

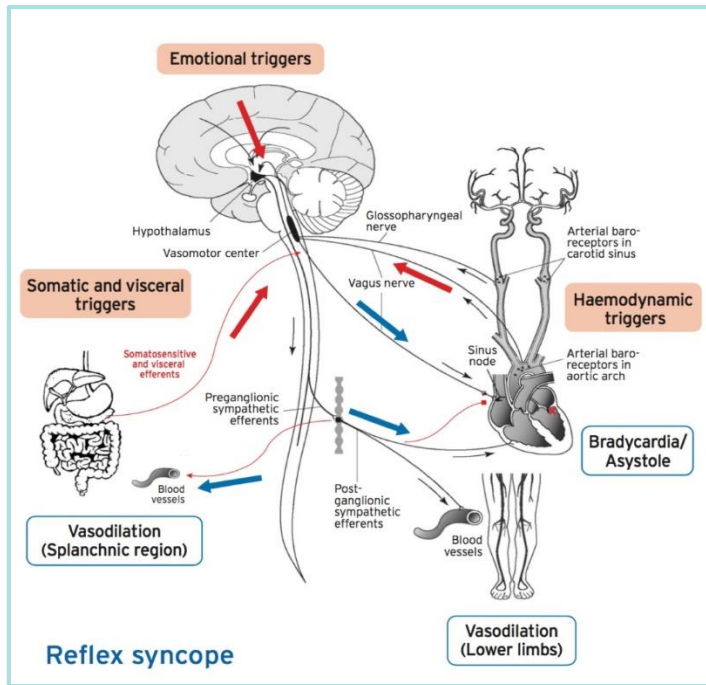
Heart Rhythm Congress

ICC, Birmingham: October 8th 2018

STARS Take Fainting to Heart: Syncope and POTs Update

ESC & ACC, AHA, HRS

What are the Differences and are they Important?



John Camm

**Professor of Clinical Cardiology, St. George's Hospital
Medical School, London**



Declaration of Competing Interests

Chairman

ESC Guidelines on Atrial Fibrillation, 2010 and Update, 2012; ACC/AHA/ESC Guidelines on VAs and SCD; 2006; NICE Guidelines on ACS and NSTEMI, 2012; NICE Guidelines on Heart Failure, 2008; Member: NICE Guidelines on AF, 2006; ESC VA and SCD Guidelines, 2015; Reviewer: AHA/ACC/HRS Guidelines on AF, 2014; ACC/AHA/HRS SVT Guidelines, 2015; ESC AF Guidelines, 2016

Steering Committees

Multiple trials involving antiarrhythmic agents, heart failure drugs and novel anticoagulants

DSMBs

Multiple trials of devices and drugs

Events Committees

One trial of novel oral anticoagulants and multiple trials of miscellaneous agents with CV adverse effects

Editorial Role

Editor-in-Chief, European Heart Journal: Case Reports and Clinical Cardiology; Editor, European Textbook of Cardiology, European Heart Journal, Electrophysiology of the Heart, and Evidence Based Cardiology

Consultant/Advisor/Speaker

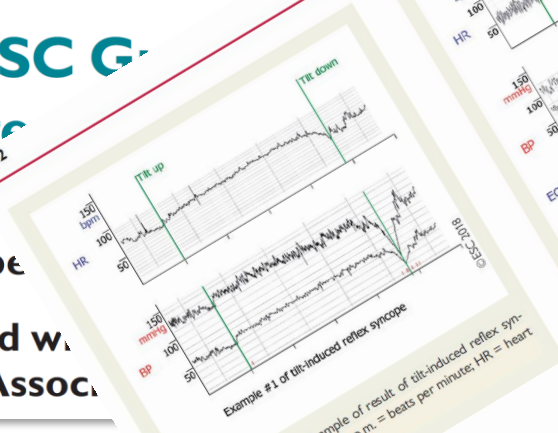
Incarda, Menarini, Milestone, Sanofi, Servier, **Bayer**, Boehringer Ingelheim, Bristol-Myers Squibb, Daiichi Sankyo, Pfizer, Boston Scientific, Abbott, Biotronik, Medtronic, GlaxoSmithKline, Anidium, Cardiac Insight, Johnson and Johnson, Novartis, Radius, Richmond Pharmacology

2018 ESC Guidelines
for the diagnosis and management of acute coronary syndromes in patients presenting without persistent ST-segment elevation

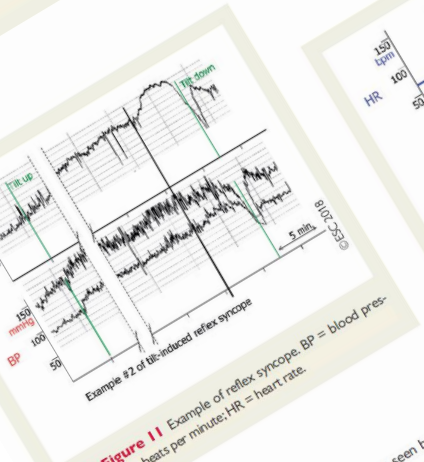
The Task Force for the European Society of Cardiology and the European Association of Cardiovascular Imaging

Developed with the European Association of Cardiovascular Imaging

ESC GUIDELINES



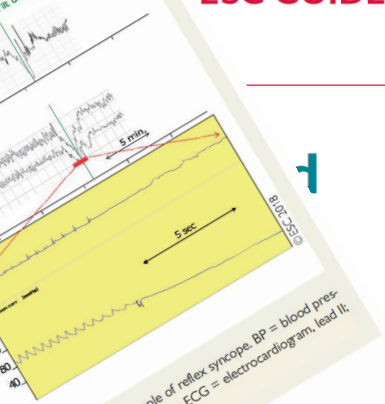
Web Figure 10 Example of result of tilt-induced reflex syncope. BP = blood pressure; b.p.m. = beats per minute; HR = heart rate.



