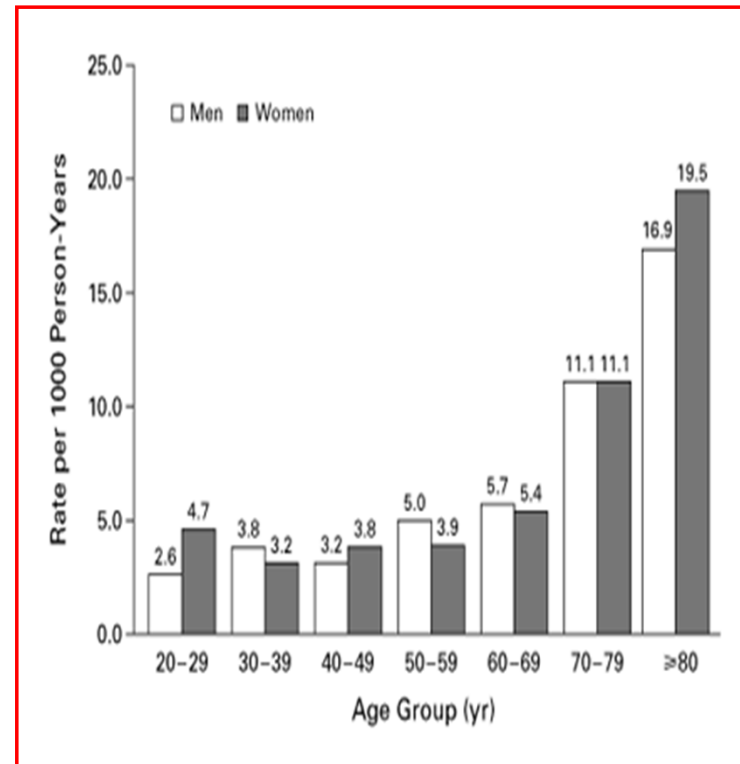
<sup>2</sup>Kapoor W. *Medicine*. 1990;69:160-175.

Annual U.S. Emergency Dept. Visits



# Syncope: High Incidence and Likely to Increase

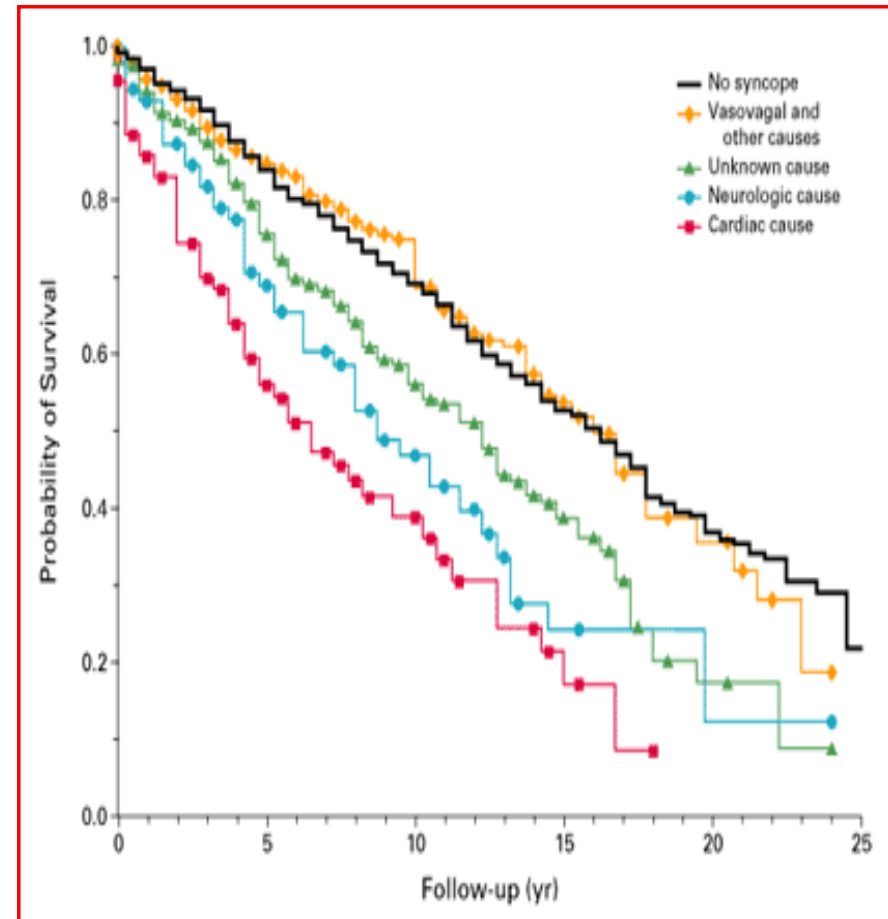
- 7814 participants followed for an average of 17 years, 822 reported syncope
- Estimated 10-year cumulative incidence of syncope was 6%
- The incidence rates increased with age, with a sharp rise at 70 years
- 22% of the study participants with syncope had a recurrence



Soteriades et al. *NEJM* 2002; 347: 878

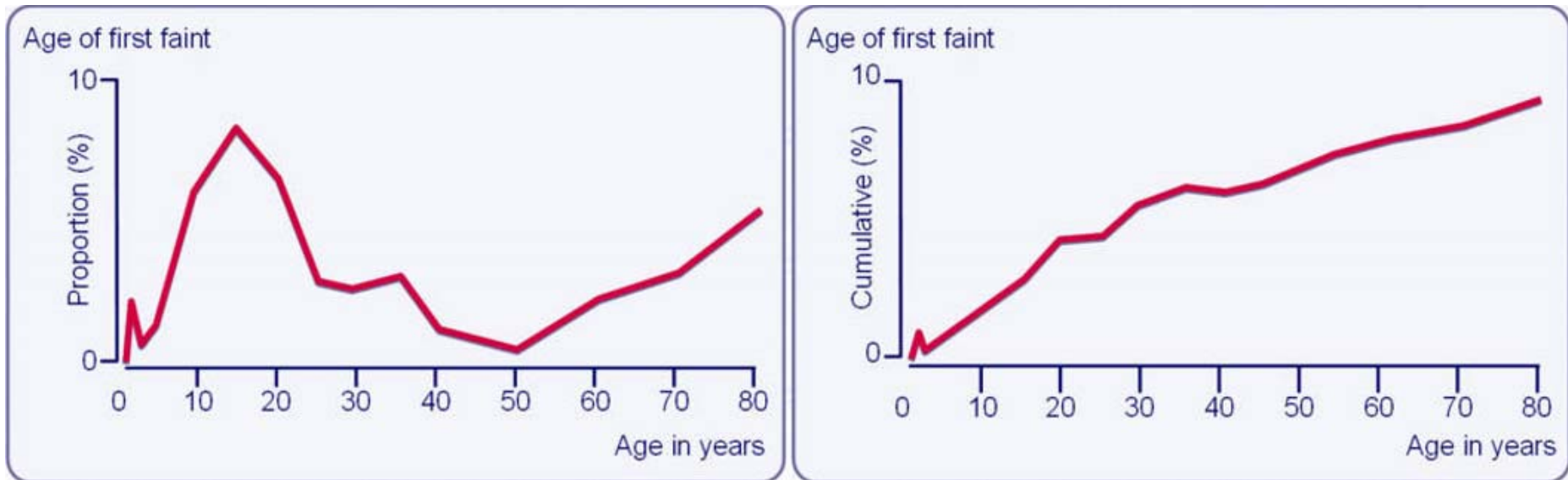
# Syncope

- 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*

# 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.

*Lombrosso et al Pediatrics 1967, Soteriades et al NEJM 2003, Ganzeboom et al Am J Cardiol 2003*

# Clarification of Definitions

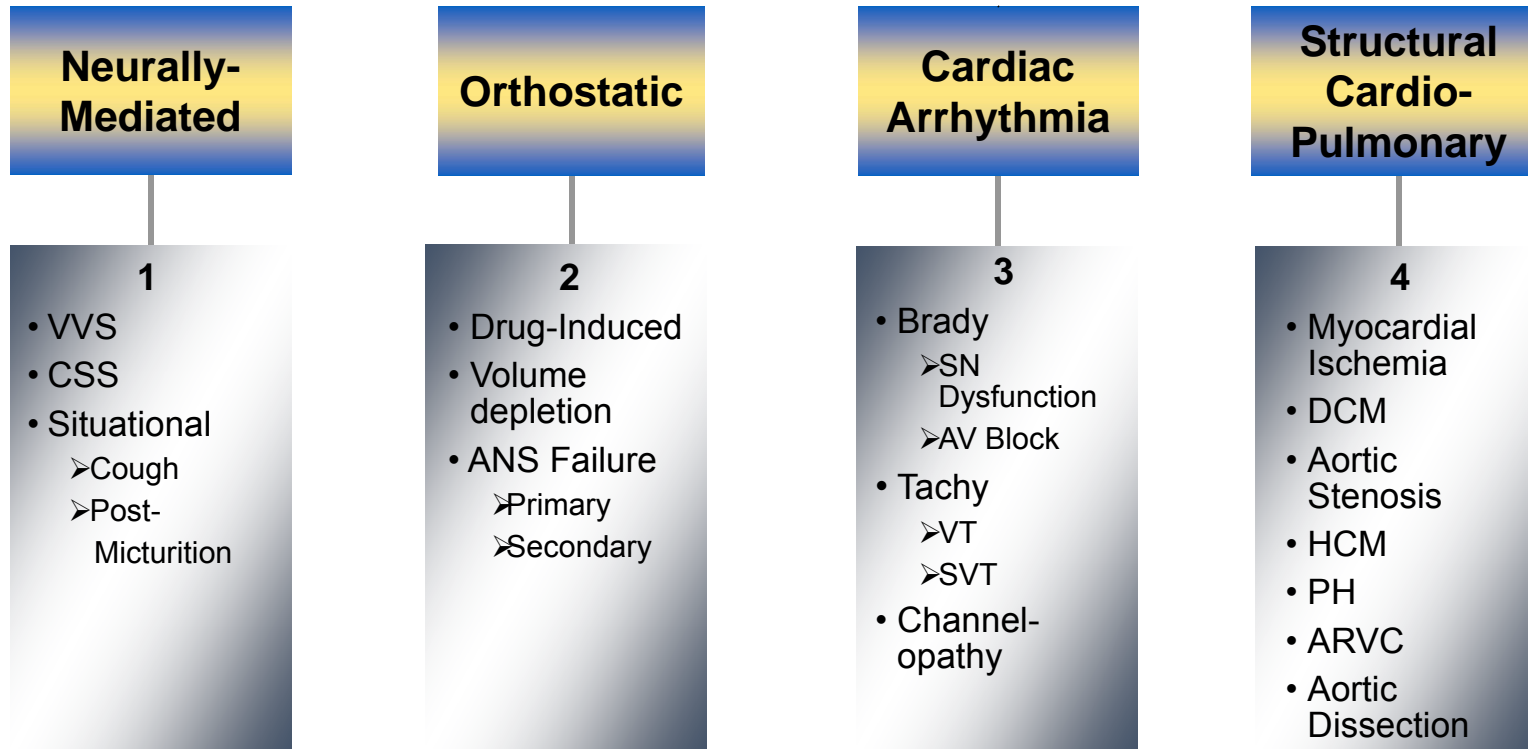
| Term                                   | Definition/Comments and References   |
|--|--|
| <b>Syncope</b>                         | <u>A symptom that presents with an abrupt, transient, complete loss of consciousness, associated with inability to maintain postural tone, with rapid and spontaneous recovery. The presumed mechanism is cerebral hypoperfusion (24,30).</u> 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). |
| <b>Loss of consciousness</b>           | A cognitive state in which one lacks awareness of oneself and one's situation, with an inability to respond to stimuli.  |
| <b>Transient loss of consciousness</b> | Self-limited loss of consciousness (30) can be divided into syncope and nonsyncope conditions. <u>Nonsyncope conditions include but are not limited to seizures, hypoglycemia, metabolic conditions, drug or alcohol intoxication, and concussion due to head trauma.</u> The underlying mechanism of syncope is presumed to be cerebral hypoperfusion, whereas nonsyncope conditions are attributed to different mechanisms.                      |
| <b>Presyncope (near-syncope)</b>       |  |



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

# Aetiology

## Causes of True Syncope



**Unexplained Causes = Approximately 1/3**

# 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)

## 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., laughter, 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).

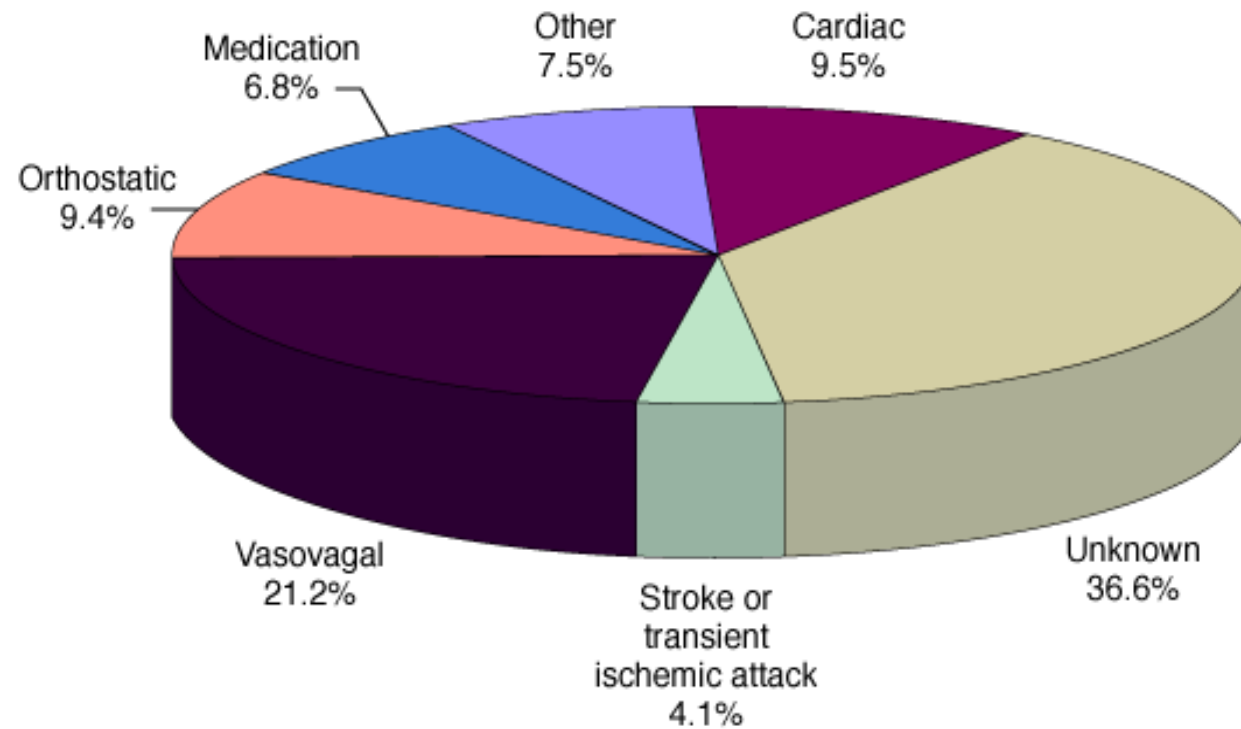
#### Drug induced bradycardia and tachyarrhythmias

#### 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



# Frequency of the causes of syncope according to age

| Age        | Source | Reflex % | OH % | CV % | Non-Sync. % | Unexplained % | Setting  |
|------------|--------|----------|------|------|-------------|---------------|----------|
| < 40 yrs   | †      | 51       | 2.5  | 1.1  | 18          | 27            | ED & CPU |
| 40-60 yrs  | †      | 37       | 6    | 3    | 19          | 34            | ED & CPU |
| < 65 years | ‡      | 68.5     | 0.5  | 12   |             | 19            | CD       |
| 60/65 yrs  | ‡      | 52       | 3    | 34   |             | 11            | CD       |
|            | §      | 62       | 8    | 11   |             | 14            | GD       |
|            | †      | 25       | 8.5  | 13   | 12.5        | 41            | ED & CPU |
| > 75 yrs   | §      | 36       | 30   | 16   |             | 9             | GD       |

† = Olde Norkcamp

‡ = Del Rosso

§ = Ungar

**ED** = emergency department

**CPU** = chest pain unit

**CD** = cardiology department

**GD** = geriatric department

# Unexplained Syncope: ISSUE Classification

- **Type 1 Asystole.** RR pause  $\geq 3$  seconds **63%**
  - 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 **5%**
  - 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 **18%**
  - 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 **14%**
  - Type 4 A. Progressive sinus tachycardia
  - Type 4 B. Atrial fibrillation
  - Type 4 C. Supraventricular tachycardia (except sinus)
  - Type 4 D. Ventricular tachycardia

# Frequency of the causes of syncope according to presence of CVD disease

**TABLE 1. CAUSES OF SYNCOPE ACCORDING TO SEX AND THE PRESENCE OR ABSENCE OF CARDIOVASCULAR DISEASE AT BASE LINE.**

| CAUSE                               | CARDIOVASCULAR<br>DISEASE ABSENT<br>(N=599) |                  | CARDIOVASCULAR<br>DISEASE PRESENT<br>(N=223) |                  | TOTAL<br>SAMPLE<br>(N=822) |
|-------------------------------------|---|------------------|--|------------------|----------------------------|
|                                     | MEN<br>(N=232)                              | WOMEN<br>(N=367) | MEN<br>(N=116)                               | WOMEN<br>(N=107) |                            |
|                                     | percent of subjects                         |                  |  |                  |                            |
| Cardiac                             | 6.5   | 3.8              | 26.7   | 16.8             | 9.5                        |
| Unknown*                            | 31.0  | 41.7             | 31.0   | 37.4             | 36.6                       |
| Stroke or transient ischemic attack | 1.7   | 2.5              | 9.5  | 9.4              | 4.1                        |
| Seizure                             | 7.3   | 3.3              | 6.9  | 2.8              | 4.9                        |
| Vasovagal                           | 24.1  | 24.5             | 11.2   | 14.0             | 21.2                       |
| Orthostatic                         | 9.5   | 10.9             | 6.9  | 6.5              | 9.4                        |
| Medication                          | 7.3   | 6.5              | 4.3  | 9.4              | 6.8                        |
| Other†                              | 13.0  | 6.8              | 3.5  | 3.7              | 7.5                        |

\*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.

