Evaluation and Management of Syncope

Anne B. Curtis, MD, MACP, FACC, FHRS, FAHA
Charles and Mary Bauer Professor and Chair
Department of Medicine
Jacobs School of Medicine & Biological Sciences
University at Buffalo
Buffalo, NY, USA

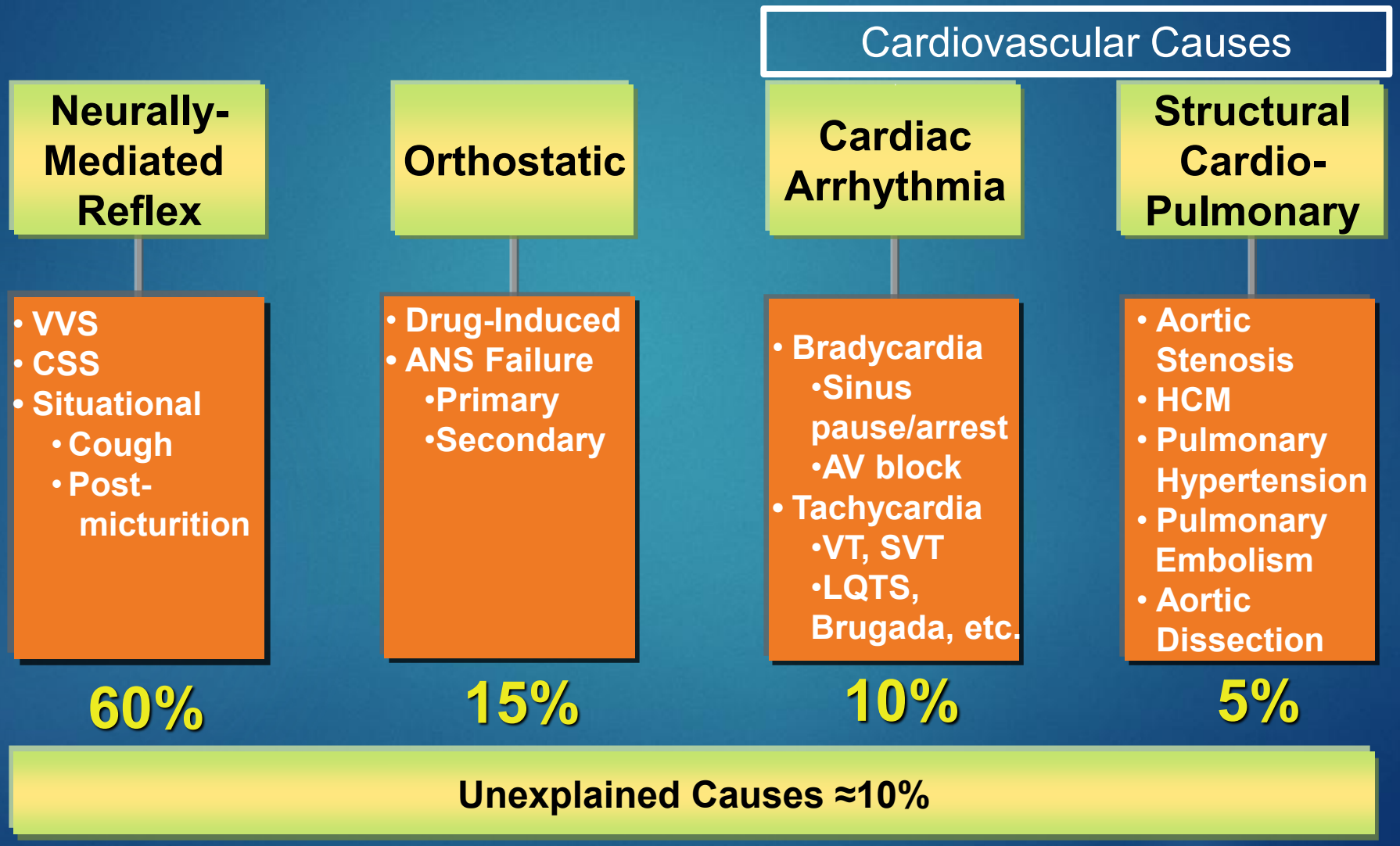
Disclosures

- Abbott: honoraria for speaking; advisory board
- Medtronic, Inc.: honoraria for speaking; data monitoring board
- Sanofi Aventis: advisory board
- Janssen Pharmaceuticals: advisory board
- Milestone Pharmaceuticals: advisory board
- Zoll: honoraria for speaking

Syncope: Definition

- A syndrome in which loss of consciousness is:
  - relatively sudden onset
  - temporary (usually <1-2 min)
  - self-terminating
  - usually rapid recovery
- Due to inadequate cerebral perfusion
- Most often due to a fall in systemic arterial pressure

Causes of Syncope



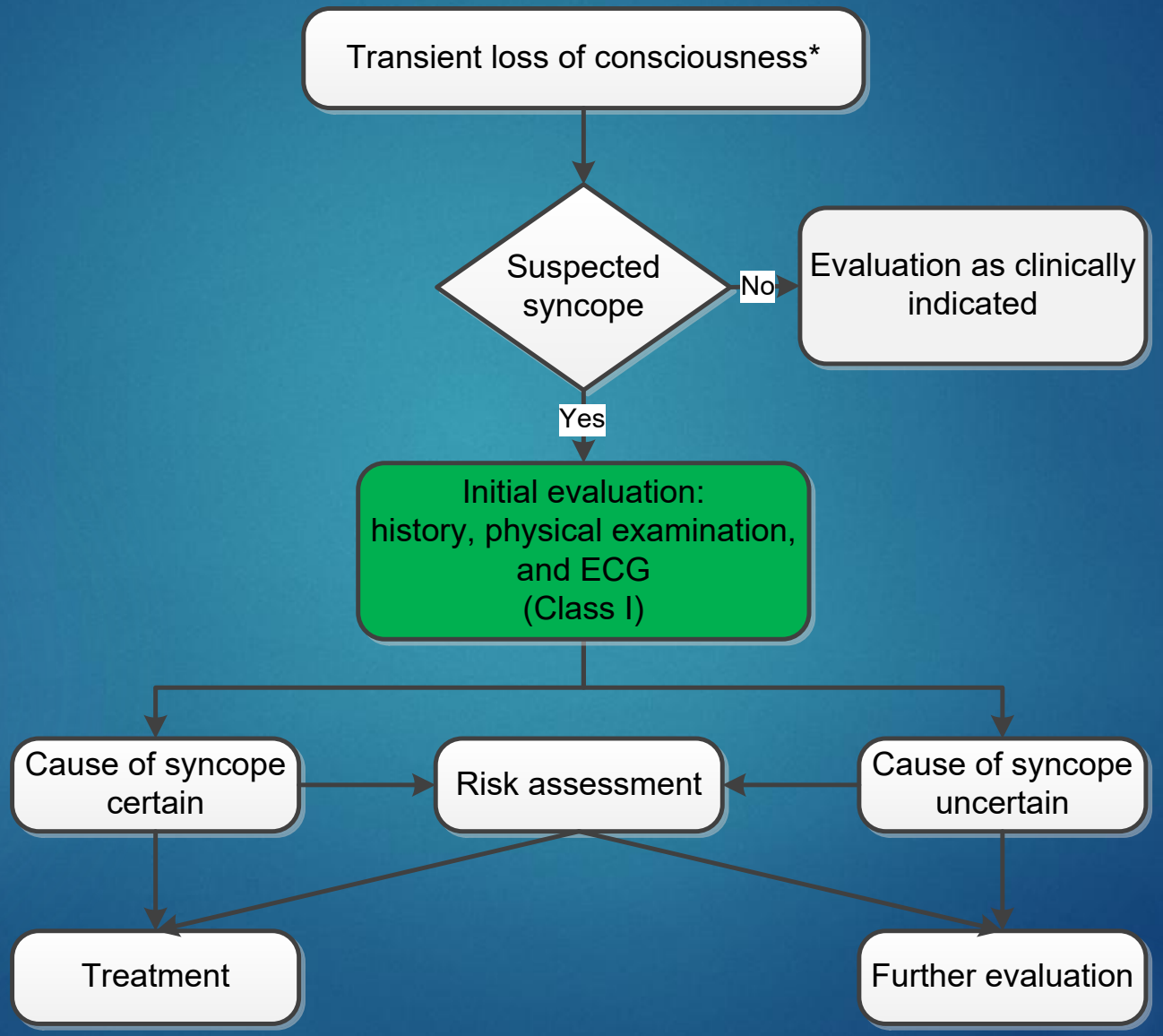
Moya A et al, ESC Syncope Guidelines, Eur Heart J 2009; 30: 2642