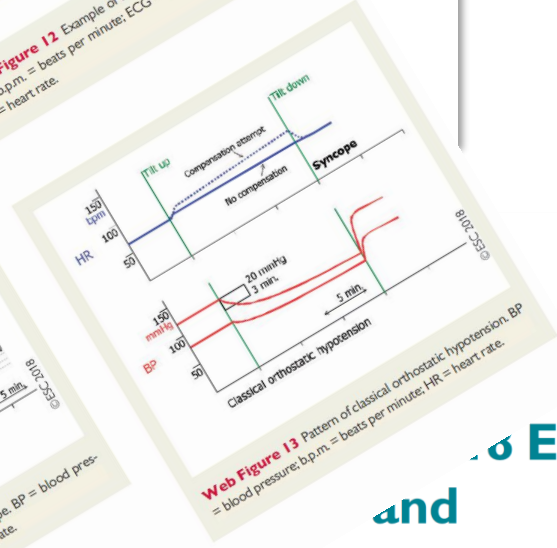
Web Figure 11 Example of reflex syncope. BP = blood pressure; b.p.m. = beats per minute; HR = heart rate.

6.3.5 Example #3 of reflex syncope
In some cases, hardly any changes in BP or HR are seen before the accelerating decrease in BP causing syncope (Web Figure 12). Here, HR decreased along with BP, resulting in a decrease in stroke volume.

The European Society of Cardiology



Web Figure 12 Example of reflex syncope. BP = blood pressure; b.p.m. = beats per minute; ECG = electrocardiogram, lead II; HR = heart rate.



Web Figure 13 Pattern of classical orthostatic hypotension. BP = blood pressure; b.p.m. = beats per minute; HR = heart rate.

ESC GUIDELINES

ESC
and

Diagnosis and management of syncope of the European Society of Cardiology (ESC)

ESC: Classes of Recommendations

Classes of recommendations	Definition	Suggested wording to use
Class I	Evidence and/or general agreement that a given treatment or procedure is beneficial, useful, effective.	Is recommended/ is indicated.
Class II	Conflicting evidence and/or a divergence of opinion about the usefulness/efficacy of the given treatment or procedure.	
<i>Class IIa</i>	<i>Weight of evidence/opinion is in favour of usefulness/efficacy.</i>	Should be considered.
<i>Class IIb</i>	<i>Usefulness/efficacy is less well established by evidence/opinion.</i>	May be considered.
Class III	Evidence or general agreement that the given treatment or procedure is not useful/effective, and in some cases may be harmful.	Is not recommended.

AHA: Classes of Recommendations

CLASS (STRENGTH) OF RECOMMENDATION	LEVEL (QUALITY) OF EVIDENCE‡
CLASS I (STRONG) Benefit >>> Risk Suggested phrases for writing recommendations: <ul style="list-style-type: none"> Is recommended Is indicated/useful/effective/beneficial Should be performed/administered/other Comparative-Effectiveness Phrases†: <ul style="list-style-type: none"> Treatment/strategy A is recommended/indicated in preference to treatment B Treatment A should be chosen over treatment B 	LEVEL A <ul style="list-style-type: none"> High-quality evidence‡ from more than 1 RCT Meta-analyses of high-quality RCTs One or more RCTs corroborated by high-quality registry studies
CLASS IIa (MODERATE) Benefit >> Risk Suggested phrases for writing recommendations: <ul style="list-style-type: none"> Is reasonable Can be useful/effective/beneficial Comparative-Effectiveness Phrases†: <ul style="list-style-type: none"> Treatment/strategy A is probably recommended/indicated in preference to treatment B It is reasonable to choose treatment A over treatment B 	LEVEL B-R (Randomized) <ul style="list-style-type: none"> Moderate-quality evidence‡ from 1 or more RCTs Meta-analyses of moderate-quality RCTs
CLASS IIb (WEAK) Benefit ≥ Risk Suggested phrases for writing recommendations: <ul style="list-style-type: none"> May/might be reasonable May/might be considered Usefulness/effectiveness is unknown/unclear/uncertain or not well established 	LEVEL B-NR (Nonrandomized) <ul style="list-style-type: none"> Moderate-quality evidence‡ from 1 or more well-designed, well-executed nonrandomized studies, observational studies, or registry studies Meta-analyses of such studies
CLASS III: No Benefit (MODERATE) Benefit = Risk <i>(Generally, LOE A or B use only)</i> Suggested phrases for writing recommendations: <ul style="list-style-type: none"> Is not recommended Is not indicated/useful/effective/beneficial Should not be performed/administered/other 	LEVEL C-LD (Limited Data) <ul style="list-style-type: none"> Randomized or nonrandomized observational or registry studies with limitations of design or execution Meta-analyses of such studies Physiological or mechanistic studies in human subjects
CLASS III: Harm (STRONG) Risk > Benefit Suggested phrases for writing recommendations: <ul style="list-style-type: none"> Potentially harmful Causes harm Associated with excess morbidity/mortality Should not be performed/administered/other 	LEVEL C-EO (Expert Opinion) Consensus of expert opinion based on clinical experience

COR and LOE are determined independently (any COR may be paired with any LOE).

A recommendation with LOE C does not imply that the recommendation is weak. Many important clinical questions addressed in guidelines do not lend themselves to clinical trials. Although RCTs are unavailable, there may be a very clear clinical consensus that a particular test or therapy is useful or effective.

* The outcome or result of the intervention should be specified (an improved clinical outcome or increased diagnostic accuracy or incremental prognostic information).

† For comparative-effectiveness recommendations (COR I and IIa; LOE A and B only), studies that support the use of comparator verbs should involve direct comparisons of the treatments or strategies being evaluated.