# Conditions Uncommonly Associated With Syncope

|                                       |  |   |
|---------------------------------------|--|---|
| Cardiac tumors (572)                  | Triad of obstruction, embolic, and systemic signs and symptoms.  | Syncope is often due to obstruction to blood flow.  |
| Prosthetic valve thrombosis (573-575) | Ranges from asymptomatic to profound HF.   | May have similar presentation to a cardiac tumor, with a high risk of embolic phenomenon and obstruction.   |
| Anomalous coronary artery (576-579)   | Common cause of exertional syncope or SCD, classically in young athletes.  | Syncope can be due to Bezold Jarisch reflex, hypotension, VT, or AV block.  |
| Aortic dissection (580-582)           | Aortic dissection may manifest with neurological symptoms, myocardial infarction, and HF. Syncope can occur in as many as 13% of aortic dissections.   | 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. |
| Subclavian steal (583-587)            | 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. | Syncope is generally associated with upper-extremity activity.  |
| Coarctation of the aorta (588)        | If severe, it can result in HF or aortic dissection.   | Associated bicuspid aortic valve stenosis may be considered with syncope.   |
| Rheumatoid arthritis (589)            | Chronic, autoimmune inflammatory disorder with systemic manifestations.  | Rarely associated with complete heart block and syncope.  |

# Conditions Uncommonly Associated With Syncope

| Condition                                 | Clinical Characteristics  | Notes   |
|---|---|---|
| <b>Cardiovascular and Cardiopulmonary</b> |   |   |
| Cardiac tamponade                         | Hypotension, tachycardia, cardiogenic shock.  | Often tachycardia and hypotension; may be hypotensive and bradycardic acutely.  |
| Constrictive pericarditis<br>(533-535)    | Severe HF symptoms, including edema, exertional dyspnea, orthopnea.   | May be associated with cough syncope.   |
| LV noncompaction<br>(536-539)             | Cardiomyopathy characterized by prominent LV trabeculae and deep intertrabecular recesses, due to embryologic perturbation.                 | Syncope reported in 5%-9% of both adult and pediatric patients. The mechanism may be a tachyarrhythmia.   |
| Takotsubo cardiomyopathy<br>(540,541)     | Apical ballooning and basal hypercontractility, often due to stress. Chest pain and ECG changes consistent with ischemia are commonly seen. | Syncope is uncommon and may be multifactorial.  |
| Pulmonary embolus<br>(128,542,543)        | Hypoxemia, tachycardia; hypotension and shock leading to pulseless electrical activity cardiac arrest in severe cases.                      | 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. |
| Pulmonary arterial hypertension           | Occurs more often during exertion in younger patients.  | Syncope due to inability to augment or sustain cardiac output during exertion, followed by vasodilatation.  |

# Conditions Uncommonly Associated With Syncope

## Infiltrative

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

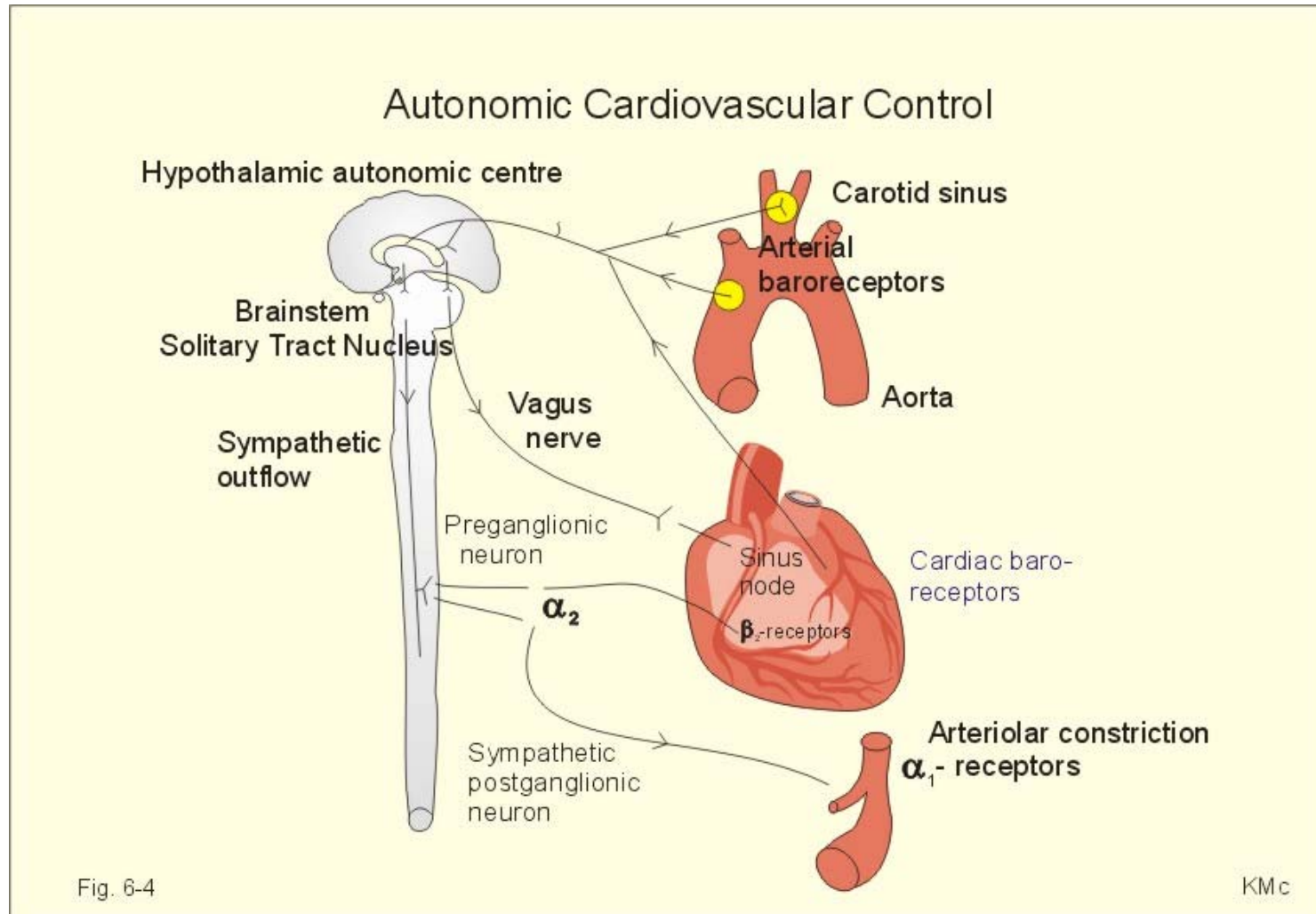
## Endocrine

|   |   |  |
|---|---|--|
| Carcinoid syndrome (602)<br>Pheochromocytoma (602,603)<br>Mastocytosis (602-609)<br>Vasoactive intestinal peptide tumor | These tumors can release vasoactive peptides and cause vasodilation, flushing, pruritus, and gastrointestinal symptoms. | Syncope is usually due to transient hypotension. |
|---|---|--|

## Hematologic

|                              |   |                            |
|------------------------------|---|----------------------------|
| Beta thalassemia major (610) | Severe anemia, multiple organ failure, and dilated cardiomyopathy due to iron overload. | Syncope may be arrhythmic. |
|------------------------------|---|----------------------------|

# Neurally Mediated Syncope: pathophysiology



# Vasovagal Syncope Classification

**Cardioinhibitory**

**Vasodepressor**

**Mixed**

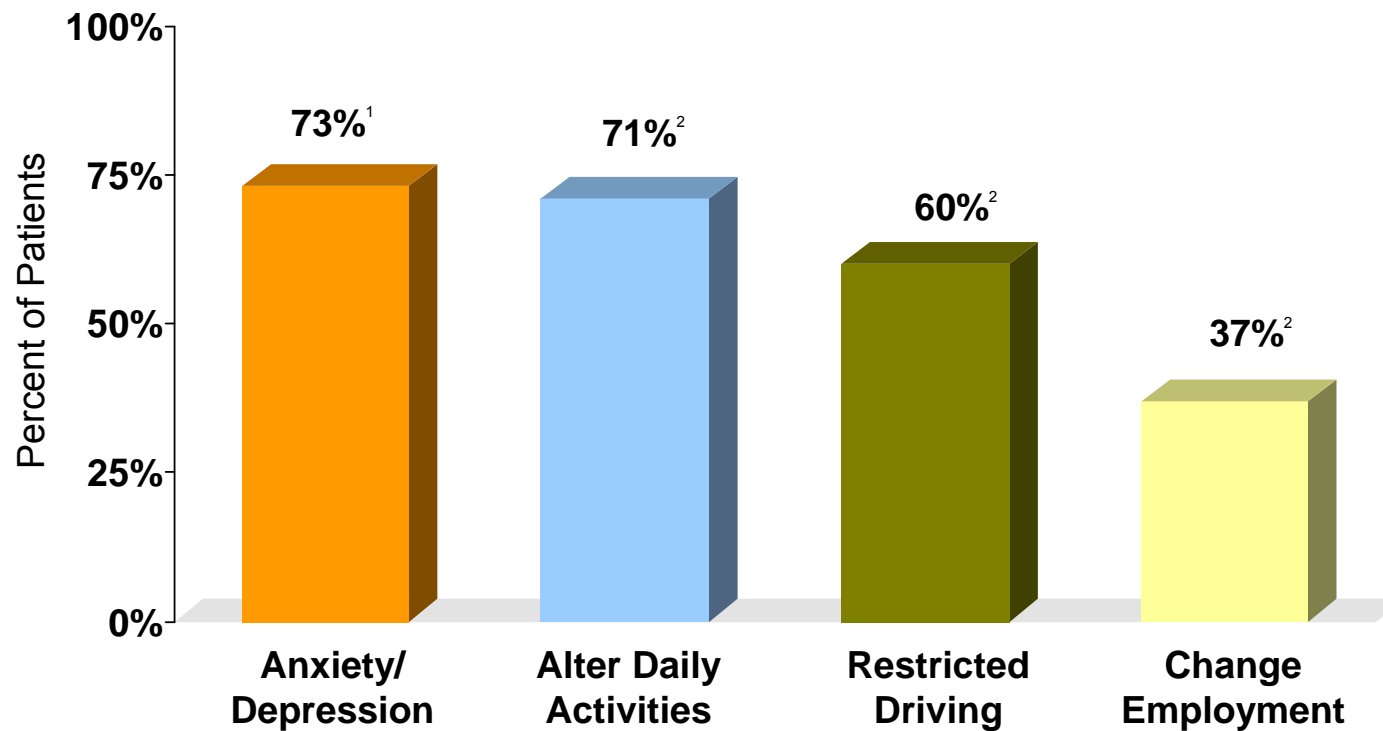
# Orthostatic syncope

- 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

# 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

# Syncope: *QOL Impact*



<sup>1</sup>Linzer M. *J Clin Epidemiol*, 1991;44:1037-1043.

<sup>2</sup>Linzer M. *J Gen Int Med*, 1994;9:181-186.

A pt with Syncope:  
how should I approach?



## Initial evaluation

The initial evaluation should answer the key questions:

1. Is there syncope or not?
2. Has the aetiological diagnosis been determined?
3. Are there data of a high risk of cardiovascular events or death?

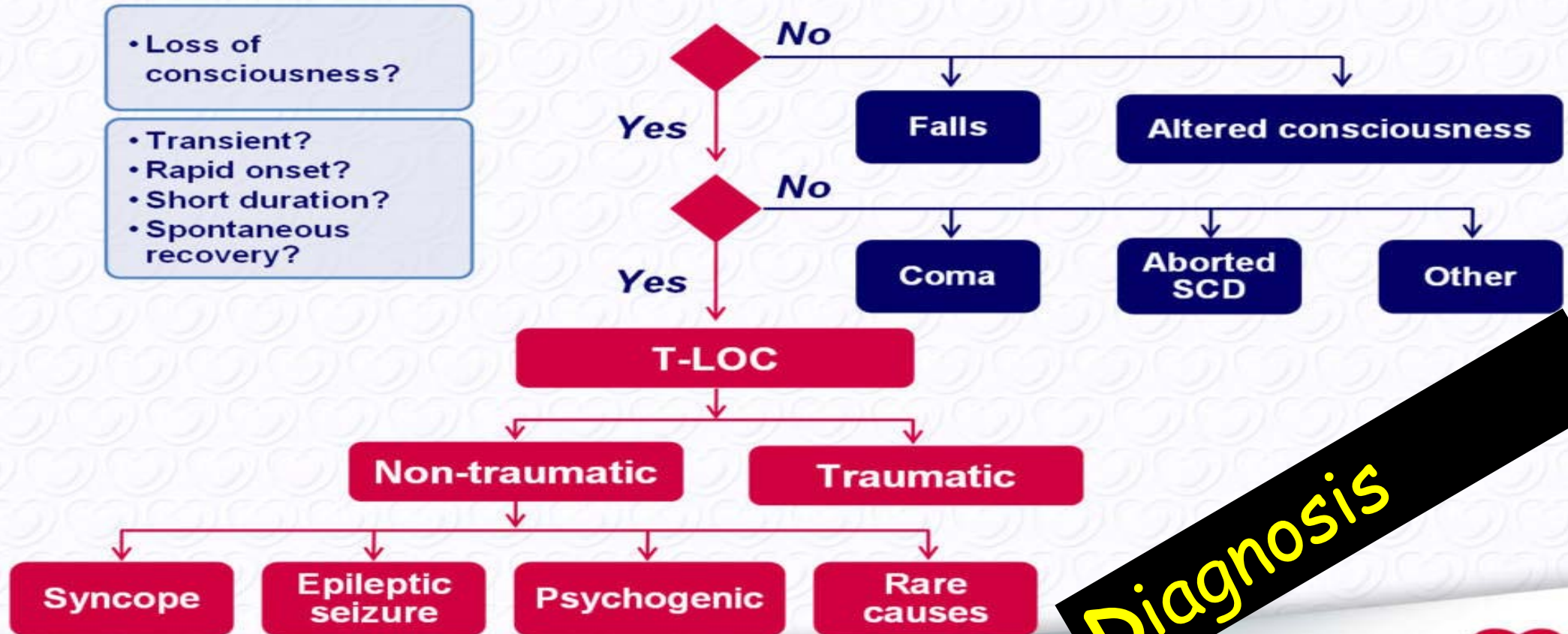
Diagnosis

Aetiology

Risk

# Syncope in the context of T-LOC

## Clinical presentation



**Diagnosis**

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

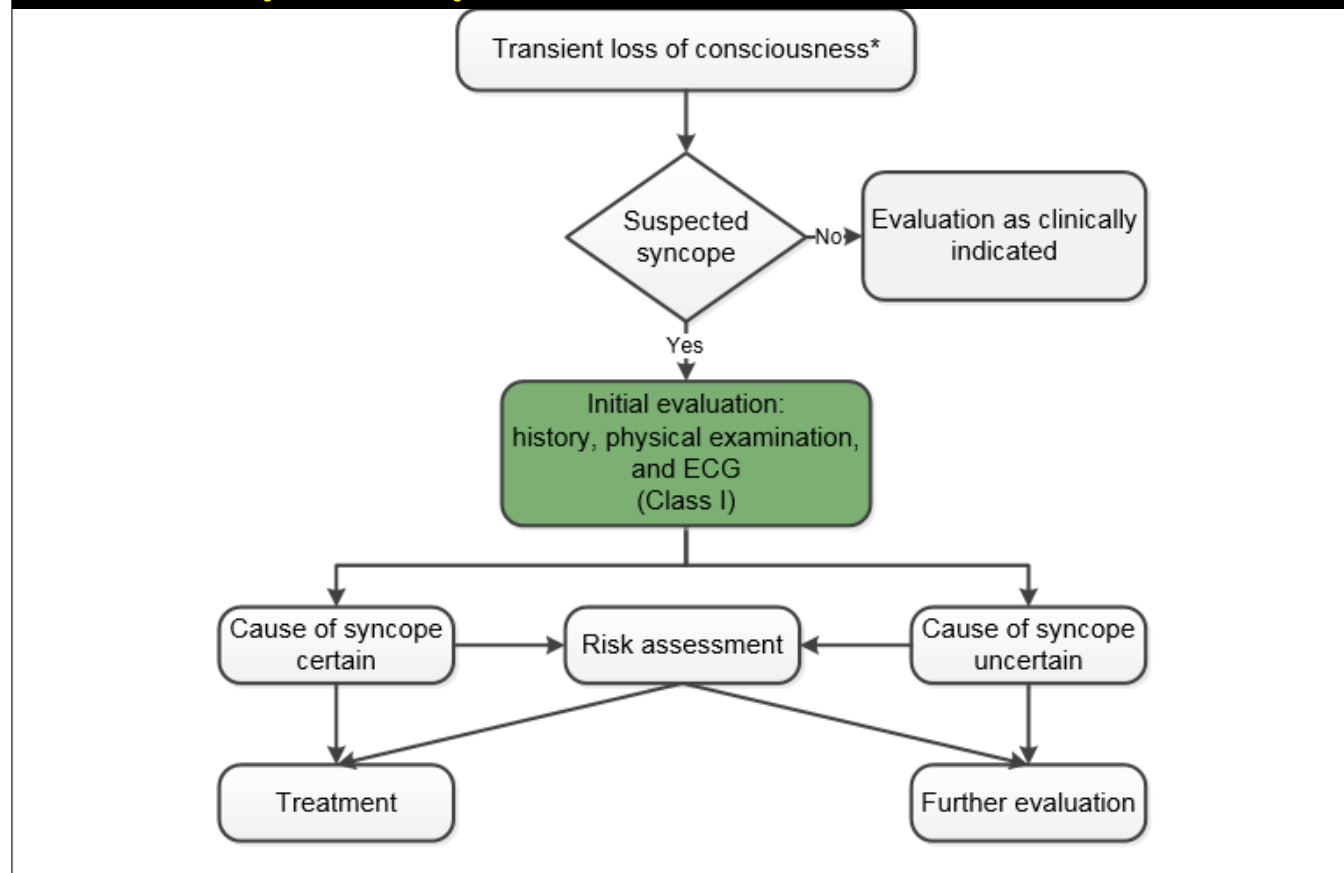
**The Task Force for the Diagnosis and Management of Syncope of the European Society of Cardiology (ESC)**

### **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



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

# Clarification of Definitions

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

## Reflex (neurally mediated) syncope

Syncope due to a reflex that causes vasodilation, bradycardia, or both (24,30,31).

### ■ 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/or 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.

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

# Clarification of Definitions

|   |   |
|---|---|
| <b>Orthostatic hypotension (OH)</b>                           | A drop in systolic BP of $\geq 20$ mm Hg or diastolic BP of $\geq 10$ mm Hg with assumption of an upright posture (31).   |
| ■ <b>Initial (immediate) OH</b>                               | A transient BP decrease within 15 s after standing, with presyncope or syncope (31,32).   |
| ■ <b>Classic OH</b>   | A sustained reduction of systolic BP of $\geq 20$ mm Hg or diastolic BP of $\geq 10$ mm Hg within 3 min of assuming upright posture (31).   |
| ■ <b>Delayed OH</b>   | A sustained reduction of systolic BP of $\geq 20$ mm Hg (or 30 mm Hg in patients with supine hypertension) or diastolic BP of $\geq 10$ mm Hg that takes $>3$ min of upright posture to develop. The fall in BP is usually gradual until reaching the threshold (31). |
| ■ <b>Neurogenic OH</b>  | 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.                   |
| <b>Psychogenic pseudosyncope</b>                              | A syndrome of <i>apparent</i> but not true loss of consciousness that may occur in the absence of identifiable cardiac, reflex, neurological, or metabolic causes (30).   |
| <b>Unexplained syncope (syncope of undetermined etiology)</b> | 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.                     |

# Clarification of Definitions

## Orthostatic intolerance

**Symptoms:** 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  $\geq 1$  of these symptoms associated with reduced ability to maintain upright posture.