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

Shen W et al., Heart Rhythm 2017;14:e155-e217

General Principles

Syncope Initial Evaluation



Basic Diagnostic Strategy

- **The Initial Evaluation**
  - History, physical exam (orthostatic blood pressure), ECG
- **Risk Assessment**
  - In-hospital vs out-of-hospital diagnostic evaluation
- **Selected Subsequent Testing**
  - **Ambulatory:**
    - ECG Monitoring (external loop recorder, mobile outpatient cardiac telemetry (MCOT), insertable loop recorder)
  - **Hospital-based:**
    - Hemodynamics/angiography, stress testing, electrophysiologic study, tilt table

Initial Evaluation

Essentials of the History

- **Concomitant disease, especially cardiac**
  - Medication history
- **Pertinent family history**
  - Cardiac disease, Unexpected death
- **Past medical history**
  - Heart disease (structural, arrhythmia)
  - Metabolic and neurologic disease
- **Circumstances of recent event(s)**
  - Eyewitness account of event
  - Warning symptoms
  - Consider unexplained 'falls' (possible amnesia in elderly)

Initial Examination

Essentials of Physical Examination

- **Vital signs**
  - Collapsed (rarely obtained) vs. post-recovery
  - Heart rate, regularity, murmurs, left ventricular hypertrophy
  - Orthostatic blood pressure change
- **CV Exam: heart or vascular disease?**
- **Carotid sinus massage**
  - Perform upright position or during tilt-table test
  - Monitor beat-to-beat blood pressure
- **Neurological exam**
  - Residual and/or new deficits?

Features Suggesting Cause of Syncope

- **Reflex (neurally-mediated)**
  - Absence of cardiac disease
  - Long history with multiple recurrences
  - Triggers including:
    - Pain, hot environment, head rotation
    - Prolonged standing, volume depletion, after strenuous exertion
- **Orthostatic**
  - After move to upright posture, may be exacerbated by:
    - Volume depletion, diuretics, vasodilators, etc
    - History of neuropathy, diabetes, alcohol abuse
- **Cardiac/Cardiovascular**
  - Structural heart disease/major ECG abnormality:
    - Including: prior myocardial infarction, hypertrophic cardiomyopathy, arrhythmogenic right ventricular cardiomyopathy, acute ischemia, AV block, channelopathy, preexcitation, etc.
  - Family history of sudden death
  - Occurrence during exercise or supine

Moya A et al, ESC Syncope Guidelines, Eur Heart J 2009; 30: 2631-71

Clinical Findings Strongly Favoring In-Hospital Diagnostic Testing

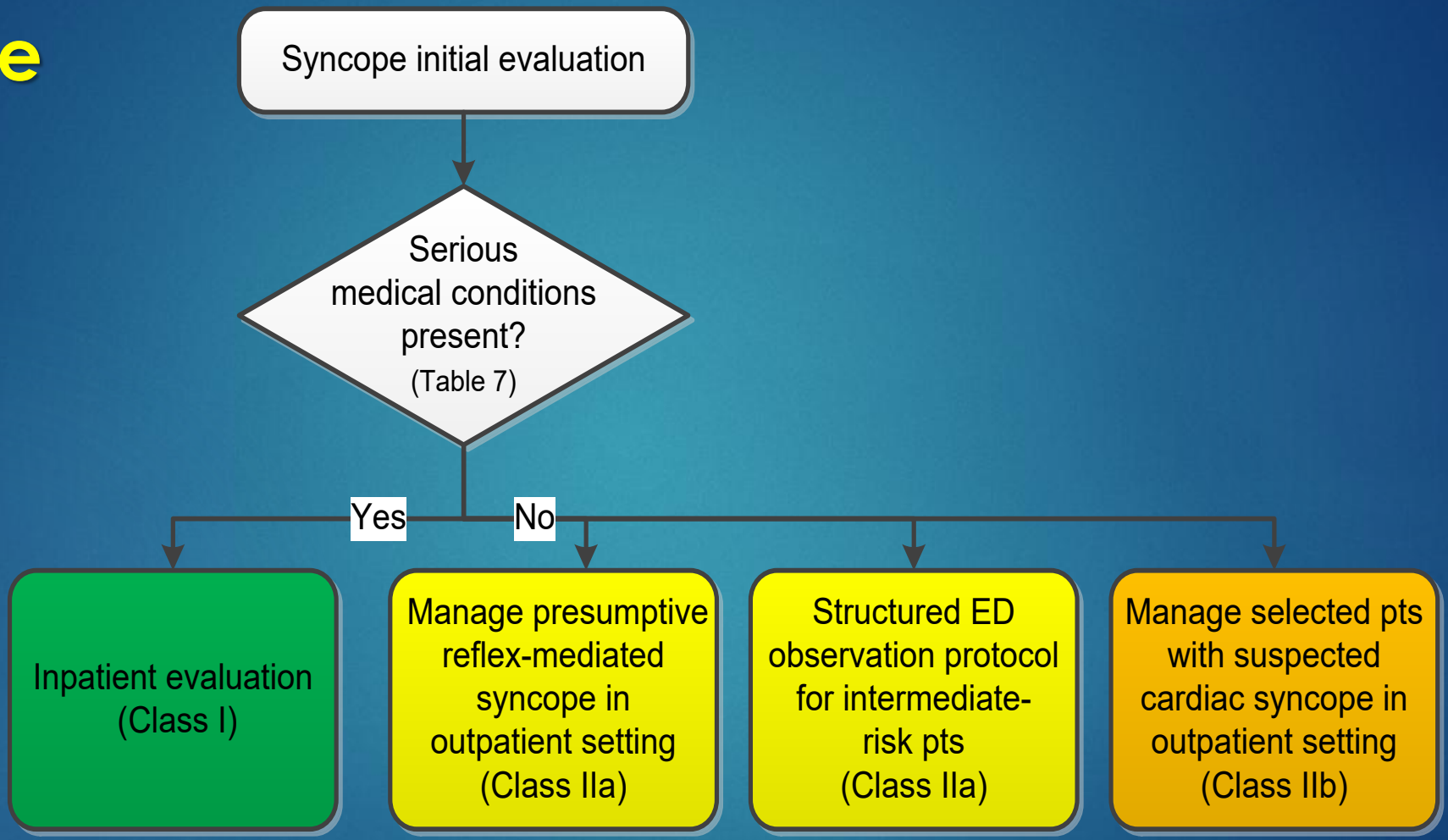
- Suspected/known clinically significant heart disease
- ECG abnormalities suggesting potential life-threatening arrhythmic cause
- Syncope during exercise or while supine
- Severe injury/accident
- Family history of premature sudden death