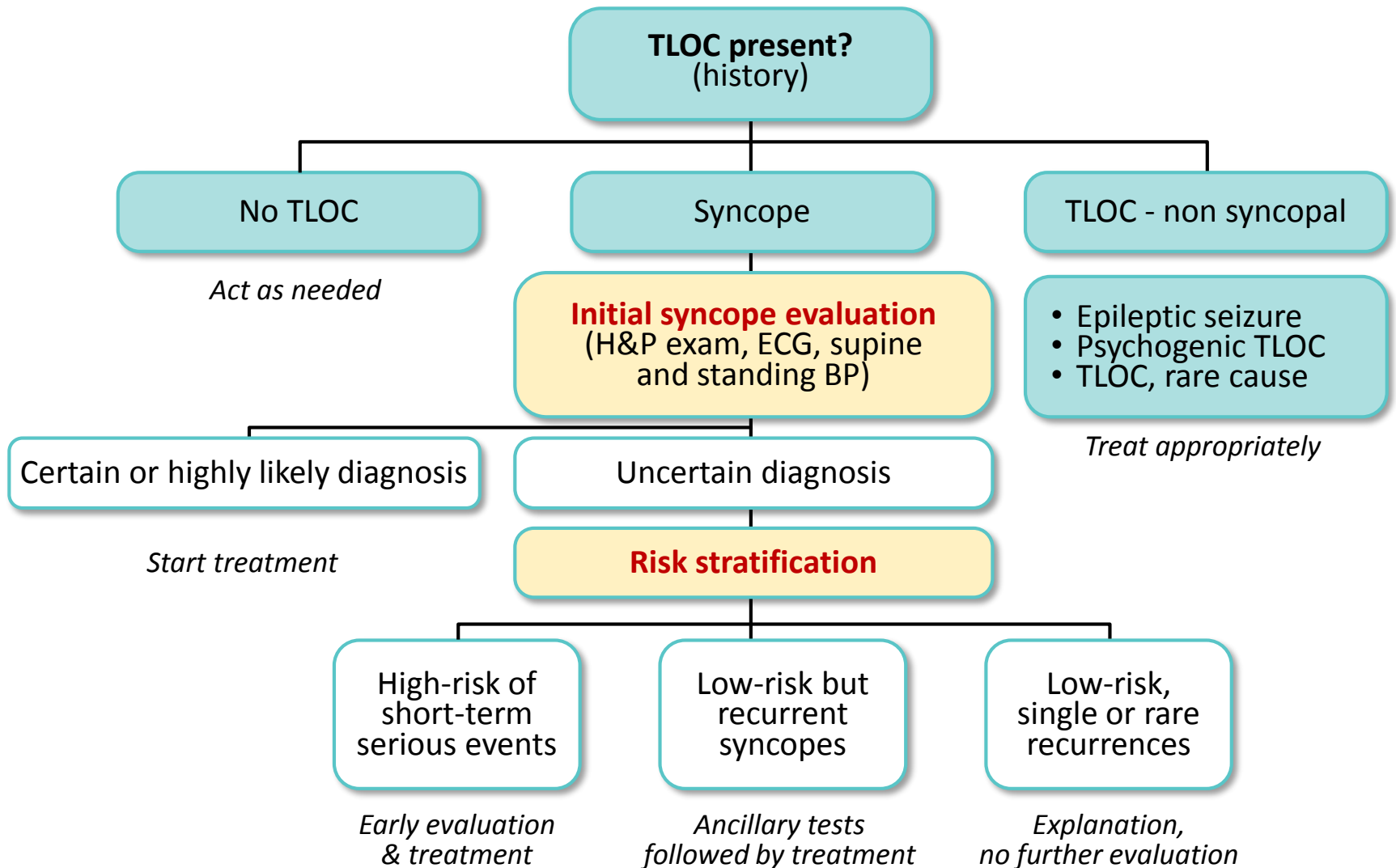
‡ The method of assessing quality is evolving, including the application of standardized, widely used, and preferably validated evidence grading tools; and for systematic reviews, the incorporation of an Evidence Review Committee.

COR indicates Class of Recommendation; EO, expert opinion; LD, limited data; LOE, Level of Evidence; NR, nonrandomized; R, randomized; and RCT, randomized controlled trial.

Definition

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

Presentation of Patient with Probable TLOC



Risk Stratification at the Initial Evaluation

Low-risk	High-risk (red flag)
Syncopal event	
<ol style="list-style-type: none">1. Associated with prodrome typical of reflex syncope (e.g. light-headedness, feeling of warmth, sweating, nausea, vomiting)2. After sudden unexpected unpleasant sight, sound, smell, or pain3. After prolonged standing or crowded, hot places4. During a meal or postprandial5. Triggered by cough, defaecation, or micturition6. With head rotation or pressure on carotid sinus (e.g. tumour, shaving, tight collars)7. Standing from supine/sitting position	<p>Major</p> <ol style="list-style-type: none">1. New onset of chest discomfort, breathlessness, abdominal pain, or headache2. Syncope during exertion or when supine.3. Sudden onset palpitation immediately followed by syncope <p>Minor (high risk only if associated with structural heart disease or abnormal ECG):</p> <ol style="list-style-type: none">1. No warning symptoms or short (<10 s) prodrome2. Family history of SCD at young age3. Syncope in the sitting position

CLINICAL PRACTICE

2017

2017 ACC/AHA/HRS guideline for the 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

SYSTEMATIC REVIEW

Pacing as a treatment for reflex-mediated (vasovagal, situational, or carotid sinus hypersensitivity) syncope: A systematic review for the 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