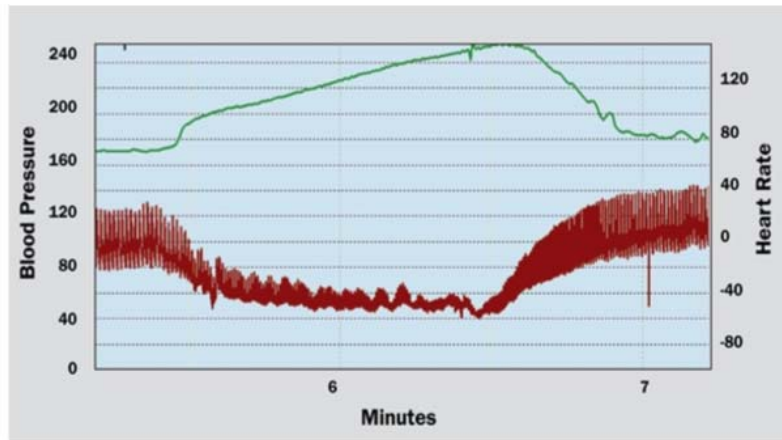
## Orthostatic tachycardia

**Findings:** A sustained increase in heart rate of  $\geq 30$  bpm within 10 min of moving from a recumbent to a quiet (nonexertional) standing position (or  $\geq 40$  bpm in individuals 12–19 y of age) (24,30,31).

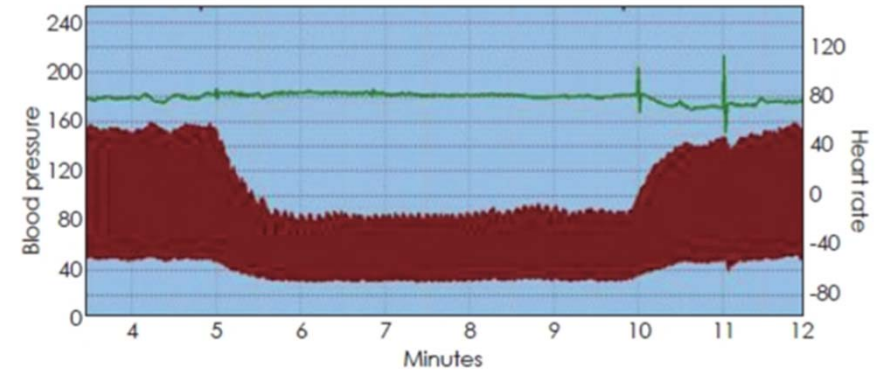
## Postural (orthostatic) tachycardia syndrome (POTS)

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  $\geq 30$  bpm during a positional change from supine to standing (or  $\geq 40$  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

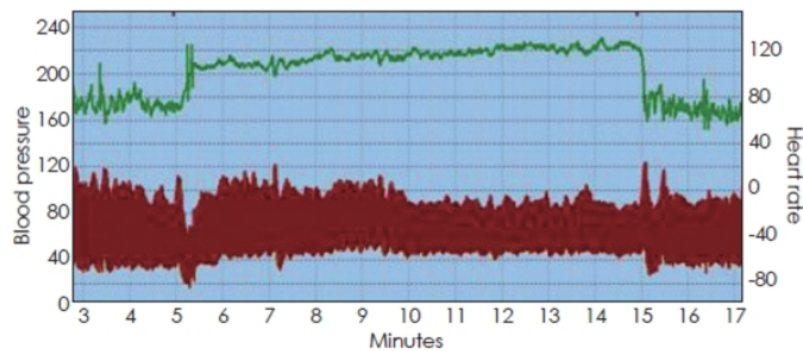


## Neurogenic orthostatic hypotension



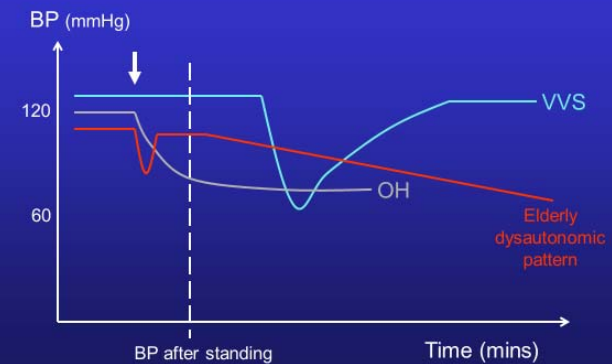
*Pronounced fall in blood pressure with a blunted heart rate response*

## POTS (postural tachycardia syndrome)



*Exaggerated heart rate response without syncope*

## BP responses in different types of syncope



# ECG

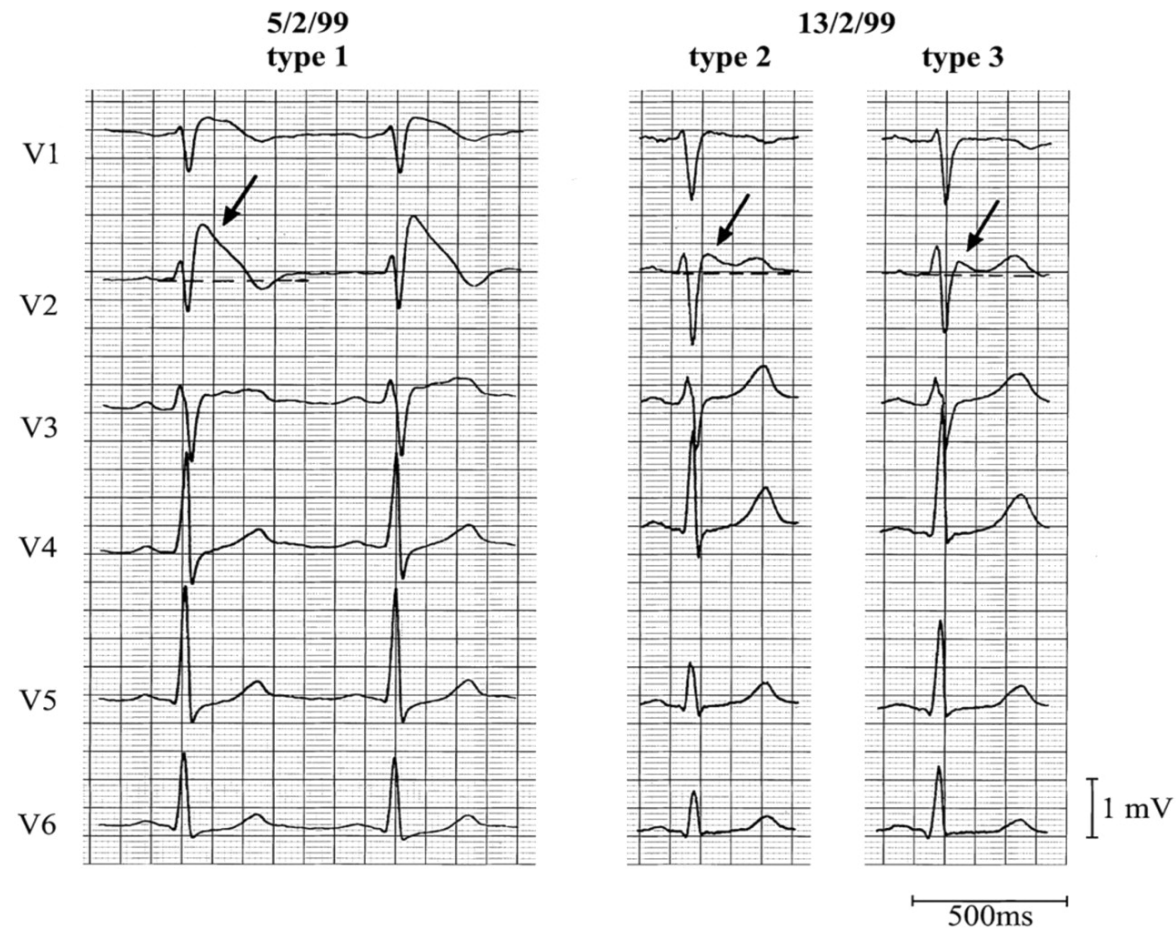
## Guidelines for the diagnosis and management of syncope (version 2009)

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

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

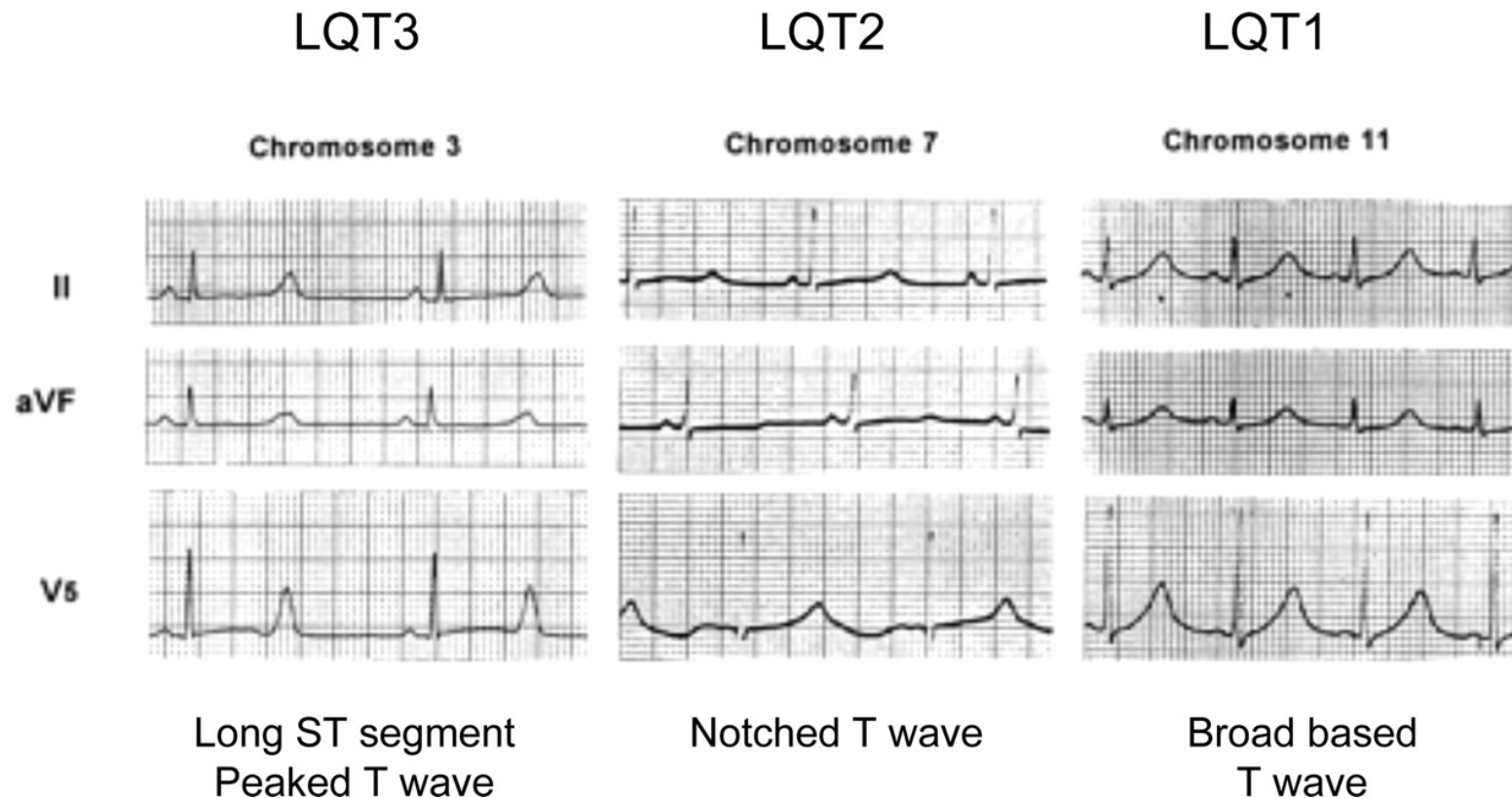
- **Abnormal in 50% of patients. Identifies potential cause in 2-11%**
  - **Pre-excitation**
  - **Conduction Delays**
  - **MI**
  - **LVH/RVH (Hypertrophic CM, Aortic Stenosis, Pulmonary HTN)**
  - **QT Interval (QTc=460) should raise suspicion**
  - **Brugada Abnormalities**
  - **Epsilon Waves (ARVC)**

# ECG changes in the Brugada syndrome

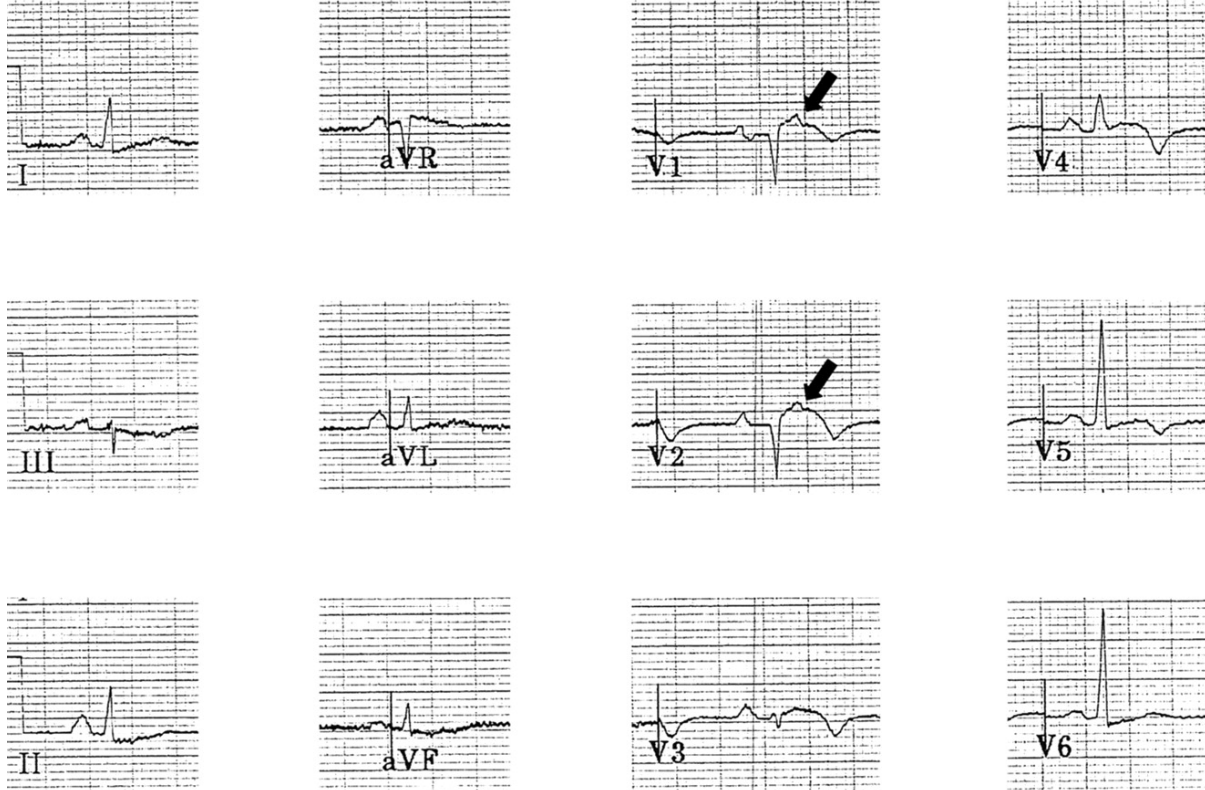


Strickberger, S. A. et al. Circulation 2006;113:316-327

# Different patterns of QT prolongation in LQTS



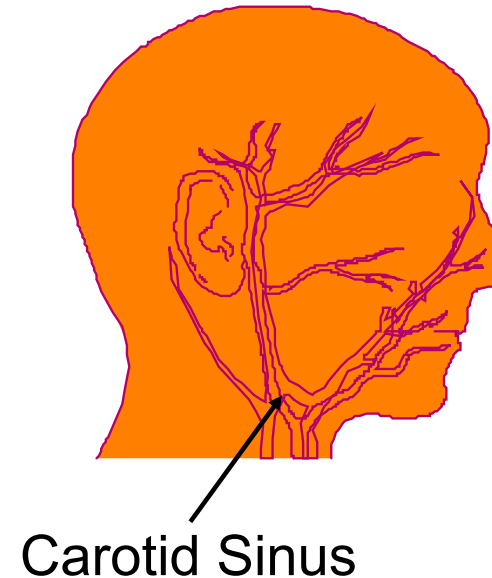
# Twelve-lead ECG in normal sinus rhythm with epsilon wave



Kenigsberg, D. N. et al. Circulation 2007;115:e538-e539

## 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



# 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  
==CAROTID SINUS SYNDROME
- Contraindications
  - Carotid bruit, known but significant carotid arterial disease, previous CVA, MI last 3 months.

# CSS

## Carotid Sinus Syndrome

- Syncope clearly associated with carotid sinus stimulation is rare ( $\leq 1\%$  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

Kenny RA, et al. *J Am Coll Cardiol*. 2001;38:1491-1496.

Brignole M, et al. *Europace*. 2004;6:467-537.

Sutton R. In: *Neurally Mediated Syncope: Pathophysiology, Investigation and Treatment*. Blanc JJ, et al. eds. Armonk, NY: Futura;1996:138.