Moya A et al, ESC Syncope Guidelines, Eur Heart J 2009; 30: 2631-71

Disposition After Initial Evaluation

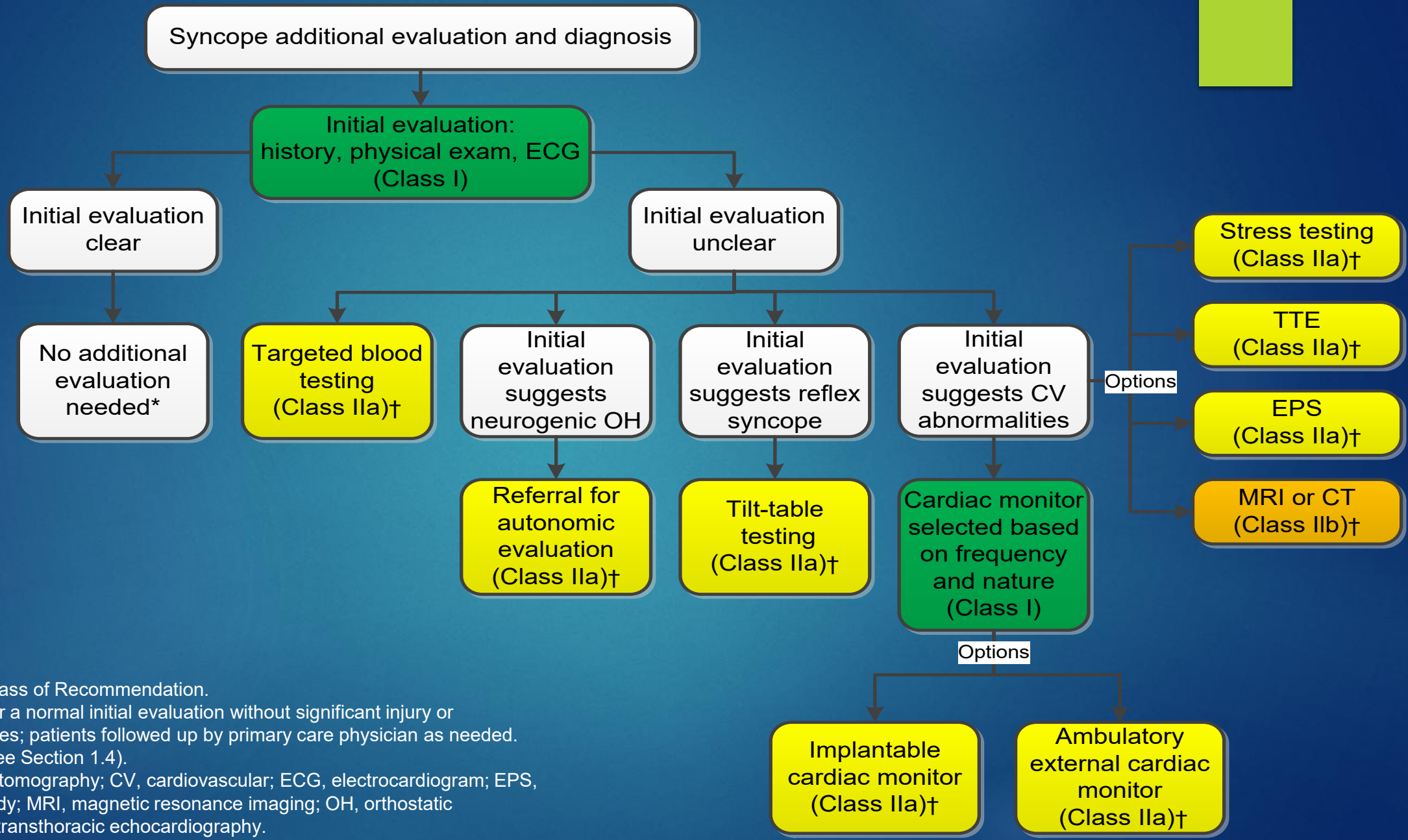
COR	LOE	Recommendations
I	B-NR	Hospital evaluation and treatment are recommended for patients presenting with syncope who have a serious medical condition potentially relevant to the cause of syncope identified during initial evaluation.
IIa	C-LD	It is reasonable to manage patients with presumptive reflex-mediated syncope in the outpatient setting in the absence of serious medical conditions.
IIa	B-R	In intermediate-risk patients with an unclear cause of syncope, use of a structured ED observation protocol can be effective in reducing hospital admission.
IIb	C-LD	It may be reasonable to manage selected patients with suspected cardiac syncope in the outpatient setting in the absence of serious medical condition.

Patient Disposition After Initial Evaluation for Syncope



ED indicates emergency department; pts, patients.

Additional Evaluation and Diagnosis



Colors correspond to Class of Recommendation.
*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.

Blood Testing

COR	LOE	Recommendations
IIa	B-NR	Targeted blood tests are reasonable in the evaluation of selected patients with syncope identified on the basis of clinical assessment from history, physical examination, and ECG.
IIb	C-LD	Usefulness of brain natriuretic peptide and high-sensitivity troponin measurement is uncertain in patients for whom a cardiac cause of syncope is suspected.
III: No Benefit	B-R	Routine and comprehensive laboratory testing is not useful in the evaluation of patients with syncope.

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.

Stress Testing

COR	LOE	Recommendation
IIa	C-LD	Exercise stress testing can be useful to establish the cause of syncope in selected patients who experience syncope or presyncope during exertion.

Cardiac Monitoring

COR	LOE	Recommendations
I	C-EO	The choice of a specific cardiac monitor should be determined on the basis of the frequency and nature of syncope events.
IIa	B-NR	To evaluate selected ambulatory patients with syncope of suspected arrhythmic etiology, the following external cardiac monitoring approaches can be useful: 1. Holter monitor 2. Transtelephonic monitor 3. External loop recorder 4. Patch recorder 5. Mobile cardiac outpatient telemetry.
IIa	B-R	To evaluate selected ambulatory patients with syncope of suspected arrhythmic etiology, an ICM can be useful.

In-Hospital Telemetry

COR	LOE	Recommendation
I	B-NR	Continuous ECG monitoring is useful for hospitalized patients admitted for syncope evaluation with suspected cardiac etiology.

Postural Blood Pressure Testing for Orthostatic Hypotension

- Sustained BP drop usually within 3-5 min standing or HUT to ≥60°
  - Systolic BP fall ≥20 mmHg, or
  - Diastolic BP fall ≥10 mmHg
- In hypertensive patients
  - Systolic BP fall of ≥30 mmHg
- In some cases symptoms may be delayed 5-15 min

Consensus statement on the definition of orthostatic hypotension, neurally mediated syncope and the postural tachycardia syndrome.

Freeman R, Wieling W, Axelrod FB, Benditt DG, Benarroch E, Biaggioni I, Cheshire WP, Chelimsky T, Cortelli P, Gibbons CH, et al.
Auton Neurosci. 2011 Apr 26; 161(1-2):46-8. Epub 2011 Mar 9.