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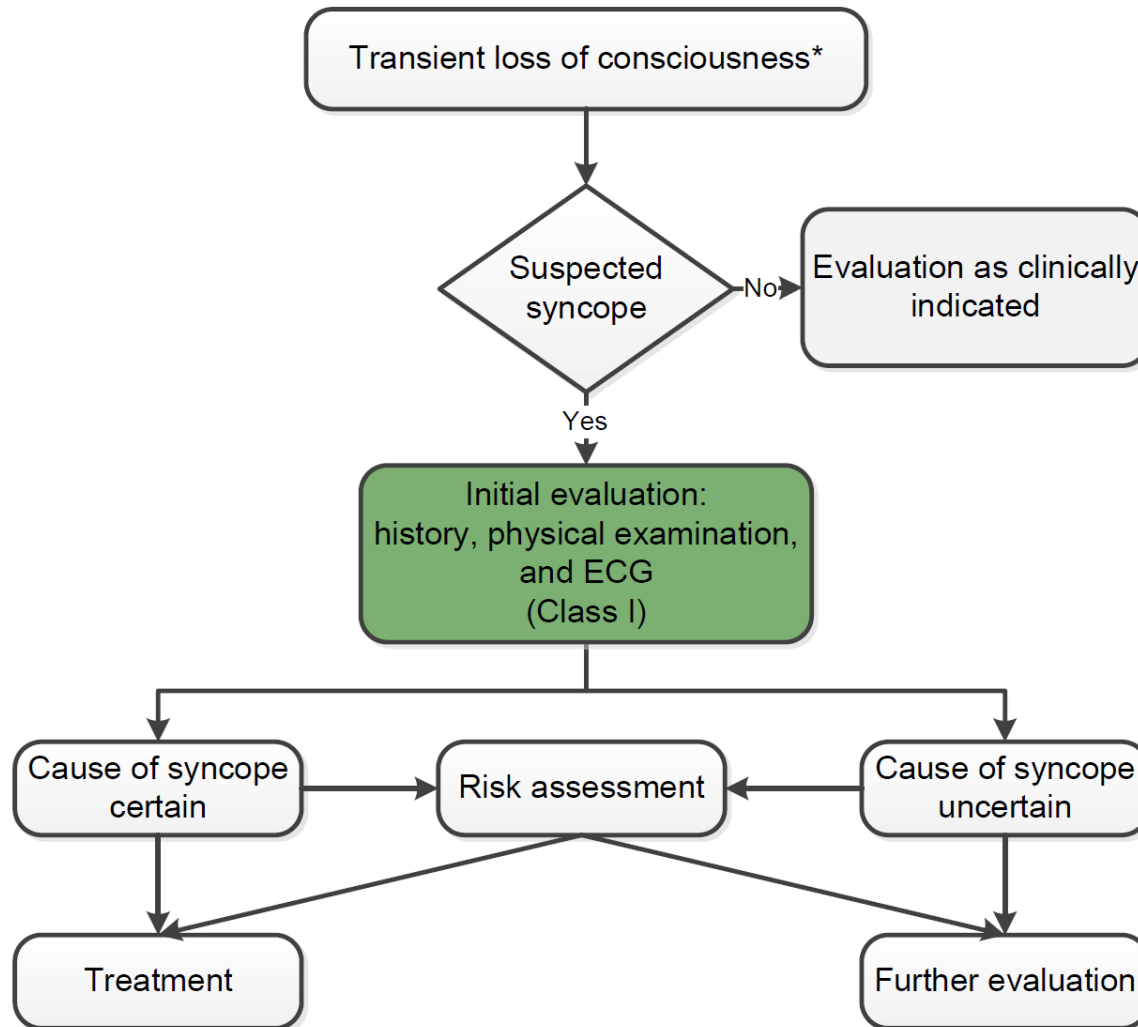
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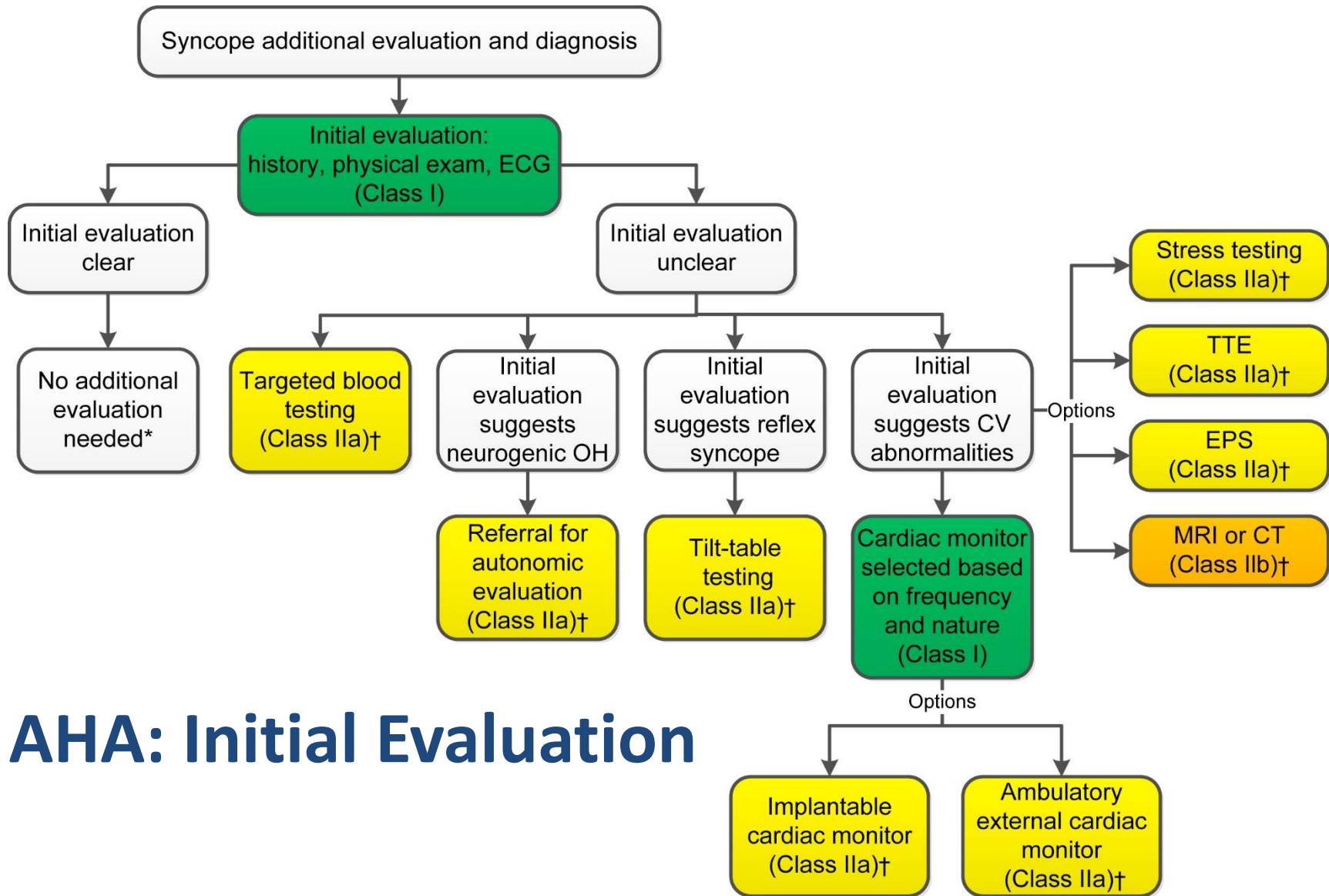
AHA: Initial Evaluation



Syncope Risk Scores

TABLE 5 Examples of Syncope Risk Scores

Study/Reference	Year	Sample N	Events N (%)	Outcome Definition	ED Events*	Predictors	NPV (%)†
Martin (65)	1997	252	104 (41%)	1-y death/arrhythmia	Yes	Abnormal ECG‡; >45 y of age; VA; HF	93
Sarasin (54)	2003	175	30 (17%)	Inpatient arrhythmia	Yes	Abnormal ECG‡; >65 y of age; HF	98
OESIL (47)	2003	270	31 (11%)	1-y death	N/A	Abnormal ECG‡; >65 y of age; no prodrome; cardiac history	100
SFSR (52)	2004	684	79 (12%)	7-d serious events§	Yes	Abnormal ECG‡; dyspnea; hematocrit; systolic BP <90 mm Hg; HF	99
Boston Syncope Rule (50)	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 (49)	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 (48)	2008	676	41 (6%)	10-d serious events¶	Yes	Abnormal ECG‡; trauma; no prodrome; male sex	—
Syncope Risk Score (55)	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 (53)	2010	550	40 (7%)	30-d serious events#	Yes	Abnormal ECG‡; B-natriuretic peptide; hemoglobin; O ₂ Sat; fecal occult blood	98