# 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.

| Class | Level |
|-------|-------|
| I     | B     |
| III   | C     |
| I     | B     |

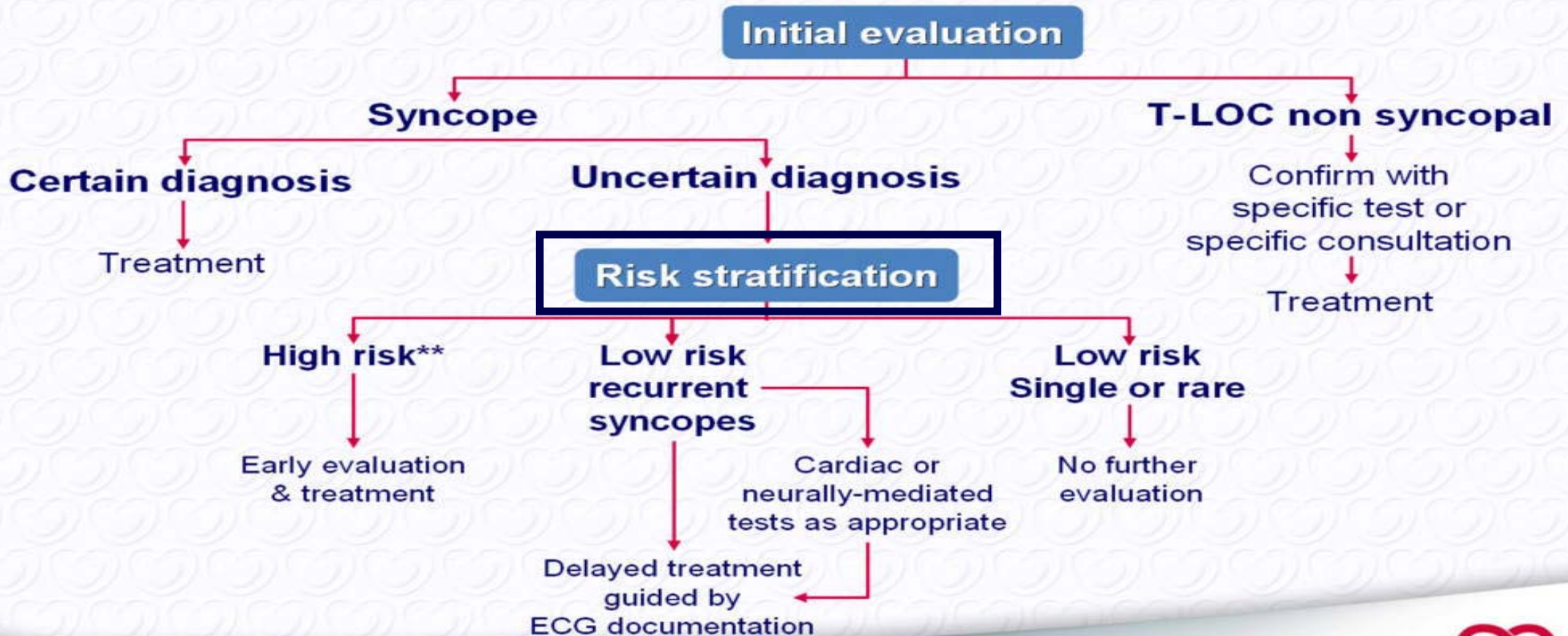
*"Syncope may be an acute result of major hemodynamic abnormalities or a manifestation of serious underlying disease"*

## Risk stratification



# Diagnostic flowchart in patients with suspected T-LOC

## T-LOC – suspected 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

## More Often Associated With Noncardiac Causes of Syncope

---

- Younger age
  - No known cardiac disease
  - Syncope only in the standing position
  - Positional change from supine or sitting to standing
  - Presence of prodrome: nausea, vomiting, feeling warmth
  - Presence of specific triggers: dehydration, pain, distressful stimulus, medical environment
  - Situational triggers: cough, laugh, micturition, defecation, deglutition
  - Frequent recurrence and prolonged history of syncope with similar characteristics
- 

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

# Short and long term morbidity and mortality risk of syncope

## Short-Term Risk Factors ( $\leq 30$ d)

### History: Outpatient Clinic or ED Evaluation

Male sex (74,85,101,102)

Older age ( $>60$  y) (88)

No prodrome (68)

Palpitations preceding loss of consciousness (83)

Exertional syncope (83)

Structural heart disease (70,83,88,101,103)

HF (74,83,85,88)

Cerebrovascular disease (70)

Family history of SCD (70)

Trauma (68,101)

### Physical Examination or Laboratory Investigation

Evidence of bleeding (83)

Persistent abnormal vital signs (70)

Abnormal ECG (68,72,74,75,105)

Positive troponin (75)

## Long-Term Risk Factors ( $>30$ d)

Male sex (68,90)

Older age (67,74,75,90)

Absence of nausea/vomiting preceding syncopal event (93)

VA (68,90)

Cancer (68)

Structural heart disease (68,103)

HF (90)

Cerebrovascular disease (68)

Diabetes mellitus (104)

High CHADS-2 score (95)

Abnormal ECG (84,90,93)

Lower GFR

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

# Scoring for prediction of serious events in pts with syncope

| Study/<br>Reference         | Year | Sample<br>N | Events<br>N (%) | Outcome<br>Definition | ED<br>Events* | Predictors  | NPV<br>(%)+ |
|-----------------------------|------|-------------|-----------------|-----------------------|---------------|---|-------------|
| Martin (90)                 | 1997 | 252         | 104 (41%)       | 1-y death/arrhythmia  | Yes           | Abnormal ECG‡; >45 y of age; VA; HF   | 93          |
| Sarasin (74)                | 2003 | 175         | 30 (17%)        | Inpatient arrhythmia  | Yes           | Abnormal ECG‡; >65 y of age; HF   | 98          |
| OESIL (67)                  | 2003 | 270         | 31 (11%)        | 1-y death             | N/A           | Abnormal ECG‡; >65 y of age; no prodrome; cardiac history   | 100         |
| SFSR (72)                   | 2004 | 684         | 79 (12%)        | 7-d serious events§   | Yes           | Abnormal ECG‡; dyspnea; hematocrit; systolic BP <90 mm Hg; HF   | 99          |
| Boston Syncope<br>Rule (70) | 2007 | 293         | 68 (23%)        | 30-d serious events   | Yes           | 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 | 100         |
| Del Rosso (69)              | 2008 | 260         | 44 (17%)        | Cardiac etiology      | N/A           | Abnormal ECG‡/cardiac history; palpitations; exertional; supine; precipitant (a low-risk factor); autonomic prodrome (low-risk factors)   | 99          |
| STePS (68)                  | 2008 | 676         | 41 (6%)         | 10-d serious events¶  | Yes           | Abnormal ECG‡; trauma; no prodrome; male sex  | —           |
| Syncope Risk<br>Score (75)  | 2009 | 2,584       | 173 (7%)        | 30-d serious events#  | No            | Abnormal ECG‡; >90 y of age; male sex; positive troponin; history of arrhythmia; systolic BP >160 mm Hg; near-syncope (a low-risk factor)   | 97          |
| ROSE (73)                   | 2010 | 550         | 40 (7%)         | 30-d serious events#  | Yes           | Abnormal ECG‡; B-natriuretic peptide; hemoglobin; O <sub>2</sub> Sat; fecal occult blood  | 98          |

IIb

B-NR

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

**CLINICAL PRACTICE GUIDELINE****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

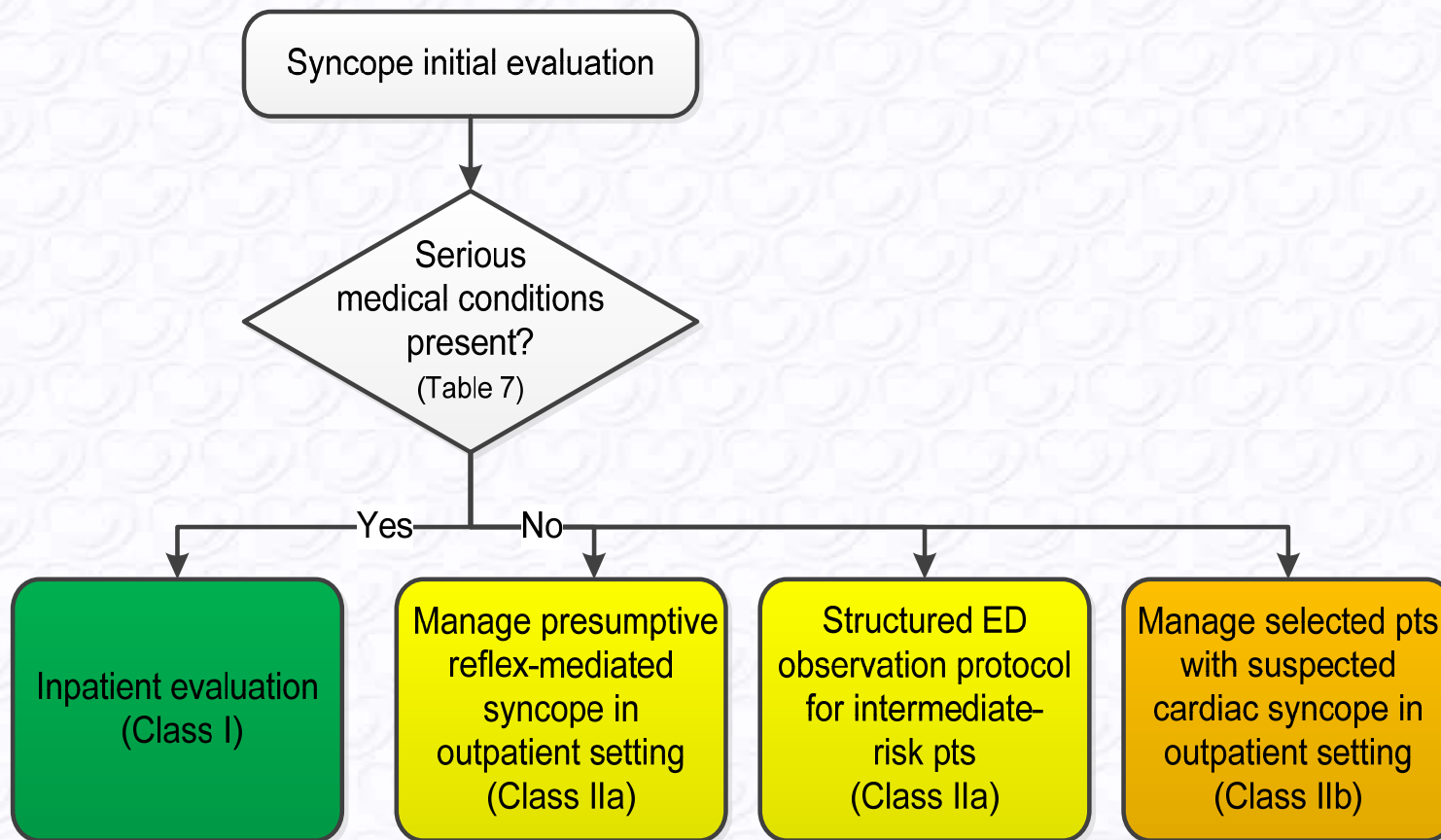
# Conditions that may impose hospital admission

**TABLE 7** Examples of Serious Medical Conditions That Might Warrant Consideration of Further Evaluation and Therapy in a Hospital Setting

| Cardiac Arrhythmic Conditions   | Cardiac or Vascular Nonarrhythmic Conditions  | Noncardiac Conditions   |
|---|---|---|
| <ul style="list-style-type: none"><li>■ Sustained or symptomatic VT</li><li>■ Symptomatic conduction system disease or Mobitz II or third-degree heart block</li><li>■ Symptomatic bradycardia or sinus pauses not related to neurally mediated syncope</li><li>■ Symptomatic SVT</li><li>■ Pacemaker/ICD malfunction</li><li>■ Inheritable cardiovascular conditions predisposing to arrhythmias</li></ul> | <ul style="list-style-type: none"><li>■ Cardiac ischemia</li><li>■ Severe aortic stenosis</li><li>■ Cardiac tamponade</li><li>■ HCM</li><li>■ Severe prosthetic valve dysfunction</li><li>■ Pulmonary embolism</li><li>■ Aortic dissection</li><li>■ Acute HF</li><li>■ Moderate-to-severe LV dysfunction</li></ul> | <ul style="list-style-type: none"><li>■ Severe anemia/gastrointestinal bleeding</li><li>■ Major traumatic injury due to syncope</li><li>■ Persistent vital sign abnormalities</li></ul> |

HCM indicates hypertrophic cardiomyopathy; HF, heart failure; ICD, implantable cardioverter-defibrillator; LV, left ventricular; SVT, supraventricular tachycardia; and VT, ventricular tachycardia.

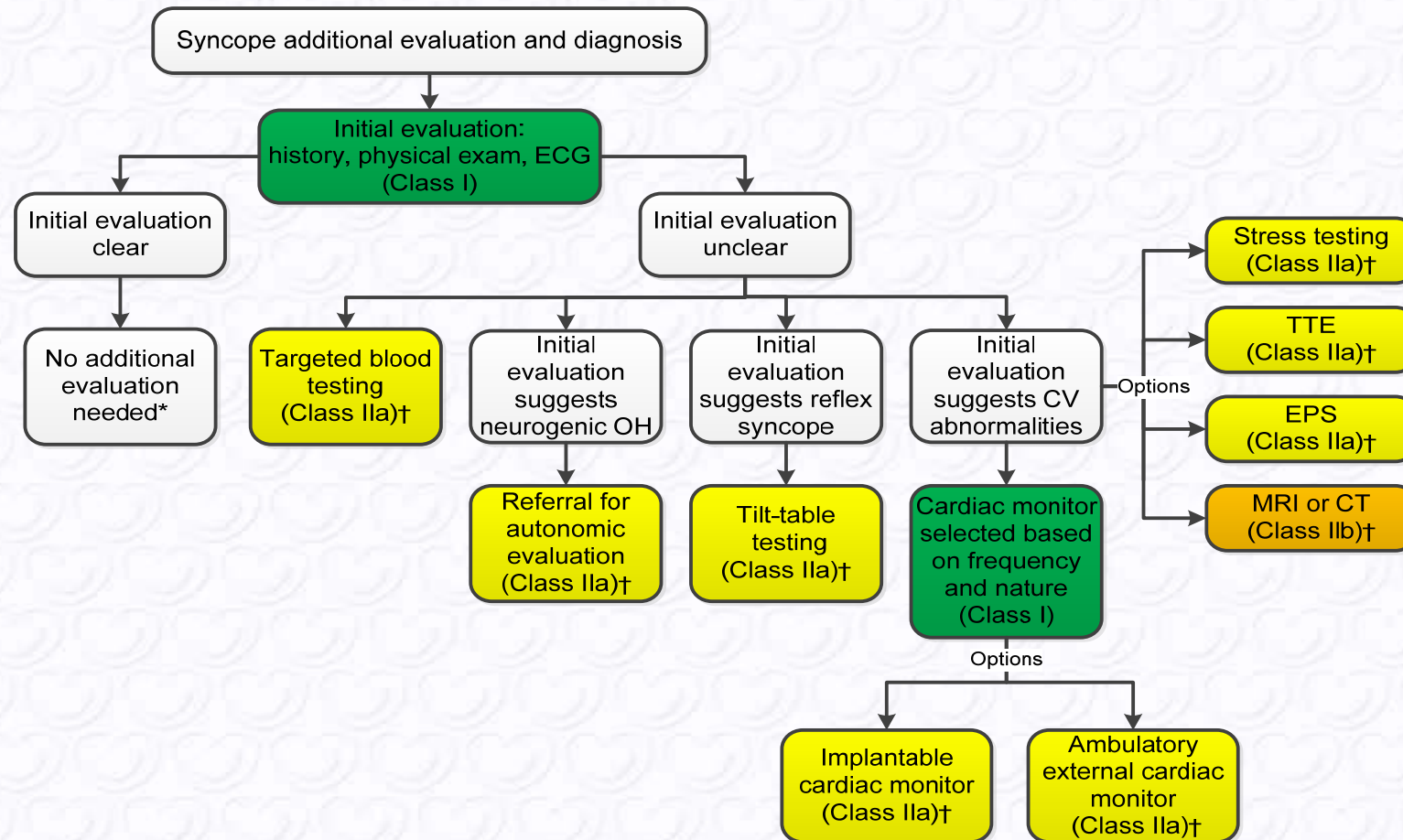
## Patient Disposition After Initial Evaluation for Syncope



**Further evaluation**



# Additional Evaluation and Diagnosis



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

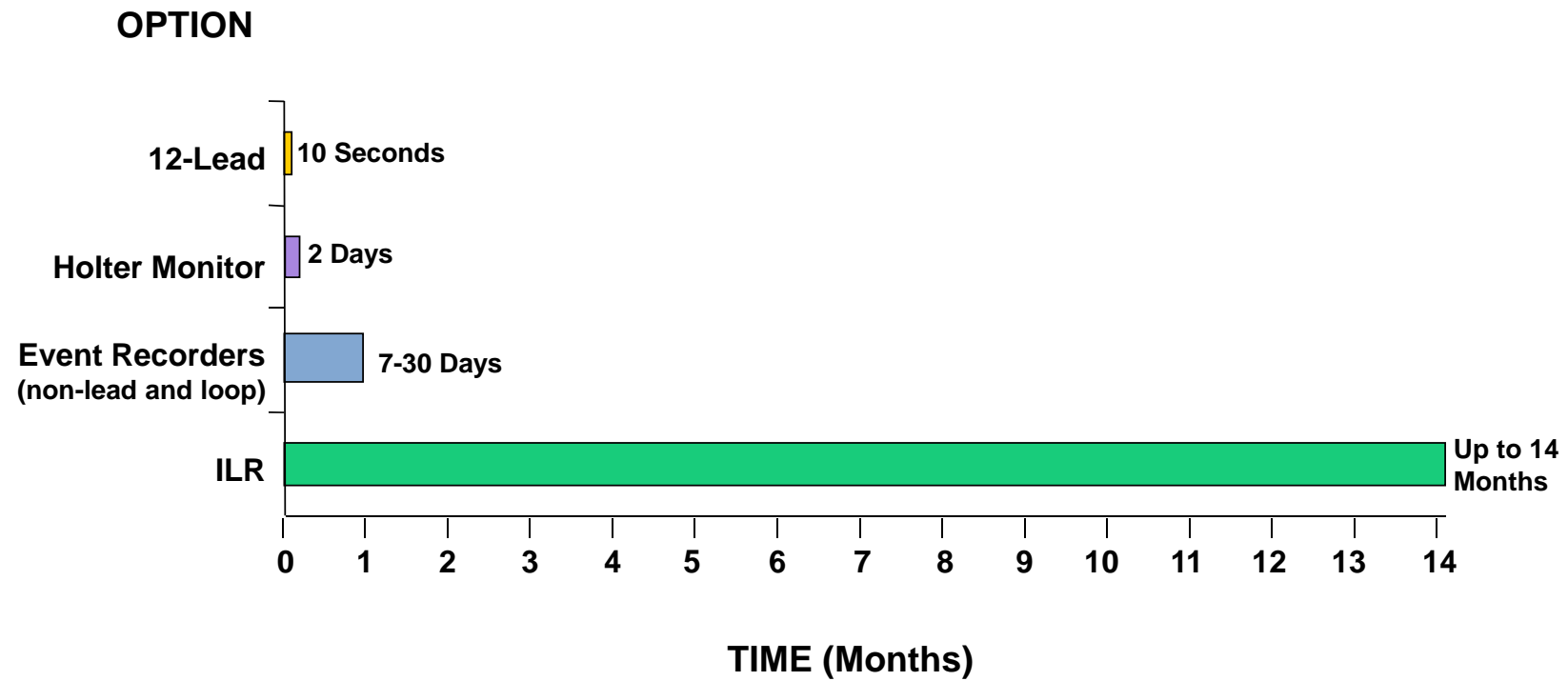
|  | Yield (%)                      |
|--|--------------------------------|
| <b>Initial Evaluation</b>                    |                                |
| History, Physical Exam, ECG, Cardiac Massage | 50-70                          |
| <b>Other Tests/Procedures</b>                |                                |
| Head-Up Tilt                                 | 27                             |
| External Cardiac Monitoring                  | 5-13                           |
| Insertable Loop Recorder (ILR)               | 43-88 <sup>3-5</sup>           |
| EP Study                                     | <2-5                           |
| Exercise Test                                | 0.5                            |
| EEG  | 0.3-0.5                        |
| MRI  | No data available <sup>6</sup> |

# Cardiovascular Testing

## Cardiac Imaging

| COR             | LOE  | Recommendations   |
|-----------------|------|---|
| IIa             | B-NR | Transthoracic echocardiography can be useful in selected patients presenting with syncope if structural heart disease is suspected.   |
| IIb             | B-NR | CT or MRI may be useful in selected patients presenting with syncope of suspected cardiac etiology.   |
| III: No Benefit | B-R  | 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



# 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 ( $\geq 1$  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  $\leq 4$  weeks.

|     |   |
|-----|---|
| I   | B |
| I   | C |
| I   | B |
| I   | B |
| I   | B |
| IIa | B |
| IIa | B |

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|     |      |   |
|-----|------|---|
| I   | C-EO | The choice of a specific cardiac monitor should be determined <u>on the basis of the frequency and nature of syncope events.</u>  |
| IIa | B-NR | To evaluate selected ambulatory patients with syncope of suspected arrhythmic etiology, the following external cardiac monitoring approaches can be useful: <ol style="list-style-type: none"> <li>1. Holter monitor</li> <li>2. <u>Transtelephonic monitor</u></li> <li>3. External loop recorder</li> <li>4. Patch recorder</li> <li>5. Mobile cardiac outpatient telemetry.</li> </ol> |
| IIa | B-R  | To evaluate selected ambulatory patients with syncope of suspected <u>arrhythmic etiology</u> , an ICM can be useful.   |

# Tilt Table 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)

- 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

|     |   |
|-----|---|
| I   | B |
| I   | C |
| IIa | C |
| IIb | C |
| IIb | C |
| IIb | C |
| III | B |
| III | C |

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

|                 |      |   |
|-----------------|------|---|
| IIa             | B-R  | If the diagnosis is <u>unclear</u> after initial evaluation, tilt-table testing can be useful for patients with suspected VVS.        |
| IIa             | B-NR | Tilt-table testing can be useful for patients with syncope and <u>suspected delayed OH</u> when initial evaluation is not diagnostic. |
| IIa             | B-NR | Tilt-table testing is reasonable to distinguish convulsive syncope from <u>epilepsy</u> in selected patients.                         |
| IIa             | B-NR | Tilt-table testing is reasonable to establish a diagnosis of <u>pseudosyncope</u> .   |
| III: No Benefit | B-R  | Tilt-table testing is not recommended to predict a response to medical treatments for VVS.  |

# 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.

I

C

- **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.