Carotid Sinus Massage (CSM)

- **Method**
  - Massage, ~10 seconds, firm but do not occlude
  - Supine and upright posture (on tilt-table)

- **Suggests Carotid Sinus Syndrome (CSS) if:**
  - >6 sec asystole* or >50 mmHg fall in systolic BP
  - Reproduction of symptoms (usually only occurs with CSM during upright posture)

* Previously 3 sec was considered adequate, but longer pause is now recommended

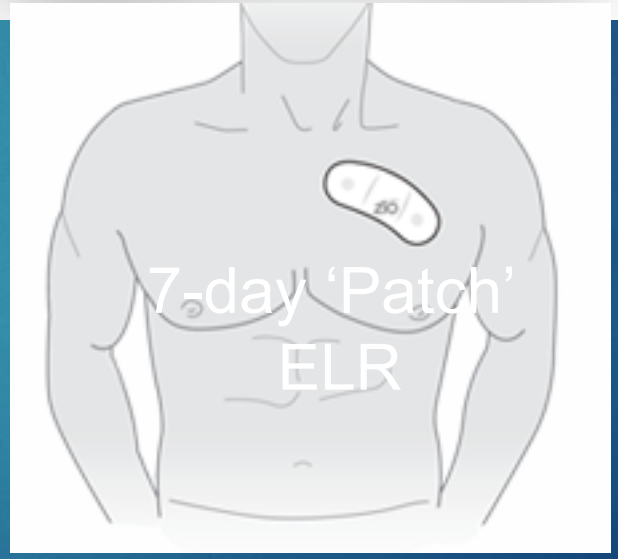
Brignole M et al Europace 2011; 13: 462-64,
Krediet CTP et al Europace 2011;13: 14-22

Additional Diagnostic Tests

Use Based on Initial Examination and Risk Stratification

- **Ambulatory ECG**
  - Wearable external monitors
  - Insertable loop recorder
- **Head-Up Tilt Test (with CSM)**
- **Electrophysiology study (EPS)**
- **Non-invasive for life-threatening VT/VF**
  - SAECG
  - Heart rate variability, HR turbulence
  - Microvolt T-wave alternans, QT dispersion

External ‘Loop’ Recorders (ELRs)

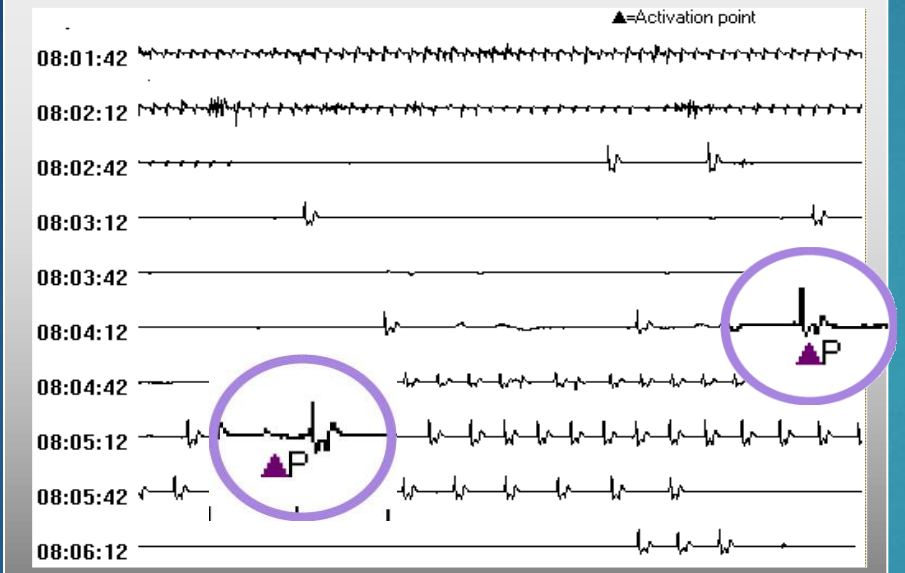


ICM Devices

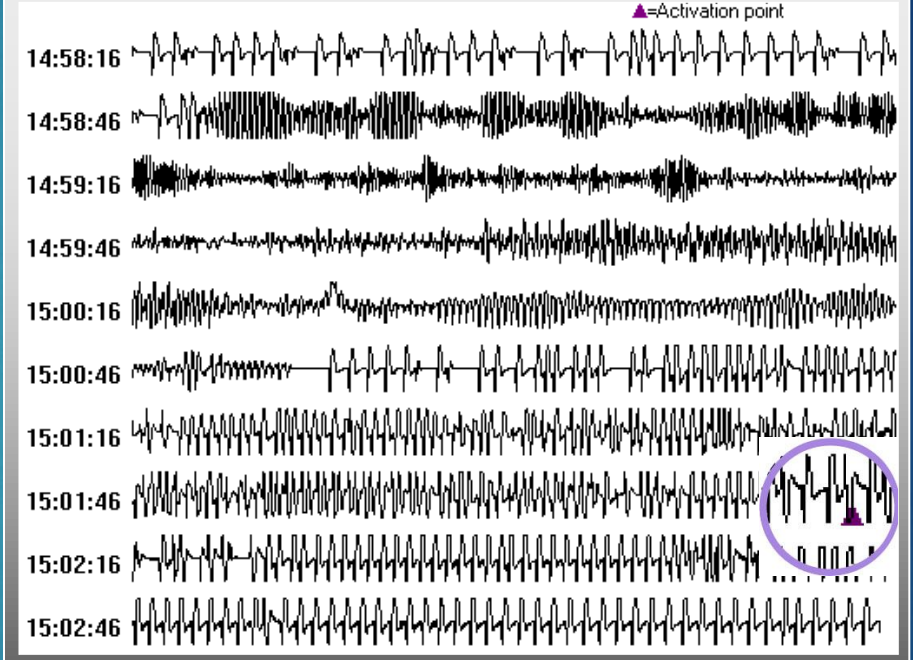

A
Medtronic
REVEAL® XT
B
Reveal LINQ™
C
ST. JUDE MEDICAL
SJM CONFIRM™
D
ST. JUDE MEDICAL
CONFIRM Rx™
DM3500
SN: 123456
E
BioMonitor 2
BIOTRONIK
BIOTRONIK
Home Monitoring