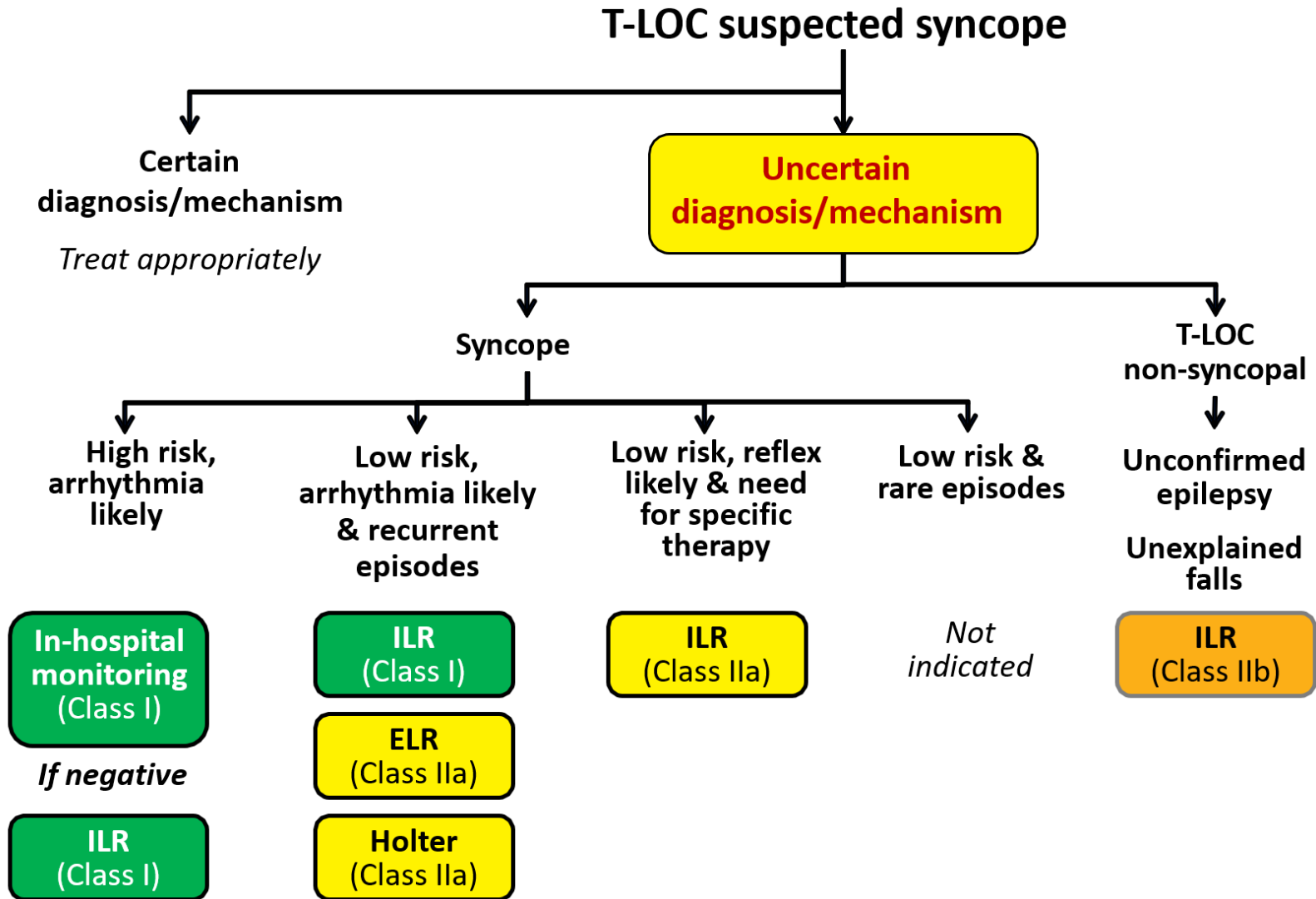
AHA: Initial Evaluation

AHA: ECG Monitoring

Recommendations for 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: <ol style="list-style-type: none">1. Holter monitor (95-99)2. Transtelephonic monitor (96,100,101)3. External loop recorder (96,100-102)4. Patch recorder (103-105)5. Mobile cardiac outpatient telemetry (106,107).
IIa	B-R	To evaluate selected ambulatory patients with syncope of suspected arrhythmic etiology, an implantable cardiac monitor can be useful (95,96,99,107-121).

ESC: ECG Monitoring



AHA: Class III Recommendations

III: No Benefit

B-NR

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 (134-136).

III: No Benefit

B-NR

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 (89,92).

III: No Benefit

B-R

Tilt-table testing is not recommended to predict a response to medical treatments for VVS (152,153).

III: No Benefit

B-NR

ICD implantation is not recommended in patients with Brugada ECG pattern and reflex-mediated syncope in the absence of other risk factors (205,206).

III: Harm

B-NR

EPS should not be performed in patients with early repolarization pattern and history of syncope in the absence of other indications (234).

III: No Benefit

B-R

Beta blockers are not beneficial in pediatric patients with VVS (371,374).

Neurological Evaluation and Tests

5. EEG, ultrasound of neck arteries, and computed tomography or magnetic resonance imaging of the brain are not indicated in patients with syncope.

III

B

III: No Benefit

B-NR

Magnetic resonance imaging and computed tomography 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 (161,162).