I

C

I

C

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

Ila

C-LD

Exercise stress testing can be useful to establish the cause of syncope in selected patients who experience syncope or presyncope during exertion.

# 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.

**I B**

**IIa B**

**IIb B**

**IIb C**

**IIb C**

**III B**

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

|                        |             |  |
|------------------------|-------------|--|
| <b>IIa</b>             | <b>B-NR</b> | EPS can be useful for evaluation of selected patients with syncope of suspected arrhythmic etiology.   |
| <b>III: No Benefit</b> | <b>B-NR</b> | 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. |

# Neurological Testing

## Autonomic Evaluation

| COR | LOE  | Recommendation  |
|-----|------|---|
| Ila | C-LD | Referral for autonomic evaluation can be useful to improve diagnostic and prognostic accuracy in selected patients with syncope and known or suspected neurodegenerative disease. |

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

# Neurological Testing

| COR             | LOE  | Recommendations   |
|-----------------|------|---|
| Ila             | C-LD | Simultaneous monitoring of an EEG and hemodynamic parameters during tilt-table testing can be useful to distinguish among syncope, pseudosyncope, and epilepsy.                             |
| III: No Benefit | B-NR | 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. |
| III: No Benefit | B-NR | 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.                 |
| III: No Benefit | B-NR | 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.                         |

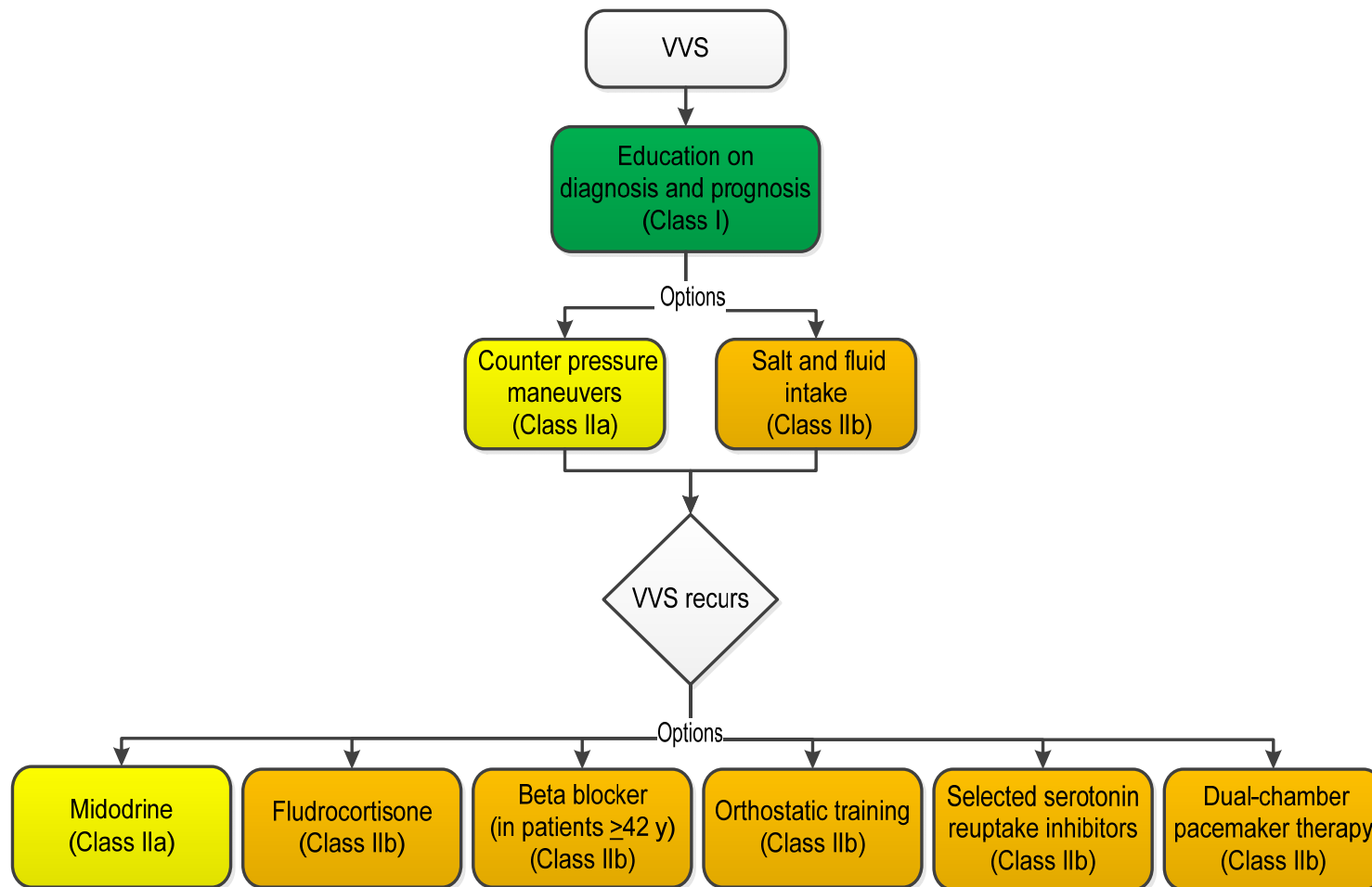
# Treatment



# Neurally Mediated Syncope



# Vasovagal Syncope



Colors correspond to Class of Recommendation in Table 1.  
VVS indicates vasovagal syncope.

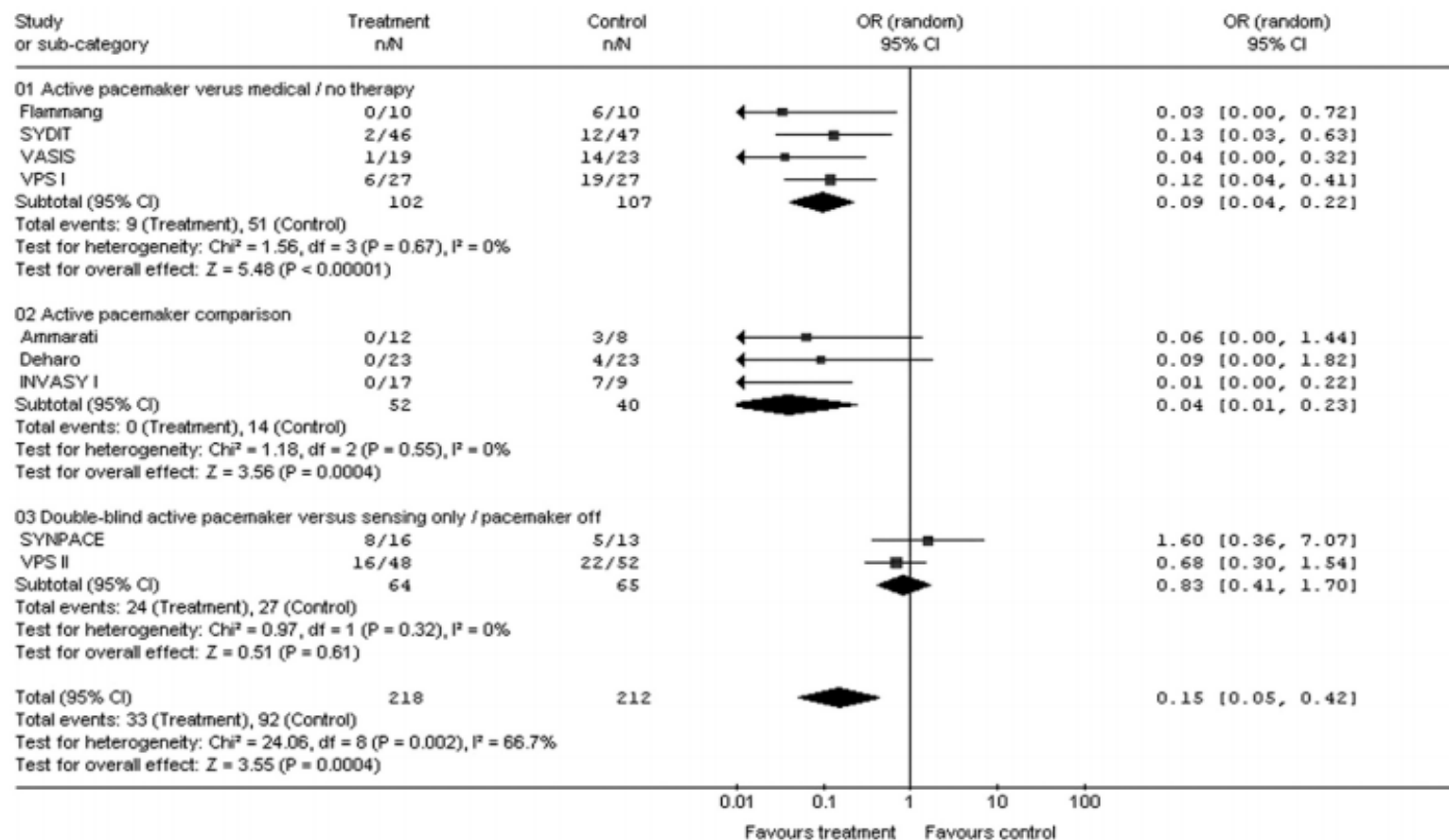


# Vasovagal Syncope: Pace or not?



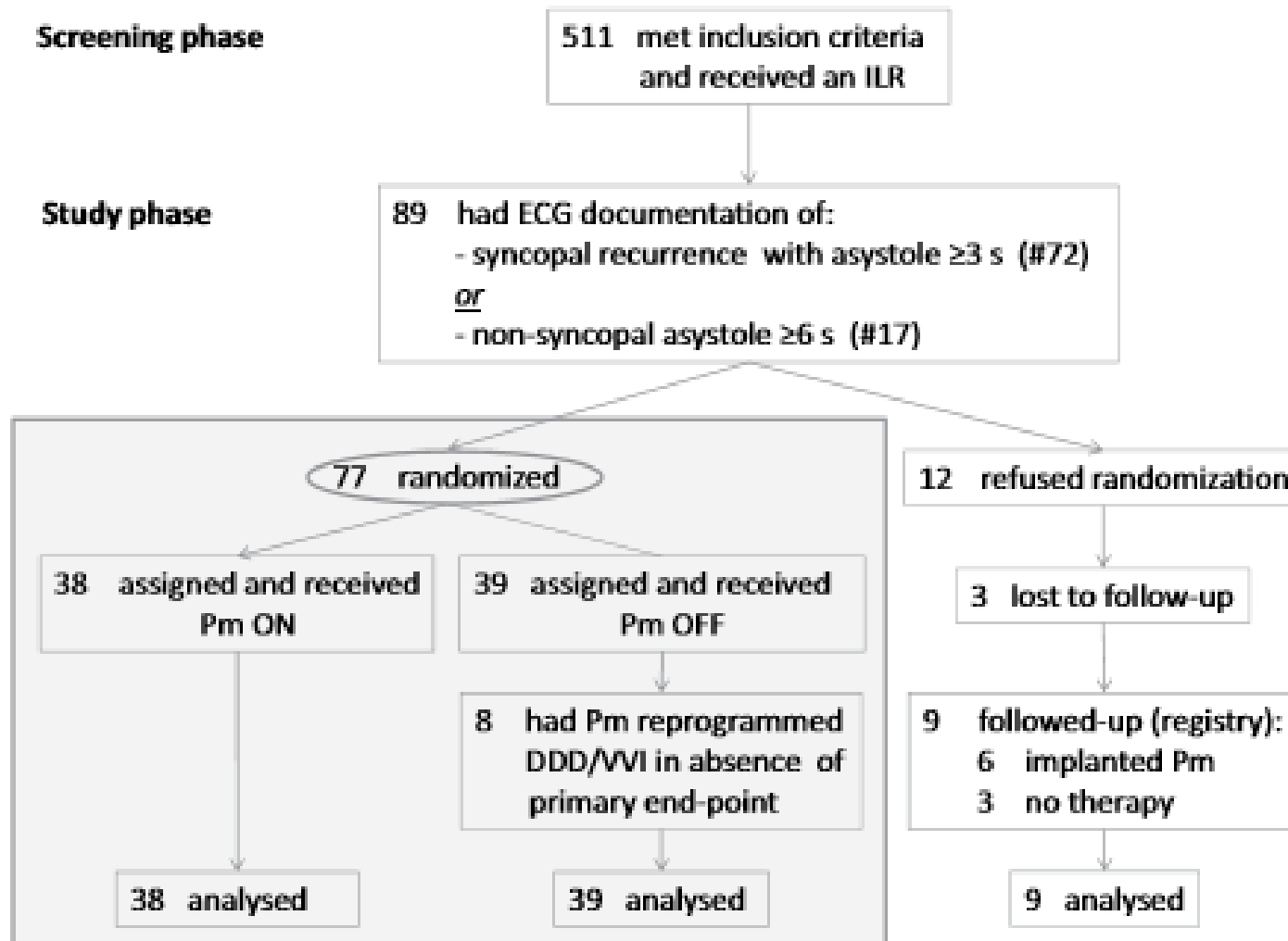
58

The American Journal of Medicine, Vol 120, No 1, January 2007



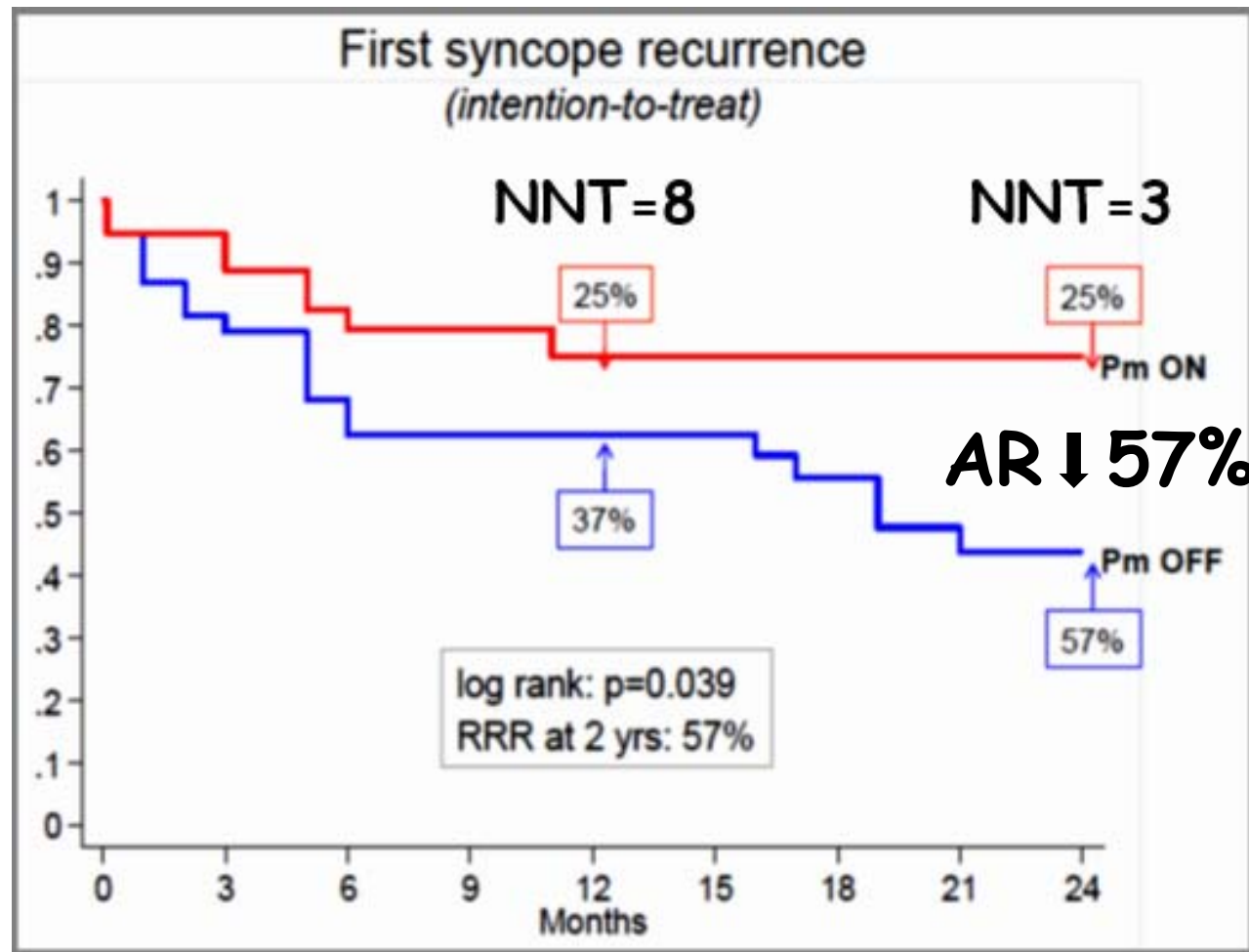
*Sachin et al Am J Med 2007*

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



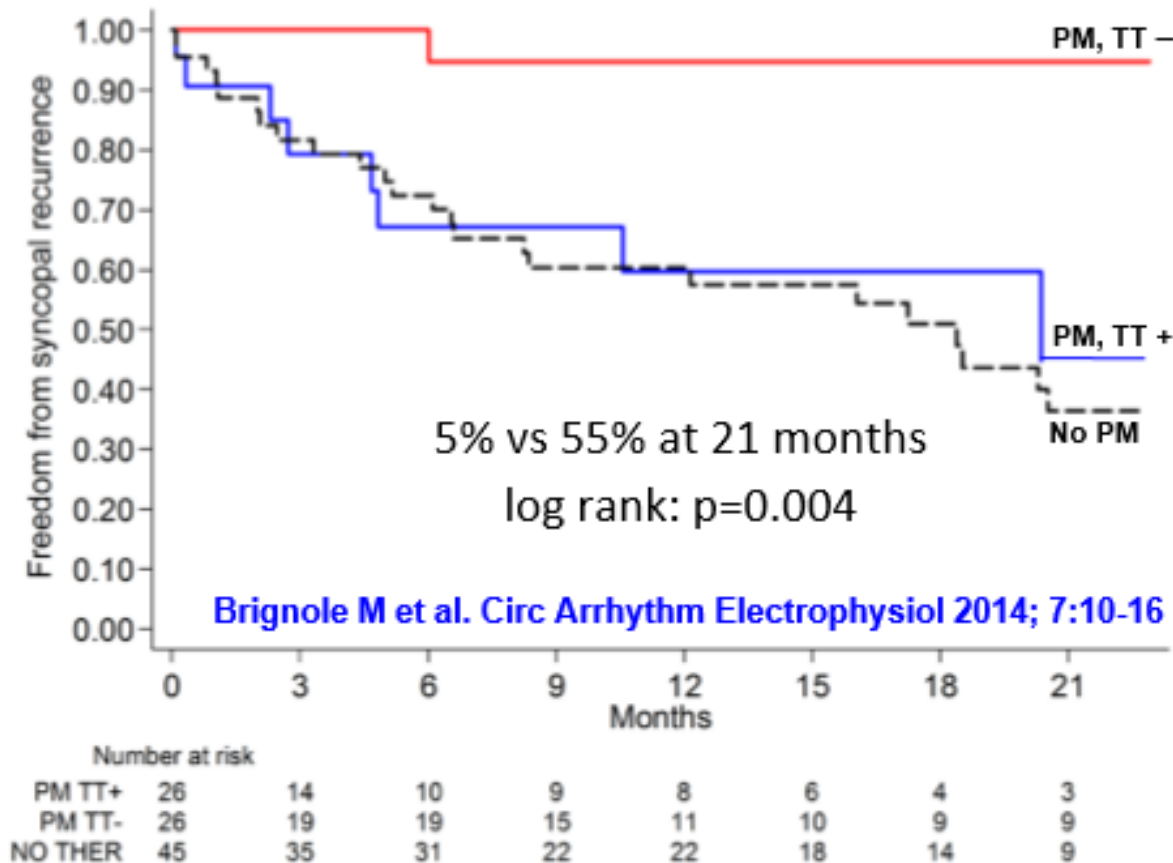
*Brignole et al Circulation 2012*

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



*Brignole et al Circulation 2012*

**Benefit of pacemaker therapy in patients with presumed neurally mediated syncope and documented asystole is greater when tilt test is negative: an analysis from the third International Study on Syncope of Uncertain Etiology (ISSUE-3).**