Symptom-Rhythm Correlation

ILR Syncope Cases with Brady- and Tachyarrhythmias



56 year old woman with refractory syncope accompanied with 'seizures



65 year old man with syncope accompanied by brief retrograde amnesia

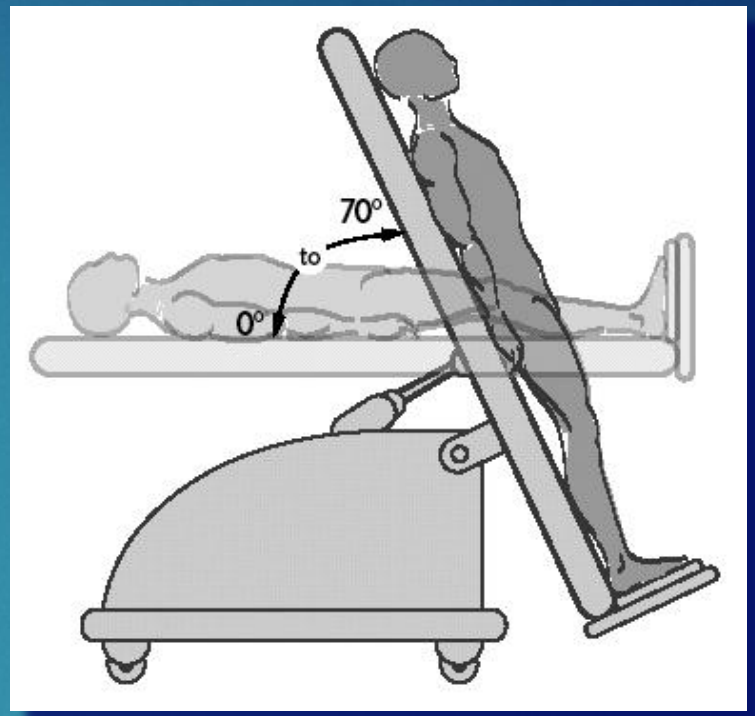
Evidence for ICMs in Syncope

Study/First Author (Year) (Ref. #)	Study Type	N	Results
RAST (2001) (30)	Randomized controlled trial	60	Diagnosis in 55% of patients in the ICM arm compared with 19% in the control (p = 0.0014)
PICTURE (2011) (31)	Multicenter prospective	570	ICMs assisted in diagnosis in 30% of patients
Solbiati et al. (2016) (18)	Systematic review	579	Patients with ICM implantation experienced higher rates of diagnosis (RR: 0.61; CI: 0.54–0.68)
Krahn et al. (2003) (32)	Randomized crossover study	60	ICM strategy was more expensive per participant but cost lower per diagnosis when compared with conventional testing
ISSUE-3 (2012) (33)	Randomized controlled trial	511	Risk of syncope recurrence in patients with ICM-detected syncope randomized to pacing arm was reduced by 57% (CI: 4%–81%)
SPRITELY (2018) (34)	Randomized pragmatic trial	115	Empirical pacemaker arm experienced lower rates of primary composite outcomes

Tilt-Table Testing

COR	LOE	Recommendations
IIa	B-R	If the diagnosis is unclear 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 suspected delayed OH when initial evaluation is not diagnostic.
IIa	B-NR	Tilt-table testing is reasonable to distinguish convulsive syncope from epilepsy in selected patients.
IIa	B-NR	Tilt-table testing is reasonable to establish a diagnosis of pseudosyncope.
III: No Benefit	B-R	Tilt-table testing is not recommended to predict a response to medical treatments for VVS.

Head-Up Tilt Test (HUT)



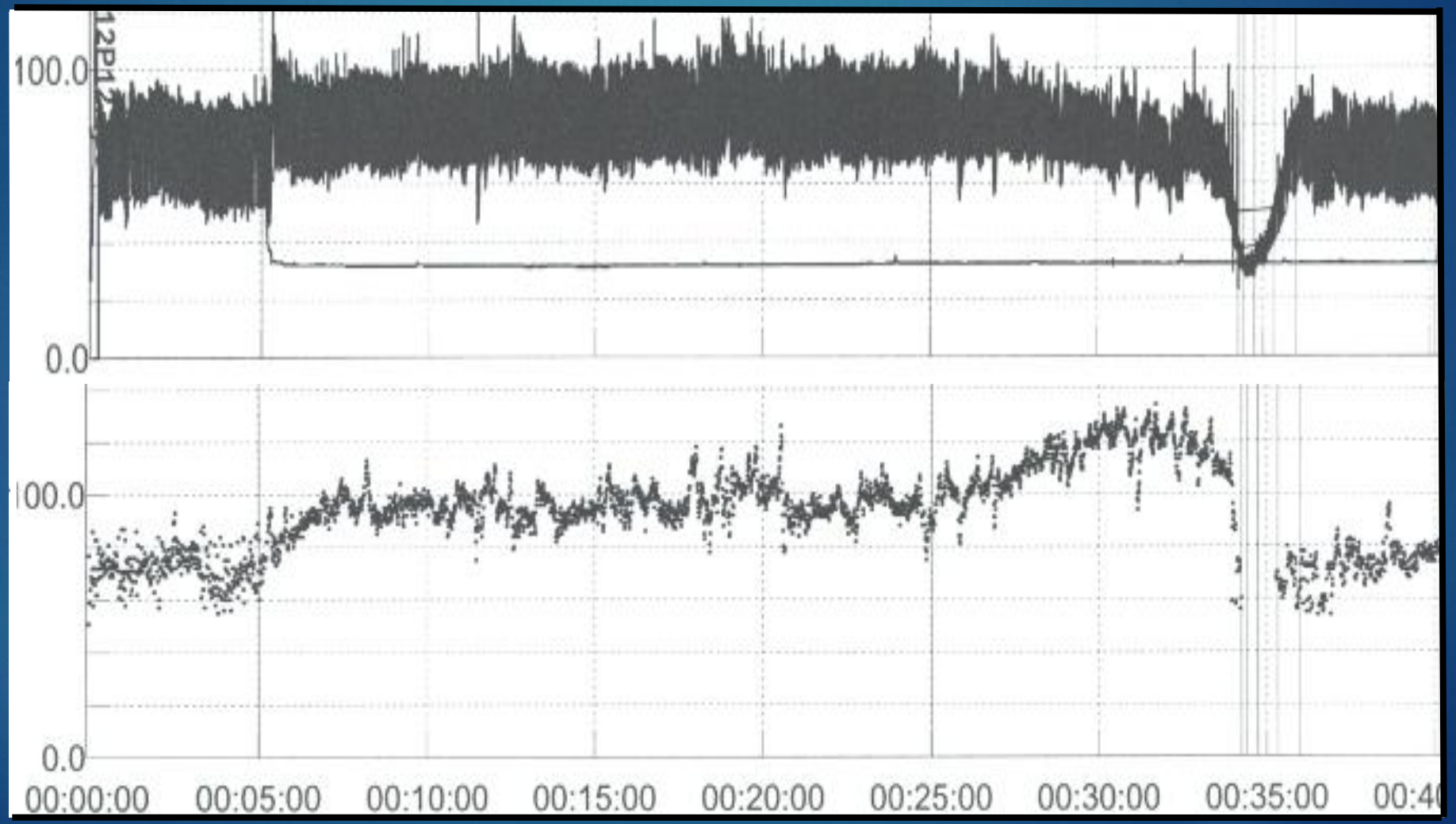
- **Protocols vary**
  - some use provocative drugs
- **Goals**
  - Unmask VVS susceptibility
  - Reproduce symptoms
  - Patient learns VVS warning symptoms
  - Patient more confident of diagnosis
- **Not recommended for predicting treatment benefit**

VVS: Typical HUT Protocol

- Supine rest period 5-15 min
- Tilt to 60-70°for 20 min
- Positive end-point: syncope with reproduction of symptoms
- If negative, then add drug provocation while still upright
  - Nitroglycerine 0.4mg SL, or
  - Isoproterenol 1-5 mcg/min, to increase HR to 125% baseline
- Extend tilt after drug, duration 10-15 minutes

Moya A et al, ESC Syncope Guidelines,
Eur Heart J 2009; 30: 2631-71

Vasovagal Syncope: Hypotension and Bradycardia Triggered by HUT



Courtesy R Sutton DSc

EP Testing for Syncope Evaluation

Principal Diagnostic Findings

- **Most useful in structural heart disease patients**
- **Useful diagnostic observations:**
  - Inducible monomorphic VT
  - SNRT > 3000 ms or CSNRT > 600 ms
  - Inducible SVT with hypotension
  - HV interval ≥ 100 ms (especially in absence of inducible VT)
  - Pacing-induced infra-nodal block