III: No Benefit

B-NR

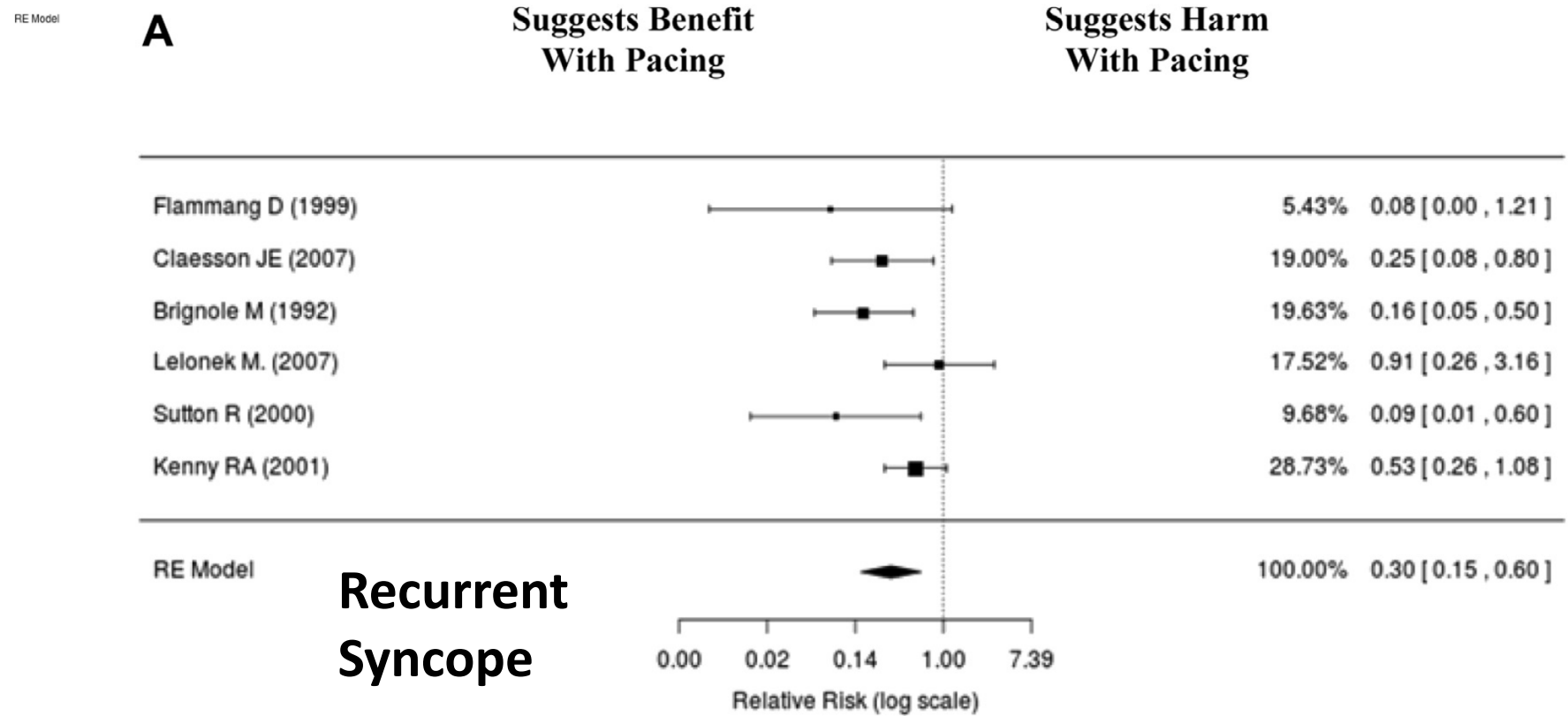
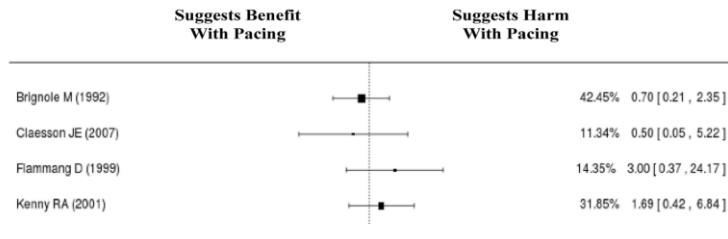
Carotid artery imaging is not recommended in the routine evaluation of patients with syncope in the absence of focal neurological findings that support further evaluation (92,161-164).

III: No Benefit

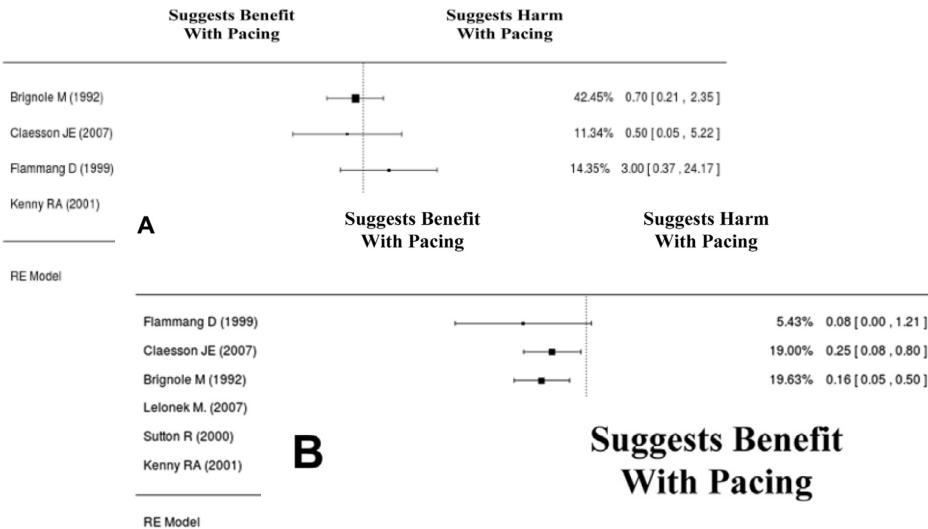
B-NR

Routine recording of an electroencephalogram is not recommended in the evaluation of patients with syncope in the absence of specific neurological features suggestive of a seizure (18,92,163-167).