**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 fu**



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

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

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

| Recommendations   | Class <sup>a</sup> | Level <sup>b</sup> | Ref. <sup>c</sup> |
|---|--------------------|--------------------|-------------------|
| <b>3) Reflex asystolic syncope.</b><br>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. | IIa                | B                  | 5, 18, 19         |
| <b>4) Asymptomatic pauses (sinus arrest or AV block).</b><br>Pacing should be considered in patients with history of syncope and documentation of asymptomatic pauses >6 s due to sinus arrest, sinus-atrial block or AV block.         | IIa                | C                  | -                 |
| <b>5) Pacing is not indicated in reversible causes of bradycardia.</b>  | III                | C                  | -                 |

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

**Pacemakers in Vasovagal Syncope**

| <b>COR</b>              | <b>LOE</b>              | <b>Recommendation</b>  |
|-------------------------|-------------------------|--|
| <b><u>I<b>b</b></u></b> | <b>B-R<sup>SR</sup></b> | 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. |

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

| Carotid Sinus Syndrome |     |  |
|------------------------|-----|--|
| COR                    | LOE | Recommendations  |
| <u>Ila</u>             | B-R | Permanent cardiac pacing is reasonable in patients with carotid sinus syndrome that is <u>cardioinhibitory</u> or mixed.       |
| <u>Ilb</u>             | B-R | It may be reasonable to implant a dual-chamber pacemaker in patients with carotid sinus syndrome who require permanent pacing. |

SAFE PACE study: Kenny et al JACC 2001  
Pacing reduced falls 70%, Syncopal events 53%, Injurious events 70%

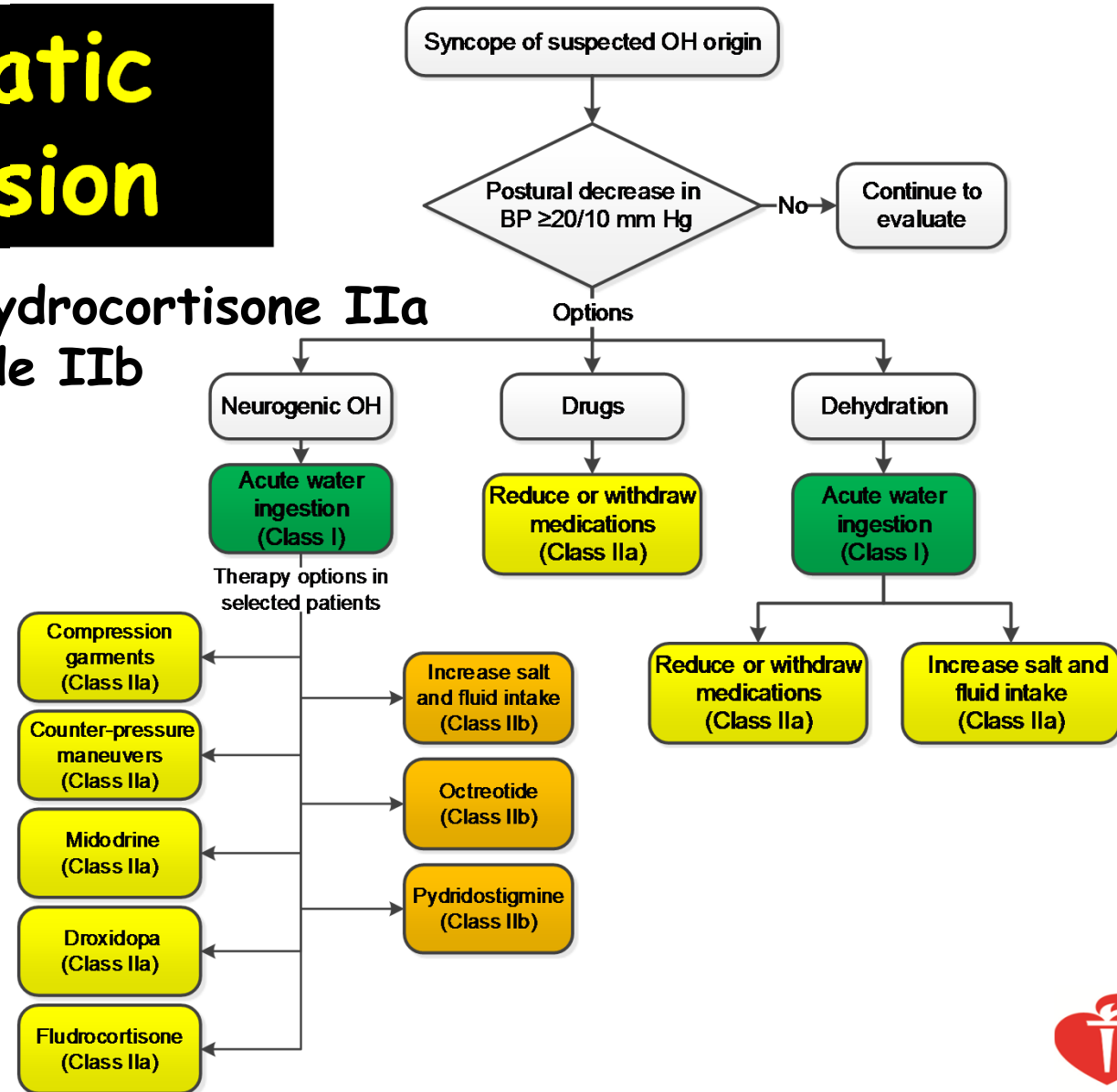
[Heart](#). 2009 Mar;95(5):405-9. doi: 10.1136/hrt.2008.153189. Epub 2009 Jan 5.

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

[Parry SW](#)<sup>1</sup>, [Steen N](#), [Bexton RS](#), [Tynan M](#), [Kenny RA](#).

# Orthostatic Hypotension

Midodrine, Droxidopa, Hydrocortisone IIa  
 Puridostigmine, Octreotide IIb



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

**LBBB and syncope?**



# LBBB and syncope: EPS

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.

Am J Cardiol 1999;83:1334-7

The positive predictive value is  $\geq 80\%$  to identify the patients who will develop 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.

Eur Heart J 2011;32:1533-1541

Eur Heart J 2009;30:2631-2671

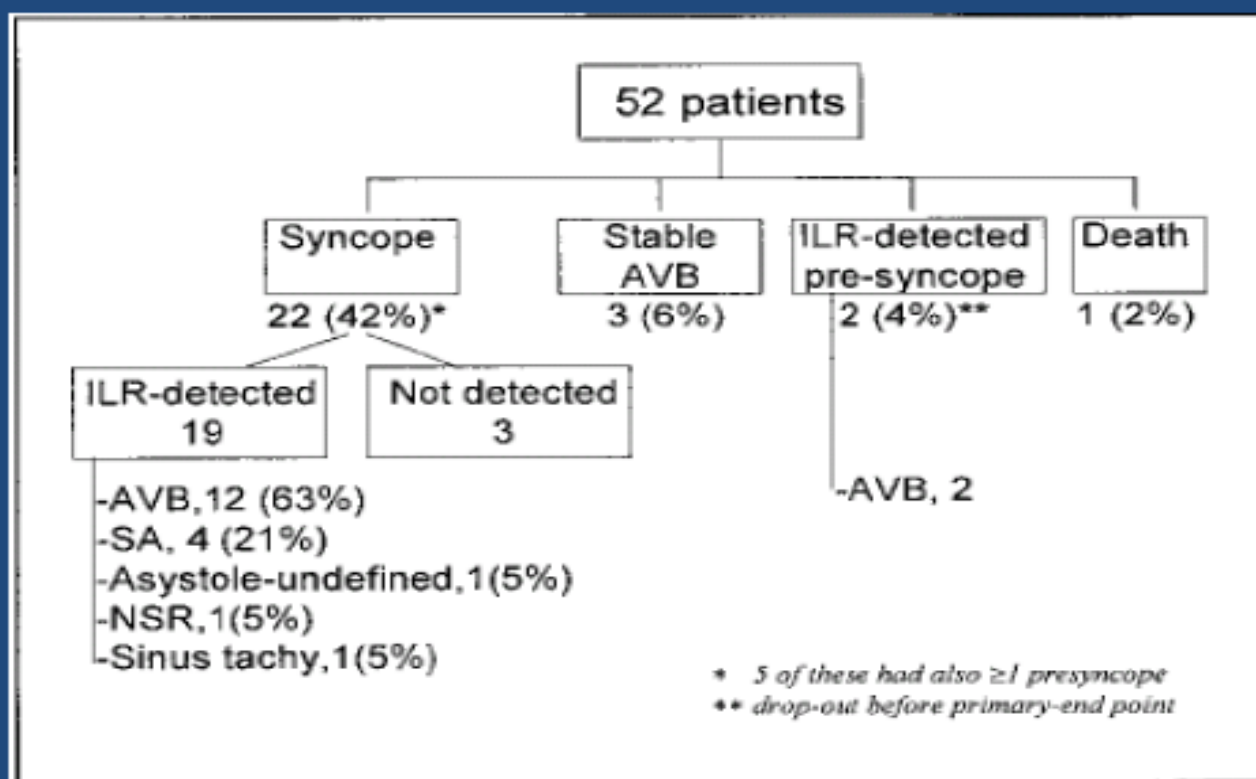
# Bundle Branch Block and Syncope: HV interval to predict AV Block Progression Rate

|                         |                                    |   |
|-------------------------|------------------------------------|---|
| Scheinman et al<br>1983 | HV interval                        | $< 70 \rightarrow 3.5\%$<br>$\geq 70 \rightarrow 12\%$<br>$\geq 100 \rightarrow 25\%$ |
| Bergfeldt<br>1994       | HV interval after<br>Dysopiramide  | $47\% \rightarrow 75\%$   |
| Petrac<br>1996          | A – V Block after atrial<br>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 Donateo, MD; on behalf of the International Study on Syncope of Uncertain Etiology (ISSUE) Investigators\*

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



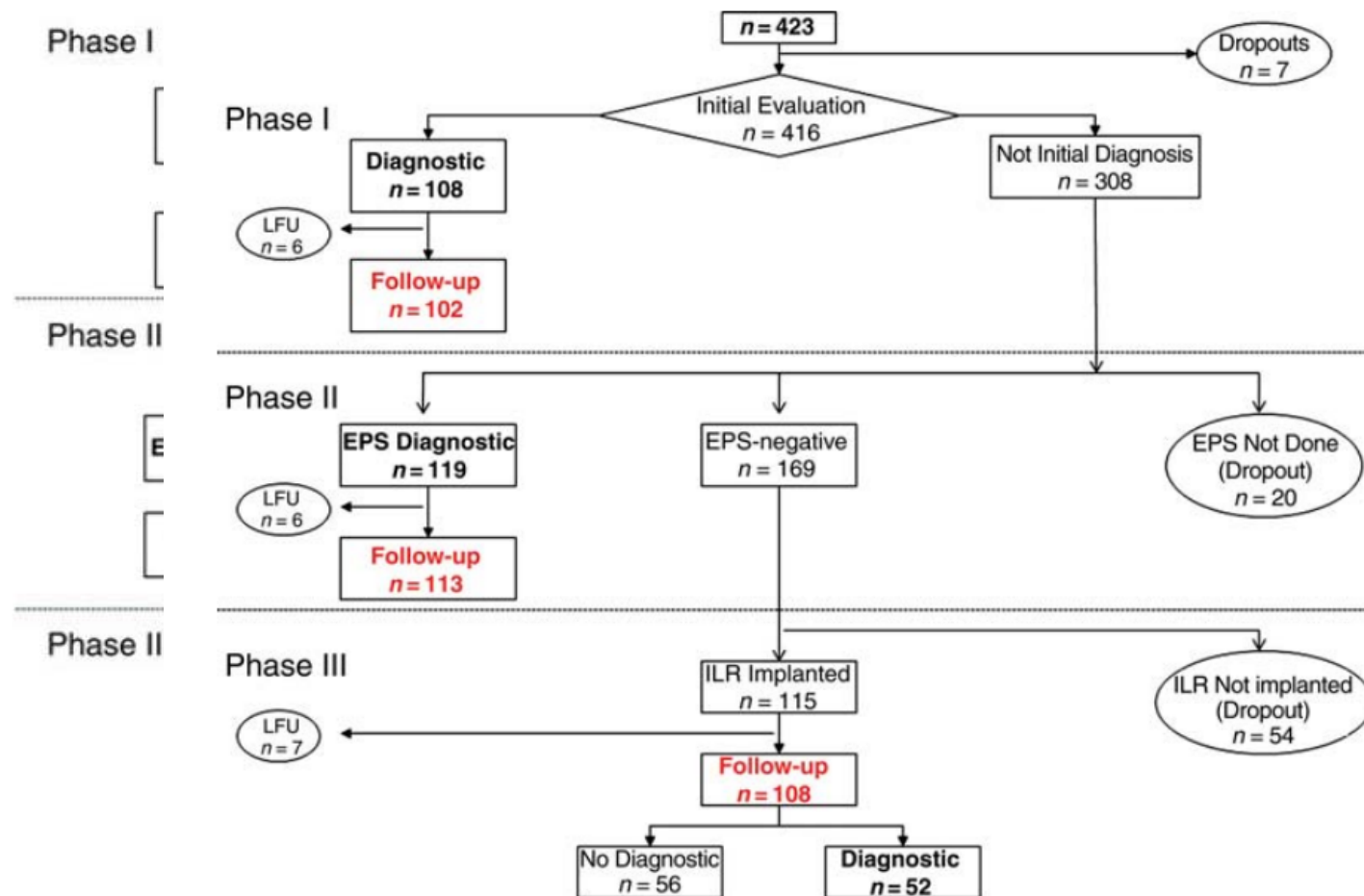
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(*Circulation*. 2001;104:2045-2050.)

|                          |          |
|--------------------------|----------|
| Asystole → PMK           | 22 (42%) |
| Non asystolic syncope    | 5 (9.1%) |
| Non syncope recurrences  | 24 (46%) |
| Death during colonoscopy | 1 (2%)   |

# 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

| Diagnosis                  |                 | n  |
|----------------------------|-----------------|----|
| Analysed patients, n = 323 |                 |    |
| Initial evaluation         |                 |    |
| (Phase I), n = 102         |                 |    |
|                            | A-VB            | 52 |
|                            | Alt BB          | 4  |
|                            | SS              | 6  |
|                            |                 | 13 |
|                            | CSS             | 6  |
|                            | Neurally        | 9  |
|                            | Orth            |    |
|                            |                 |    |
|                            | pulmonary       |    |
| EPS                        | Bradyarrhythmia | 70 |
|                            |                 |    |
|                            |                 | 4  |
|                            |                 | 12 |
|                            |                 | 14 |
|                            |                 | 12 |
|                            |                 | 1  |
| II                         | Bradyarrhythmia | 36 |
|                            |                 |    |
|                            |                 | 5  |
|                            | SA              | 7  |
|                            | Non-arrhythmic  | 3  |
|                            | VT/VF           | 1  |
|                            | Brady/tachy     | 56 |
|                            | No diagnosis    |    |

**Diagnosis**

Analysed patients,  $n = 323$

Initial evaluation (Phase I),  $n = 102$

CSS

Neurally

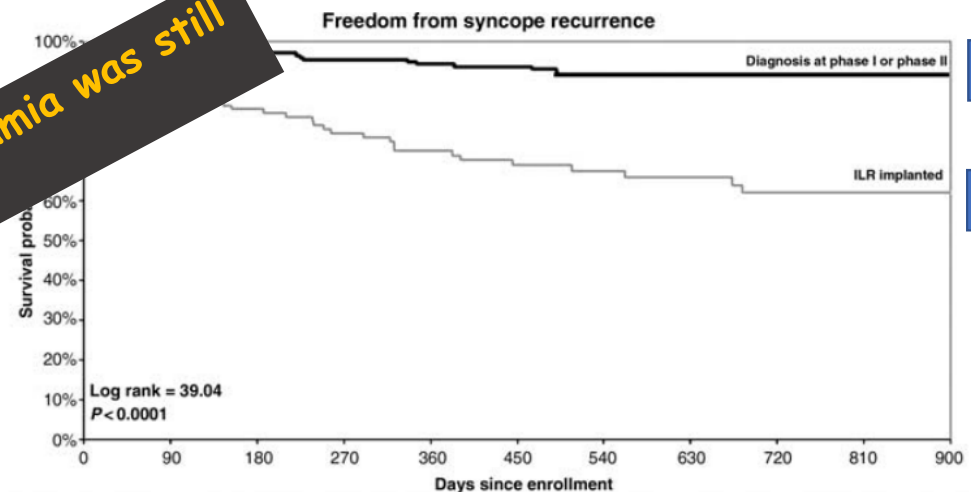
Orth

-6% Phase I

**Mortality rate=6%**  
**Phase I, II: 6% vs Phase III**  
**with a negative EPS.**

45% of the patients were documented by ILR

| Diagnosis | 215 | 204 |
|-----------|-----|-----|
| ILR       | 108 | 94  |



|           |     |     |     |     |     |     |     |     |    |    |   |
|-----------|-----|-----|-----|-----|-----|-----|-----|-----|----|----|---|
| Diagnosis | 215 | 204 | 188 | 176 | 159 | 137 | 120 | 103 | 85 | 14 | 9 |
| ILR       | 108 | 94  | 86  | 74  | 65  | 53  | 44  | 39  | 27 | 7  | 4 |