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

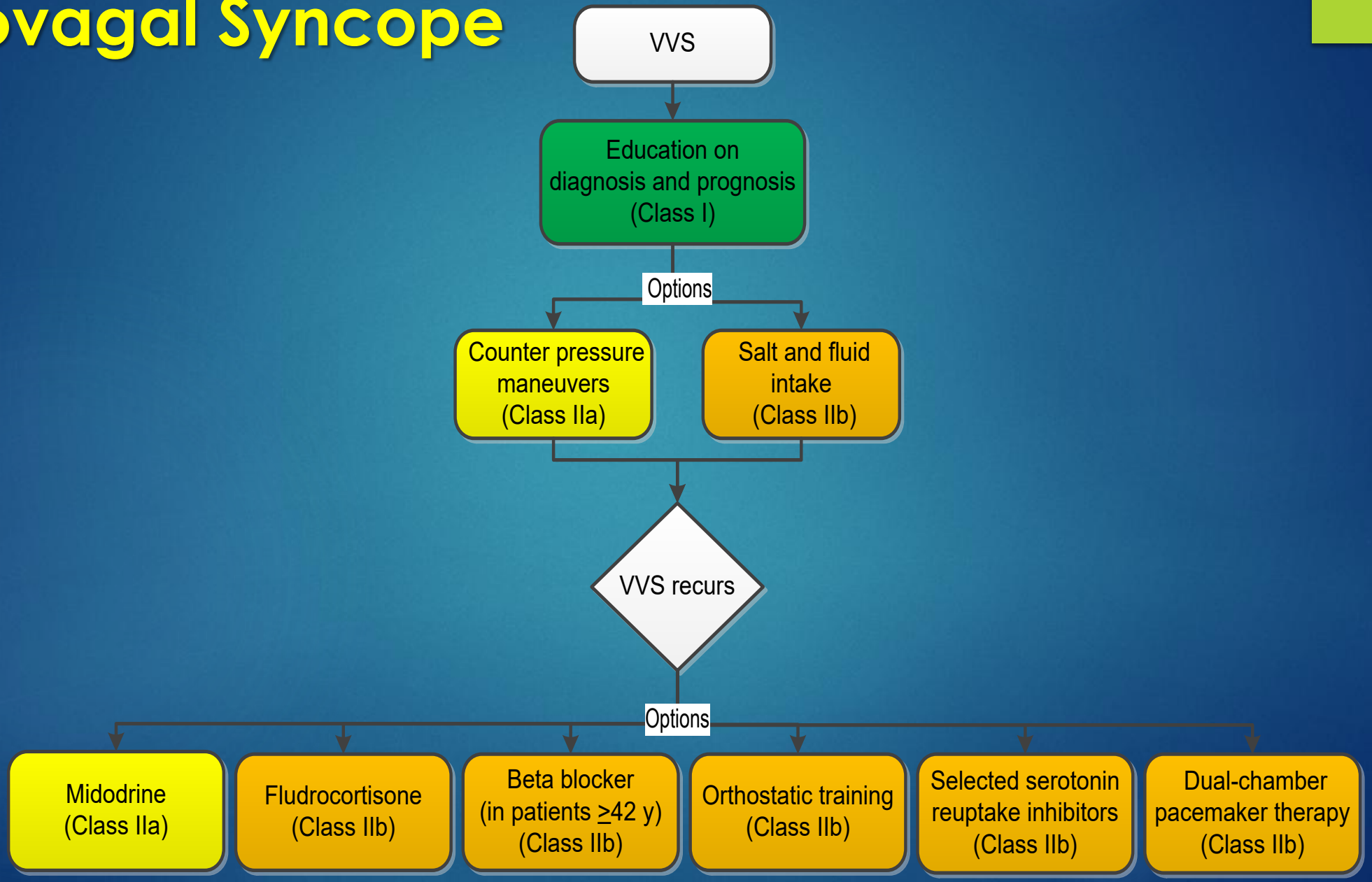
Specific Conditions

- Reflex (Neurally-mediated) Syncope (NMS)
  - Vasovagal, Carotid Sinus Syndrome (CSS), etc.
- Orthostatic Hypotension
  - Autonomic dysfunction (1°, 2°)
  - Drug induced
- Cardiac Syncope
  - Structural heart disease
  - Channelopathies
    - Long QT Syndrome (idiopathic, drug-induced)
    - Brugada Syndrome

Reflex (Neurally-Mediated) Syncope

- Vasovagal Syncope (VVS)
- Carotid Sinus Syndrome (CSS)
- Situational Syncope
  - post-micturition
  - cough
  - swallow
  - defecation
  - venipuncture (blood draw)

Vasovagal Syncope

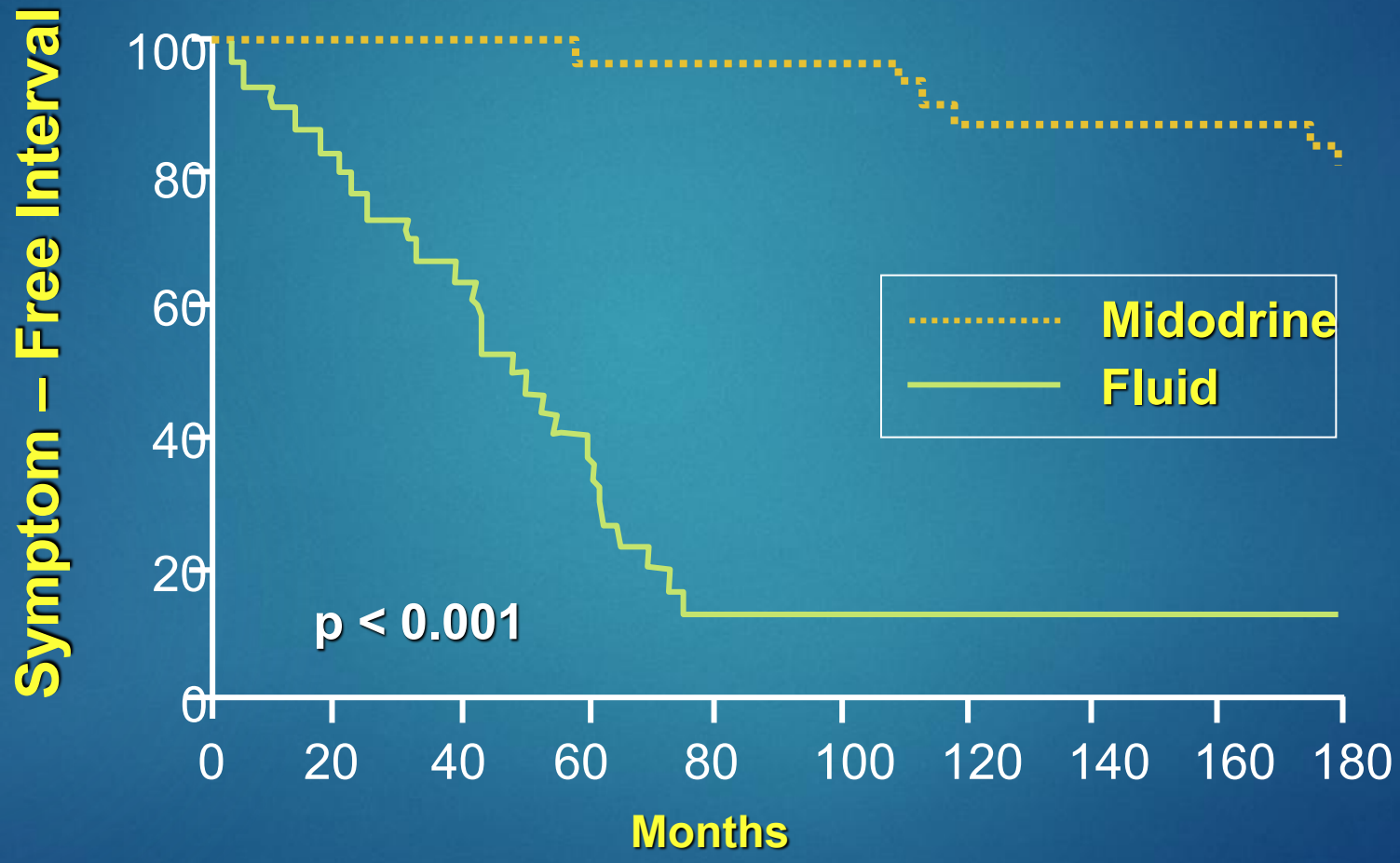


Vasovagal Syncope:
Non-Pharmacologic Treatment Strategy

- Patient education, reassurance, instruction
- Salt/Volume
  - Increased dietary salt
  - Increased volume intake
  - (e.g., electrolyte rich 'sport' drinks, beware of calories)
- Physical maneuvers
  - Standing/tilt-training
  - Muscle tensing, leg-crossing
- Support hose, abdominal binders