Pacing for Vasovagal/CSH Syncope

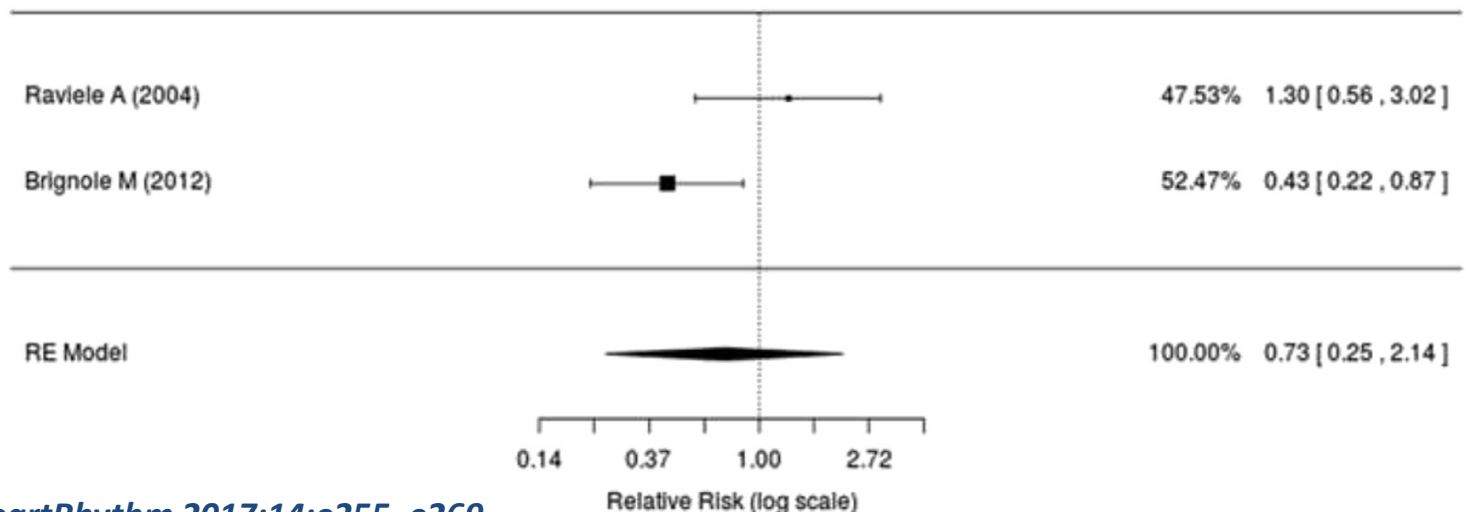


Pacing for Vasovagal/CSH Syncope



The evidence does not support the routine use of pacing for reflex-mediated syncope beyond patients with **recurrent syncope and asystole documented by implantable loop recorder**, such as those meeting the entry criteria for the ISSUE-3 trial

**Recurrent
Syncope
Double
Blind
Studies**

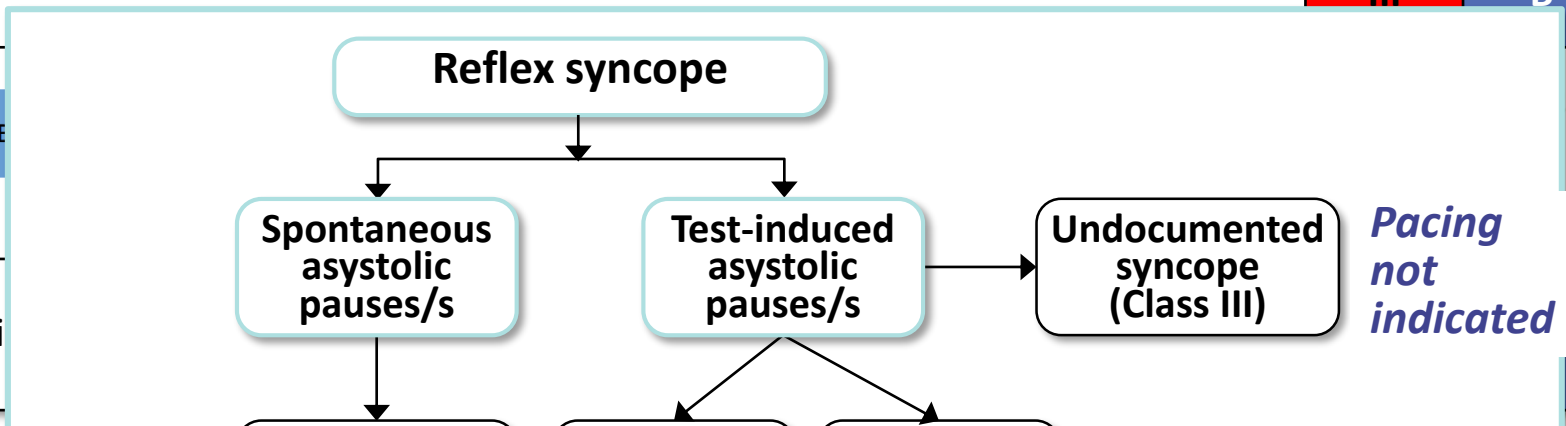


Treatment of Reflex syncope

Recommendations	Class	Level
Pharmacological therapy		
Beta-adrenergic blocking drugs are not indicated.	III	B