7%

33%

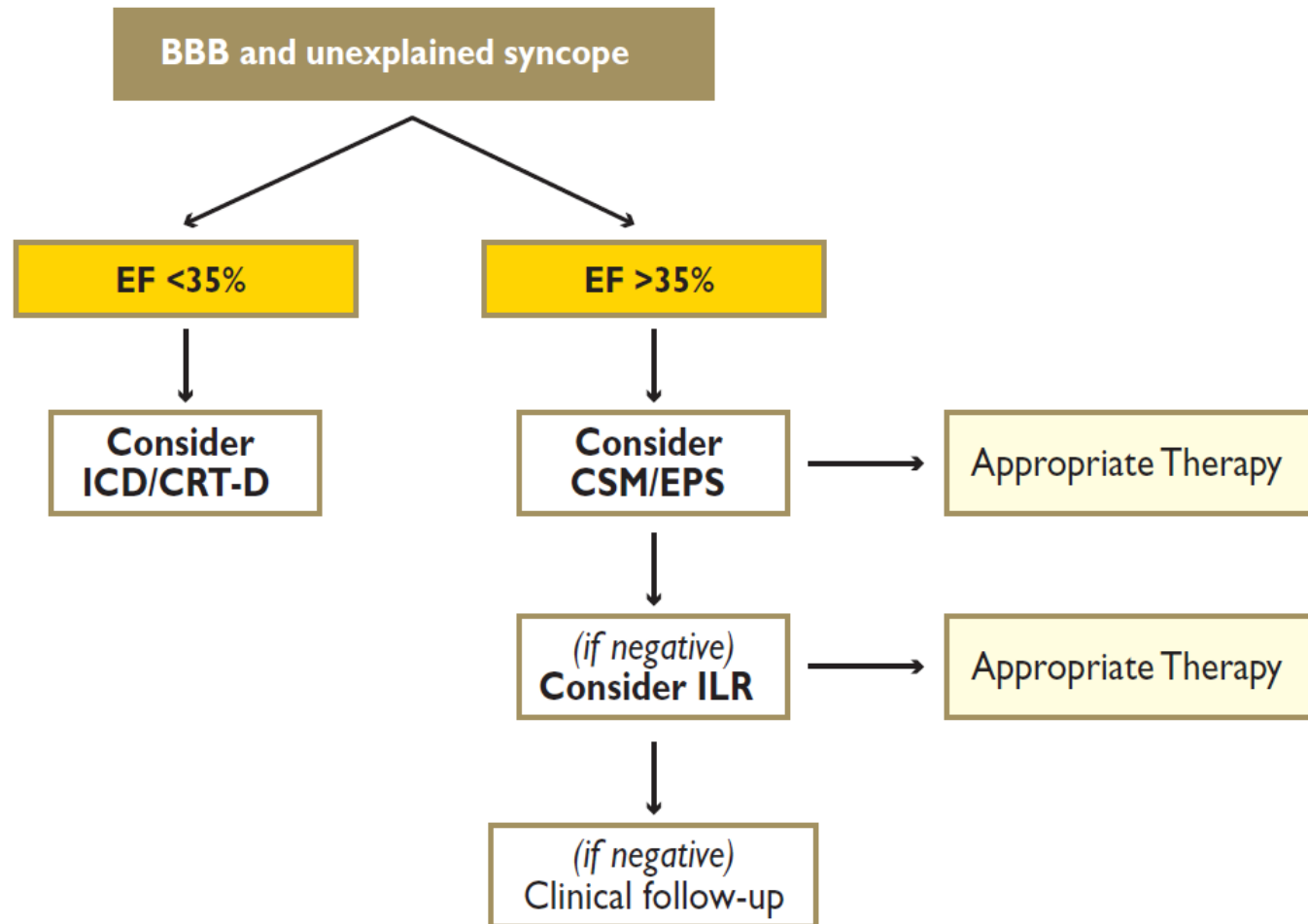
# LBBB when to pace?

- Pacing is indicated in patients with syncope, BBB, and positive EPS I B
- Pacing should be considered in patients with unexplained syncope and BBB IIa C

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

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

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



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

# Be aware that...

| Brugada Syndrome |      |   |
|------------------|------|---|
| COR              | LOE  | Recommendations   |
| <u>Ila</u>       | B-NR | ICD implantation is reasonable in patients with <u>Brugada</u> ECG pattern and syncope of suspected arrhythmic etiology.                          |
| <u>Ilb</u>       | B-NR | Invasive EPS may be considered in patients with <u>Brugada</u> ECG pattern and syncope of suspected arrhythmic etiology.                          |
| III: No Benefit  | B-NR | ICD implantation is not recommended in patients with <u>Brugada</u> ECG pattern and reflex-mediated syncope in the absence of other risk factors. |

III: Harm

B-NR

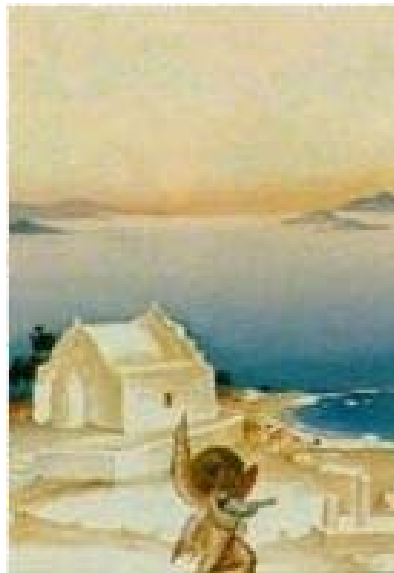
See [Online Data Supplement 42](#).

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).

# 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 Ελύτης  
Από το Άξιον Εστί:  
**Τη γλώσσα μου έδωσαν ελληνική**

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

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

Εκεί σπάρτοι και πέρκες  
ανεμόδαρτα ρήματα  
ρεύματα πράσινα μες στα γαλάζια  
όσα είδα στα σπλάχνα 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...

**THANK YOU FOR YOUR ATTENTION**

# Bundle Branch Block and Syncope

Bradycardia detection in Bundle Branch Block (B4) study



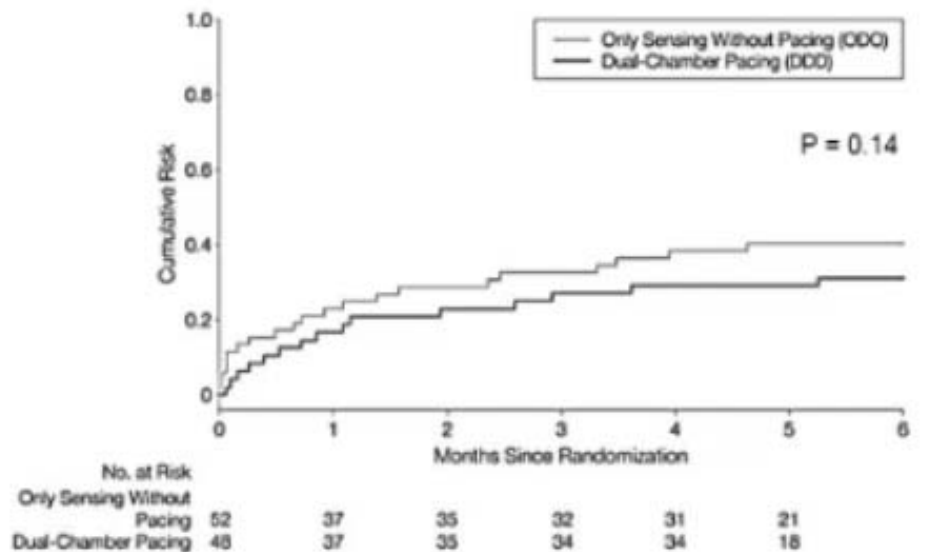
## Other Key messages:

- 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?



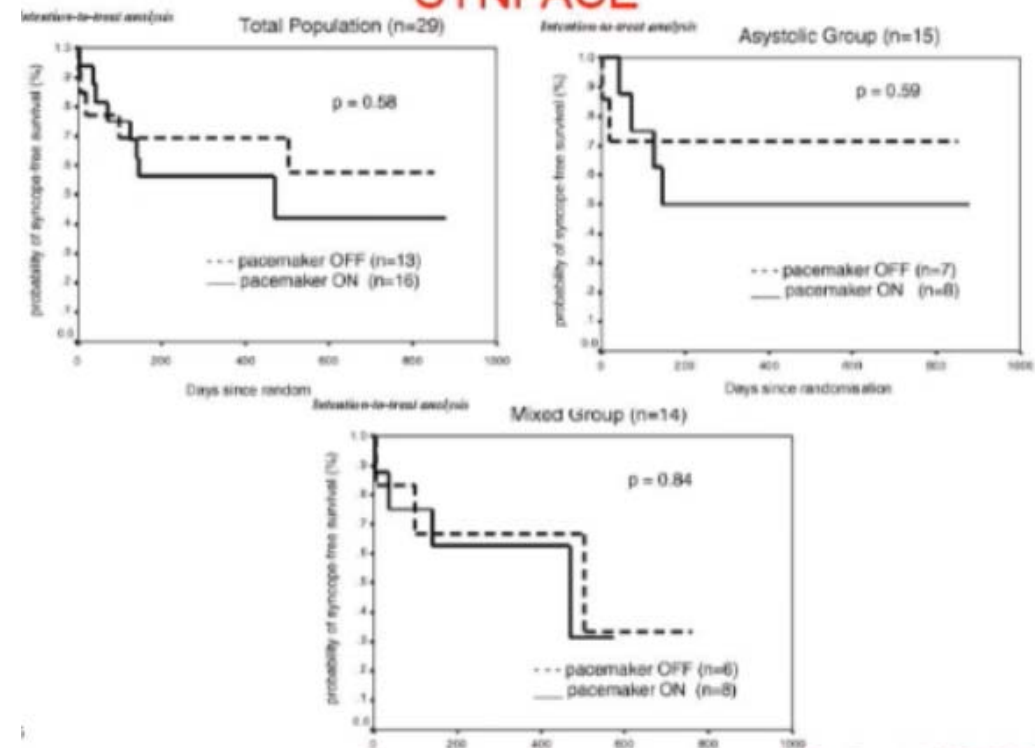
## VPS II



Relative risk reduction of 30.2% (95% confidence interval, -33.2% to 63.4%; log-rank P = .14).

*Connolly et al JAMA 2003*

## SYNPACE



*Raviele et al Eur Heart J 2004*

# 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

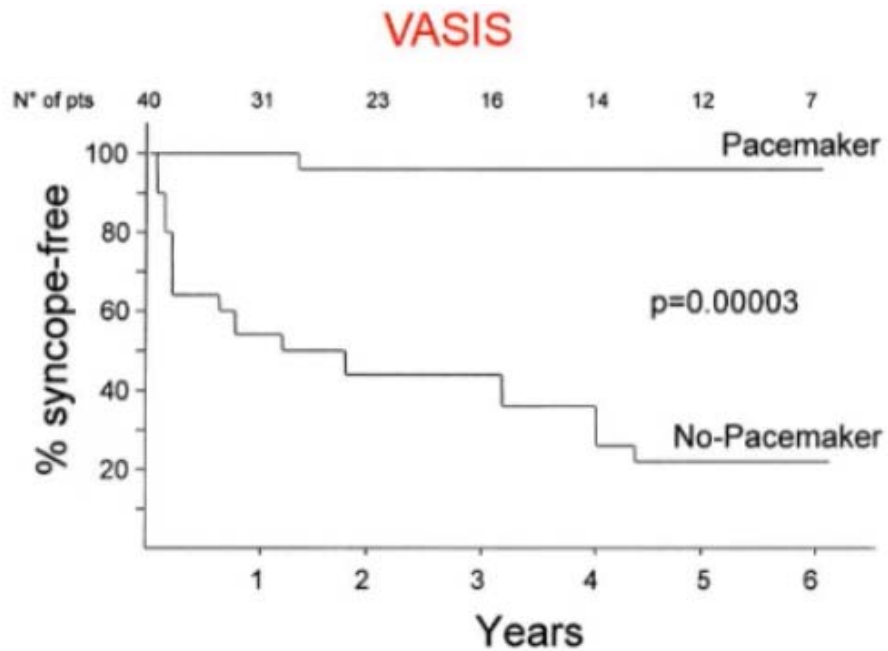
### ■ Randomized controlled trial (N=175)

- Adults > 50 years, non-accidental fall, positive CSM
- Pacing (n=87) vs. No Pacing (n=88)

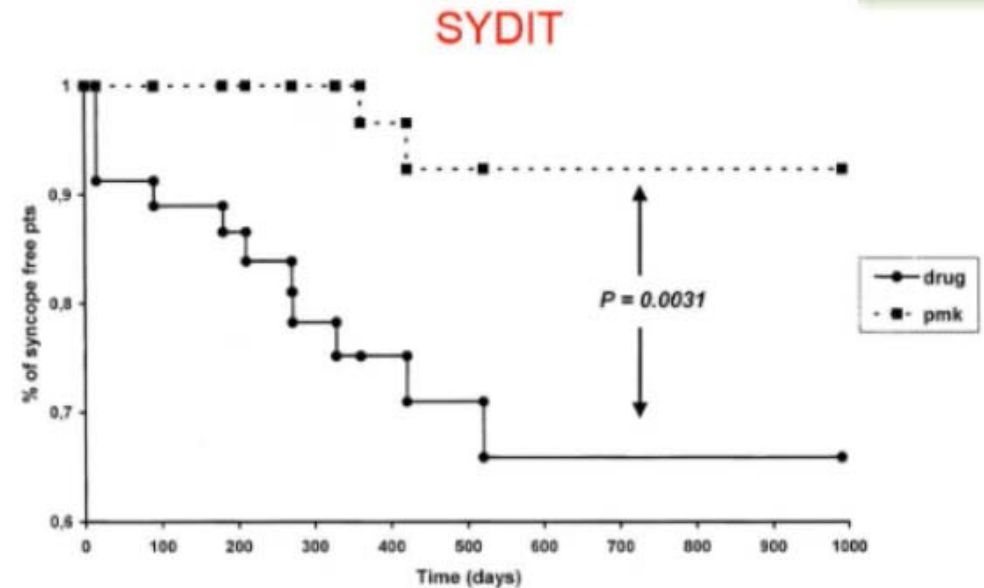
### ■ Results

- 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%

# Vasovagal Syncope: Pace or not?

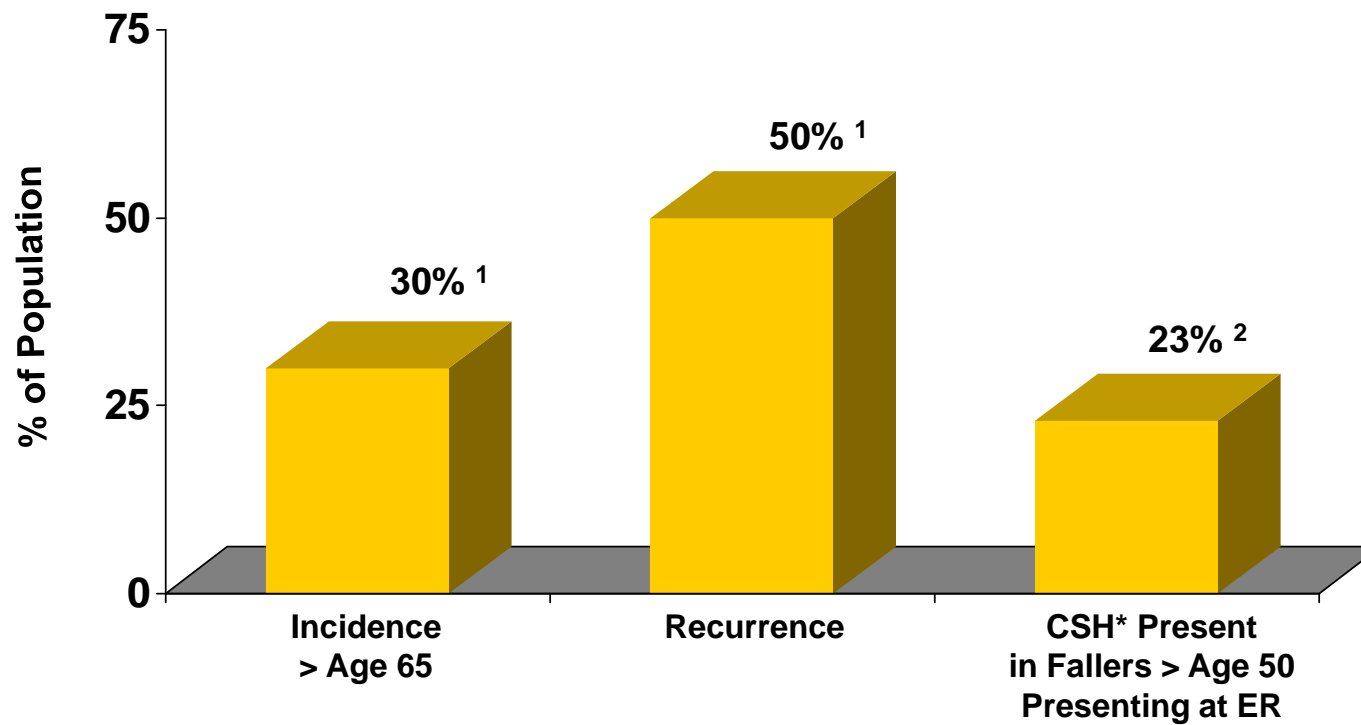


*Sutton et al Circulation 2000*



*Ammirati et al Circulation 2001*

## Falls: Incidence, Recurrence, CSH\*



\*Carotid Sinus Hypersensitivity

<sup>1</sup> *J Am Geriatr Soc.* 1995.

<sup>2</sup> Richardson D, et al. *PACE.* 1997;20:820.