* modified after Moya A et al, ESC Syncope Guidelines, Eur Heart J 2009; 30: 2631-71

Midodrine for VVS



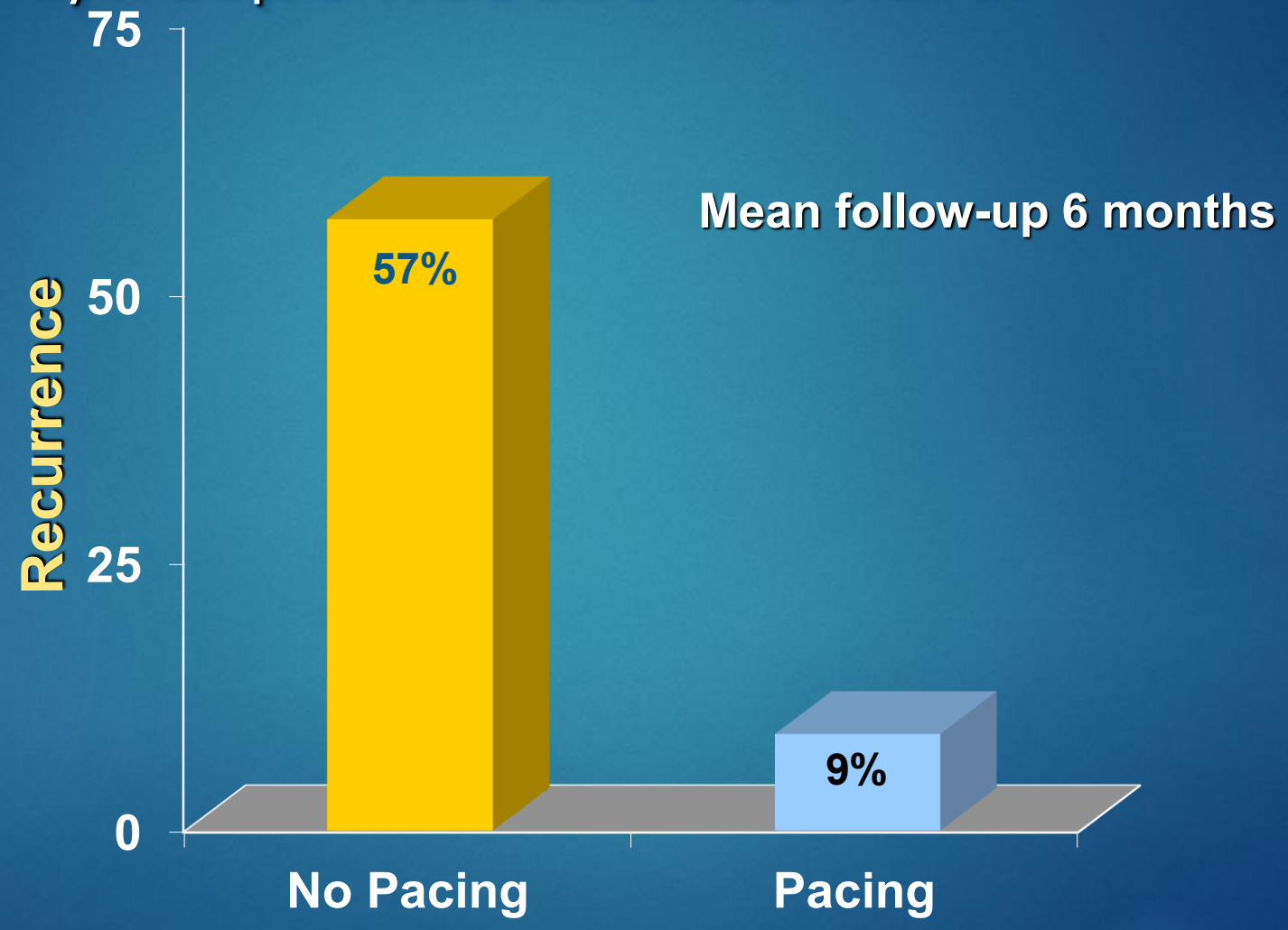
Perez-Lugones A et al JCE 2001;12:935

Pacing in VVS: Summary

- Initial studies were not double-blind and not based on documented spontaneous bradycardia
- PM implantation may create psychological responses that modify autonomic responses
- ISSUE-3 suggested that pacing therapy is effective if spontaneous bradycardia is documented