# Outcomes of syncope

**TABLE 3. HAZARD RATIOS FOR THE OUTCOMES OF INTEREST IN PARTICIPANTS WITH SYNCOPE AS COMPARED WITH PARTICIPANTS WITHOUT SYNCOPE.**

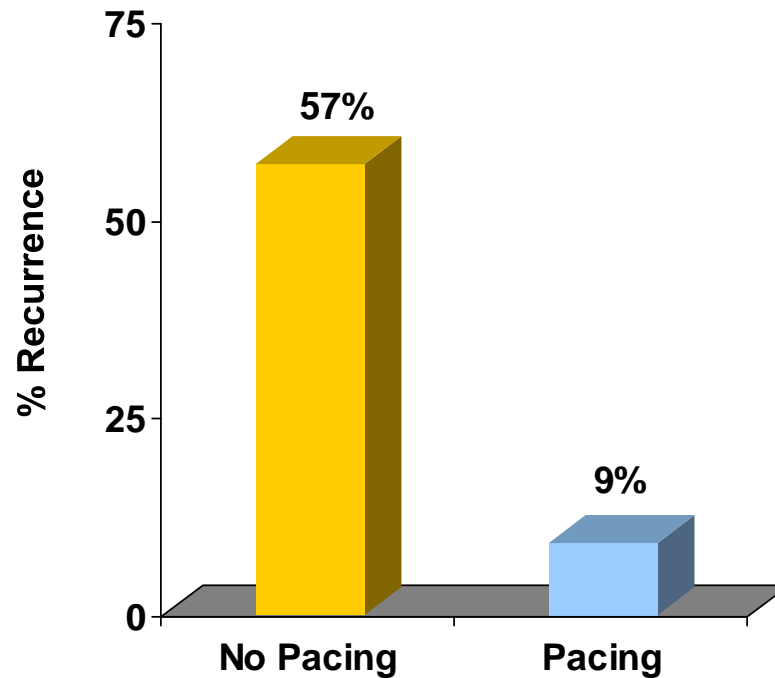
| CAUSE OF SYNCOPE   | HAZARD RATIO<br>(95% CONFIDENCE INTERVAL) |                             |
|--|---|-----------------------------|
|  | ADJUSTED FOR<br>AGE AND SEX               | MULTIVARIABLE-<br>ADJUSTED* |
| Any cause  |   |                             |
| Death from any cause                                       | 1.43 (1.25–1.64)†                         | 1.31 (1.14–1.51)†           |
| Myocardial infarction or death from coronary heart disease | 1.47 (1.15–1.88)‡                         | 1.27 (0.99–1.64)            |
| Fatal or nonfatal stroke                                   | 1.19 (0.87–1.62)                          | 1.06 (0.77–1.45)            |
| Cardiac  |   |                             |
| Death from any cause                                       | 2.41 (1.78–3.26)†                         | 2.01 (1.48–2.73)†           |
| Myocardial infarction or death from coronary heart disease | 3.56 (2.29–5.55)†                         | 2.66 (1.69–4.19)†           |
| Fatal or nonfatal stroke                                   | 2.67 (1.43–4.98)‡                         | 2.01 (1.06–3.80)§           |
| Unknown  |   |                             |
| Death from any cause                                       | 1.36 (1.13–1.65)‡                         | 1.32 (1.09–1.60)‡           |
| Myocardial infarction or death from coronary heart disease | 1.43 (1.00–2.03)§                         | 1.31 (0.92–1.86)            |
| Fatal or nonfatal stroke                                   | 0.72 (0.43–1.22)                          | 0.66 (0.39–1.11)            |
| Neurologic (including seizure)                             |   |                             |
| Death from any cause                                       | 1.98 (1.45–2.72)†                         | 1.54 (1.12–2.12)‡           |
| Myocardial infarction or death from coronary heart disease | 1.02 (0.48–2.17)                          | 0.79 (0.37–1.69)            |
| Fatal or nonfatal stroke                                   | 3.12 (1.82–5.36)†                         | 2.96 (1.69–5.18)†           |
| Vasovagal or other¶  |   |                             |
| Death from any cause                                       | 1.17 (0.95–1.44)                          | 1.08 (0.88–1.34)            |
| Myocardial infarction or death from coronary heart disease | 1.16 (0.80–1.68)                          | 1.03 (0.71–1.49)            |
| Fatal or nonfatal stroke                                   | 0.93 (0.57–1.52)                          | 0.87 (0.54–1.42)            |

Soteriades et al. *NEJM* 2002; 347: 878

# 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

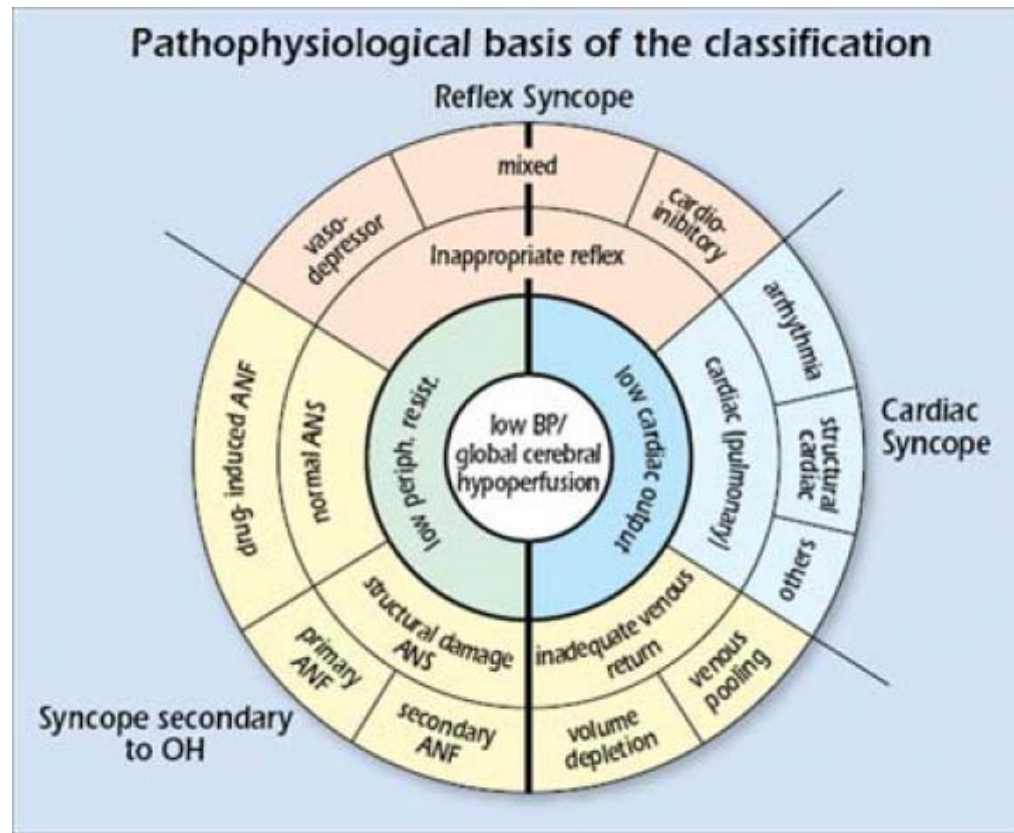
## ■ Conclusions

- 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

## 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)

### Pathophysiological Basis of Classification of syncope



# 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 Level

|   |   |
|---|---|
| I | C |
| I | C |
| I | C |
| I | C |
| I | C |
| I | C |
| I | C |

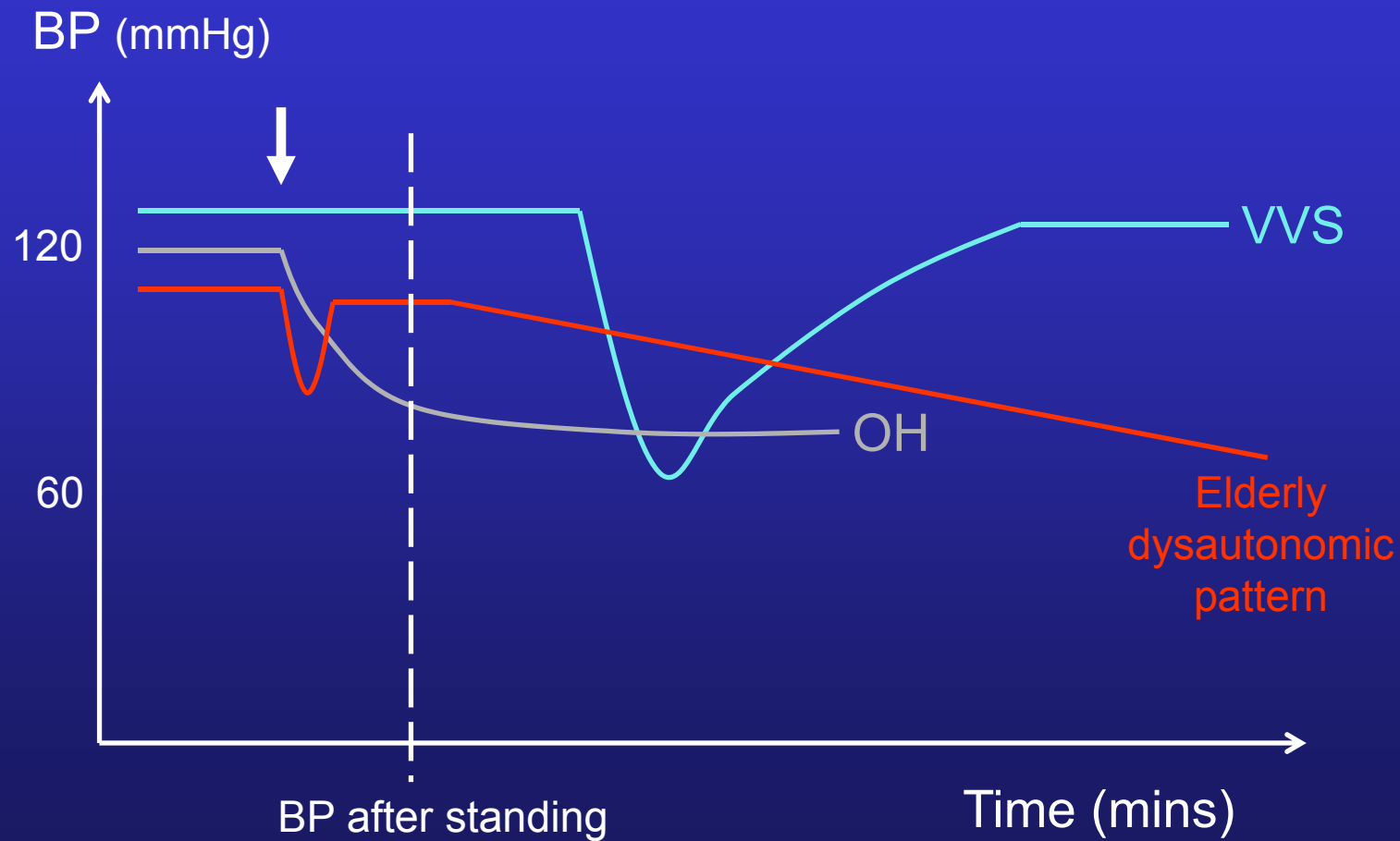
## Scoring for prediction of serious events in pts with syncope

| Study   | Risk factors   | Score                                    | Endpoints  | Results (validation cohort)  |
|---|--|--|--|--|
| <b>S. Francisco Syncope Rule<sup>48</sup></b> | -Abnormal ECG<br>-Congestive heart failure<br>-Shortness of breath<br>-Haematocrit <30%<br>-Systolic blood pressure <90 mmHg   | No risk = 0 item<br>Risk = $\geq 1$ item | Serious events at 7 days   | 98% sensitive and 56% specific   |
| <b>Martin et al.<sup>40</sup></b>             | -Abnormal ECG<br>-History of ventricular arrhythmia<br>-History of congestive heart failure<br>-Age >45 years  | 0 to 4 (1 point each item)               | 1-year severe arrhythmias or arrhythmic death                      | 0% score 0<br>5% score 1<br>16% score 2<br>27% score 3 or 4  |
| <b>OESIL score<sup>41</sup></b>               | -Abnormal ECG<br>-History of cardiovascular disease<br>-Lack of prodrome<br>-Age >65 years   | 0 to 4 (1 point each item)               | 1-year total mortality   | 0% score 0<br>0.6% score 1<br>14% score 2<br>29% score 3<br>53% score 4                            |
| <b>EGSYS score<sup>42</sup></b>               | -Palpitations before syncope (+4)<br>-Abnormal ECG and/or heart disease (+3)<br>-Syncope during effort (+3)<br>-Syncope while supine (+2)<br>-Autonomic prodrome <sup>a</sup> (-1)<br>-Predisposing and/or precipitating factors <sup>b</sup> (-1) | Sum of + and - points                    | 2-year total mortality<br><br>.....<br>Cardiac syncope probability | 2% score <3<br>21% score $\geq 3$<br><br>2% score <3<br>13% score 3<br>33% score 4<br>77% score >4 |

# 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



# 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 propranolol 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



# Situational Syncope

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



# 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)

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

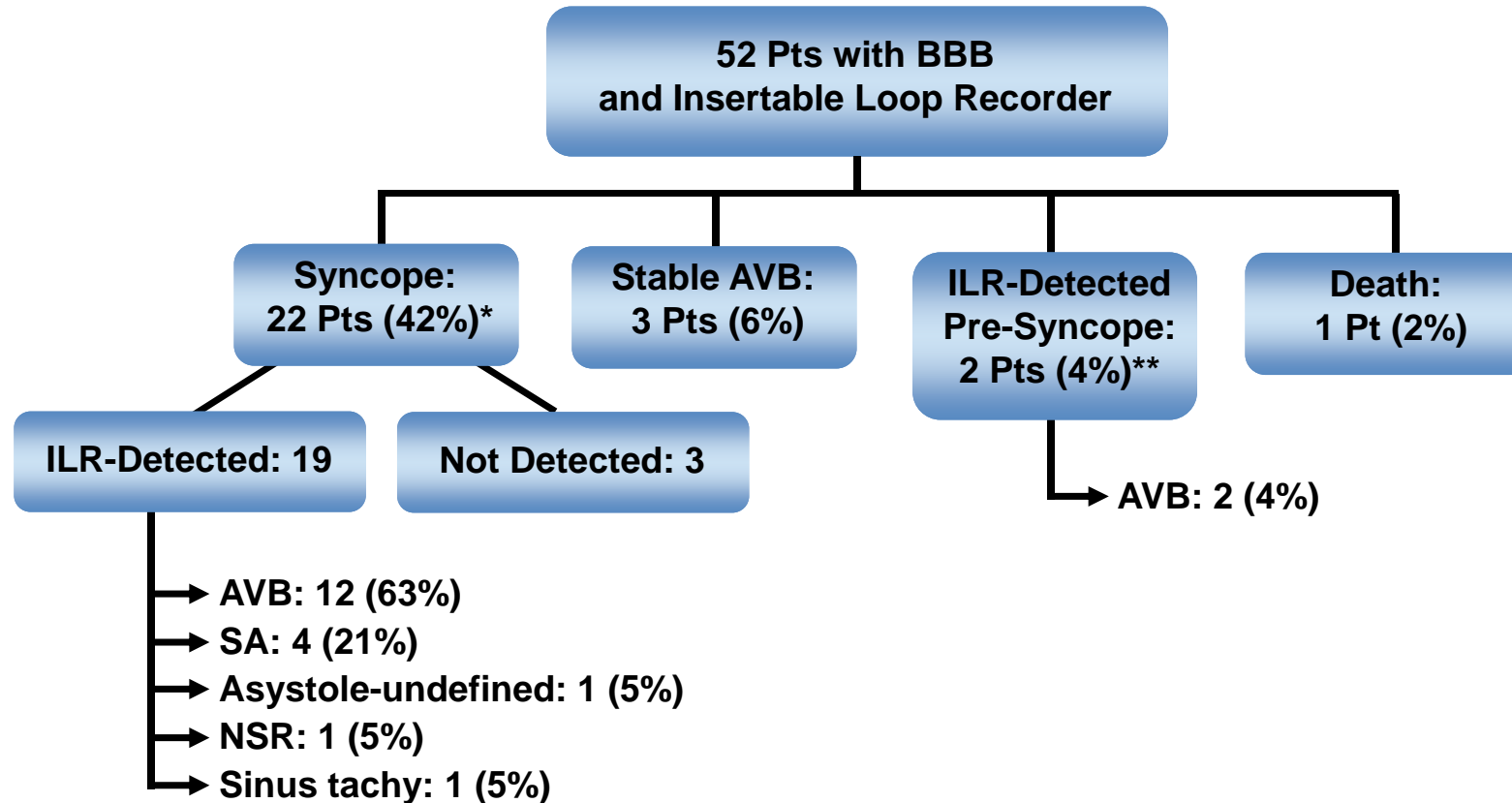
## Neurogenic Orthostatic Hypotension

|     |      |   |
|-----|------|---|
| I   | B-R  | Acute water ingestion is recommended in patients with syncope caused by neurogenic OH for occasional, temporary relief. |
| IIa | C-LD | Physical counter-pressure maneuvers can be beneficial in patients with neurogenic OH with syncope.                      |
| IIa | C-LD | Compression garments can be beneficial in patients with syncope and OH.   |
| IIa | B-R  | Midodrine can be beneficial in patients with syncope due to neurogenic OH.  |
| IIa | B-R  | Droxidopa can be beneficial in patients with syncope due to neurogenic OH.  |

|     |      |  |
|-----|------|--|
| IIa | C-LD | Fludrocortisone can be beneficial in patients with syncope due to neurogenic OH.                                       |
| IIb | C-LD | Encouraging increased salt and fluid intake may be reasonable in selected patients with neurogenic OH.                 |
| IIb | C-LD | Pyridostigmine may be beneficial in patients with syncope due to neurogenic OH who are refractory to other treatments. |
| IIb | C-LD | Octreotide may be beneficial in patients with syncope and refractory recurrent postprandial or neurogenic OH.          |

# ISSUE

## Patients with Bundle Branch Block and Negative EP Test



## ISSUE

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

#### 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 1.** CAUSES OF SYNCOPES ACCORDING TO SEX AND THE PRESENCE OR ABSENCE OF CARDIOVASCULAR DISEASE AT BASE LINE.

| CAUSE                               | CARDIOVASCULAR DISEASE ABSENT (N=599) |               | CARDIOVASCULAR DISEASE PRESENT (N=223) |               | TOTAL SAMPLE (N=822) |
|-------------------------------------|---------------------------------------|---------------|--|---------------|----------------------|
|                                     | MEN (N=232)                           | WOMEN (N=367) | MEN (N=116)                            | WOMEN (N=107) |                      |
|                                     | percent of subjects                   |               |  |               |                      |
| Cardiac                             | 6.5                                   | 3.8           | 26.7                                   | 16.8          | 9.5                  |
| Unknown*                            | 31.0                                  | 41.7          | 31.0                                   | 37.4          | 36.6                 |
| Stroke or transient ischemic attack | 1.7                                   | 2.5           | 9.5                                    | 9.4           | 4.1                  |
| Seizure                             | 7.3                                   | 3.3           | 6.9                                    | 2.8           | 4.9                  |
| Vasovagal                           | 24.1                                  | 24.5          | 11.2                                   | 14.0          | 21.2                 |
| Orthostatic                         | 9.5                                   | 10.9          | 6.9                                    | 6.5           | 9.4                  |
| Medication                          | 7.3                                   | 6.5           | 4.3                                    | 9.4           | 6.8                  |
| Other†                              | 13.0                                  | 6.8           | 3.5                                    | 3.7           | 7.5                  |

\*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*

# 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  $\geq 120$  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).