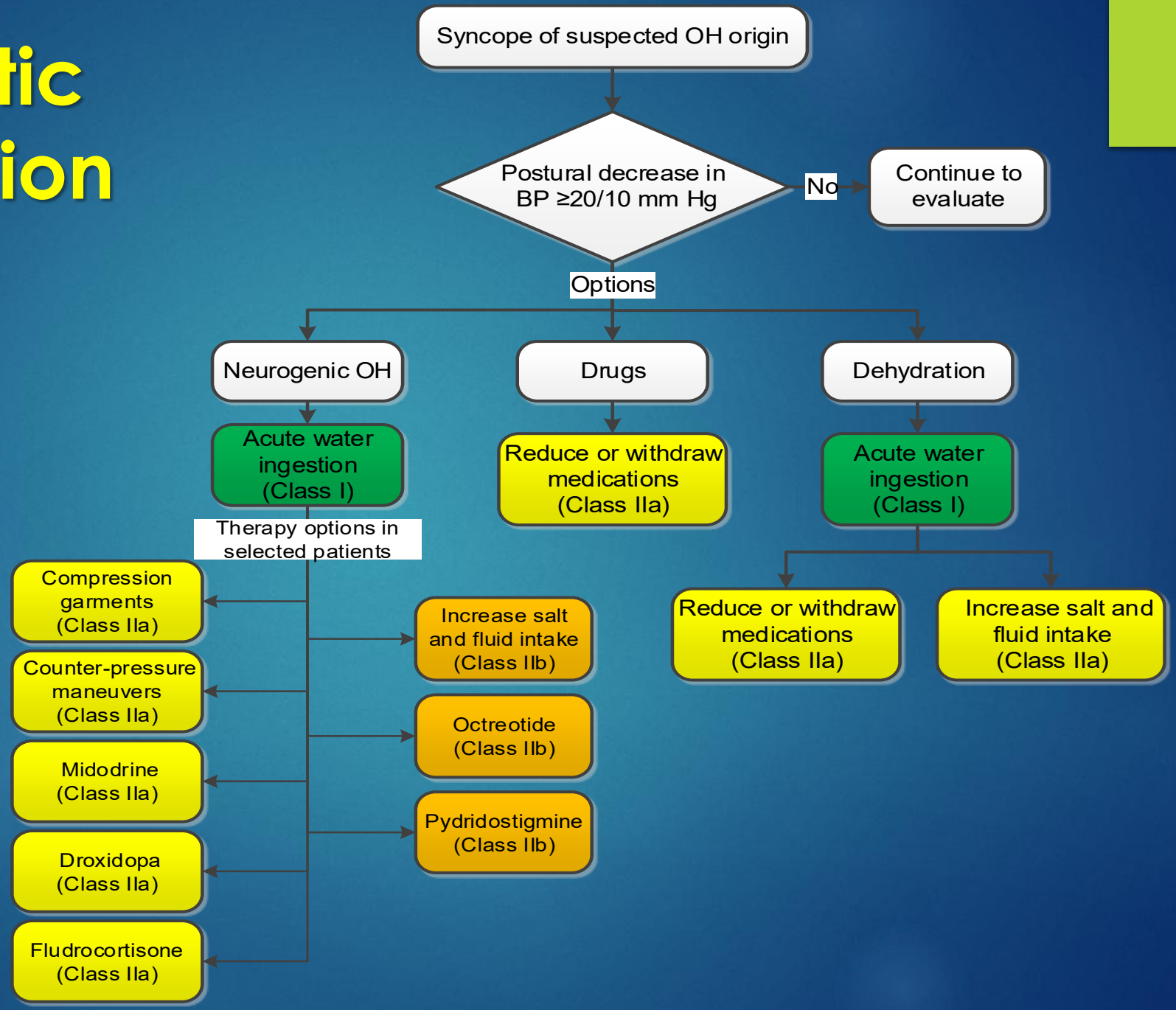
Pacing in Carotid Sinus Syndrome

Syncope Recurrence Rate

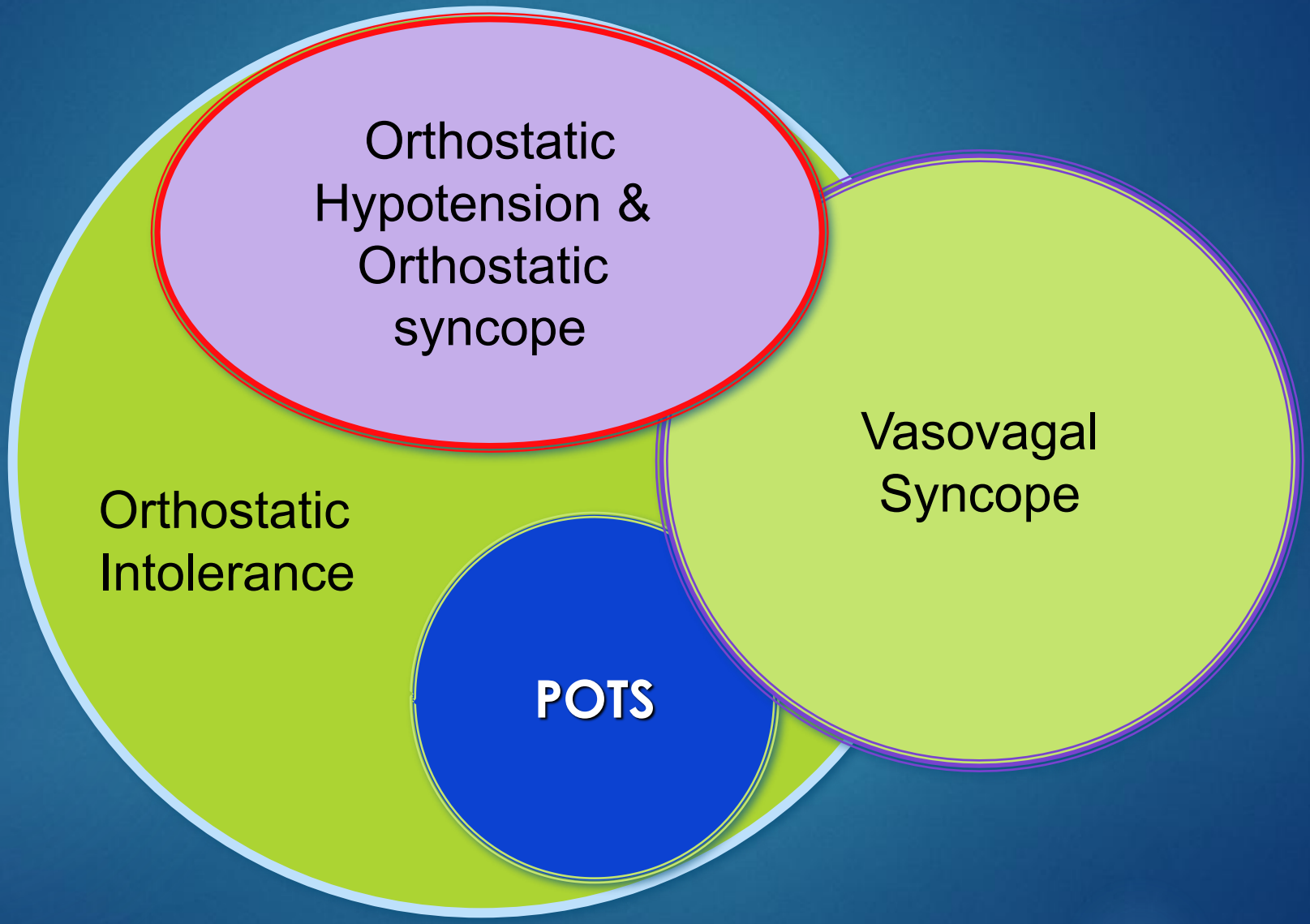


Brignole M, et al. Eur JCPE. 1992;4:247-254

Orthostatic Hypotension



Orthostatic Intolerance Syndromes



Orthostatic Intolerance: Treatment Strategies

- Patient education, injury avoidance
- Reduce or withdraw drugs
- Hydration
  - Fluids, salt, diet
  - Minimize caffeine/alcohol
- Sleeping with head of bed elevated
- (≈ 25 cm)
- Tilt Training, leg crossing, arm tensing
- Exercise (begin recumbent)
- Waist high support hose, abdominal binders
- Midodrine therapy

Cardiac Syncope: Principal Causes

- Acute MI / Ischemia (most common)
  - Acquired/congenital coronary artery disease, coronary embolism
  - Stroke (CVA)
- Hypertrophic Cardiomyopathy (HCM)
- Arrhythmogenic RV Dysplasia (ARVD)
- Acute aortic dissection
- Acute pulmonary embolus/pulmonary hypertension
- Valvular abnormalities
  - Aortic stenosis, mitral stenosis, ball thrombus/vegetation
- Atrial myxoma

Syncope Due to Cardiac Arrhythmias

- **Bradyarrhythmias**
  - Sinus arrest, exit block
  - High grade or acute complete AV block
  - Post-tachycardia pause
- **Tachyarrhythmias**
  - Atrial fibrillation/flutter with rapid ventricular rate (e.g., abrupt onset rapd rate)
  - Paroxysmal SVT or VT
  - Torsades de pointes (e.g., long QT syndrome)

Clinical and ECG Features Suggesting Cardiac Syncope

- Severe structural heart disease/heart failure present
- Syncope during exertion or while supine
- Palpitations at time of syncope
- ECG/monitor findings of:
  - Baseline wide QRS complex
  - Mobitz 1 second degree AVB
  - Sinus bradycardia <50 bpm
  - Documented nonsustained or sustained VT
  - Preexcitation, Long/Short QT, ARVD or Brugada pattern
  - Infero-lateral 'early repolarization' pattern

Moya A et al, ESC Syncope Guidelines, Eur Heart J 2009; 30: 2631-71

Conclusions

- Syncope is very common and most often has a benign prognosis
- Most important distinction to make is between cardiac and other causes of syncope
- International society guidelines provide recommendations on the optimal approach to diagnosis and treatment