IIb

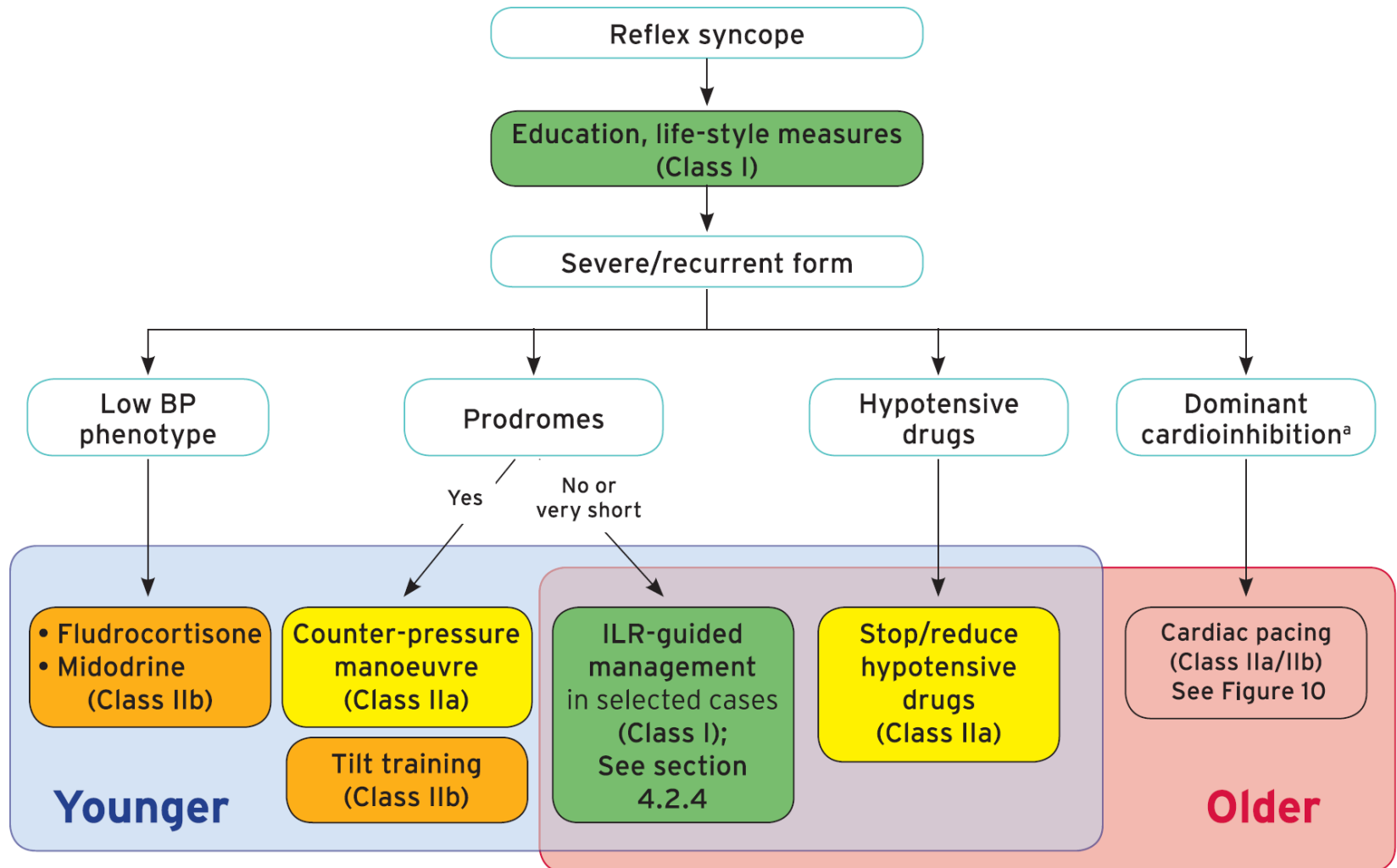
Cardiac pacing i



The use of adenosine triphosphate in the evaluation of syncope in older patients continues to evolve. In a small, single-blind trial of older patients (mean age 75 years) randomized to active pacing or back-up pacing with documented adenosine triphosphate-sensitive sinoatrial or AV block, there was a 75% risk reduction in syncope recurrence with dual-chamber pacing.

53).

ESC: Reflex Syncope

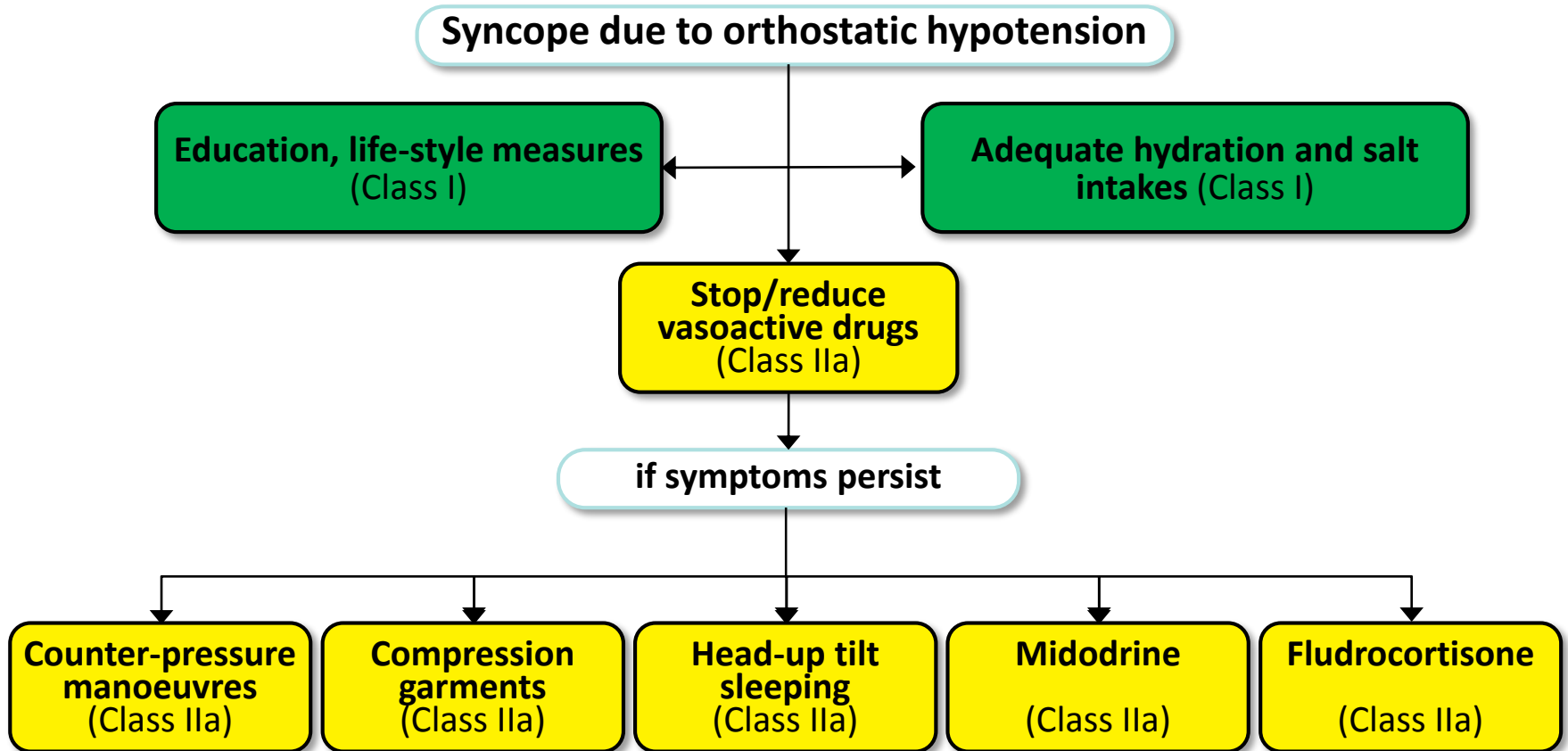


Recommendations for Reflex Syncope

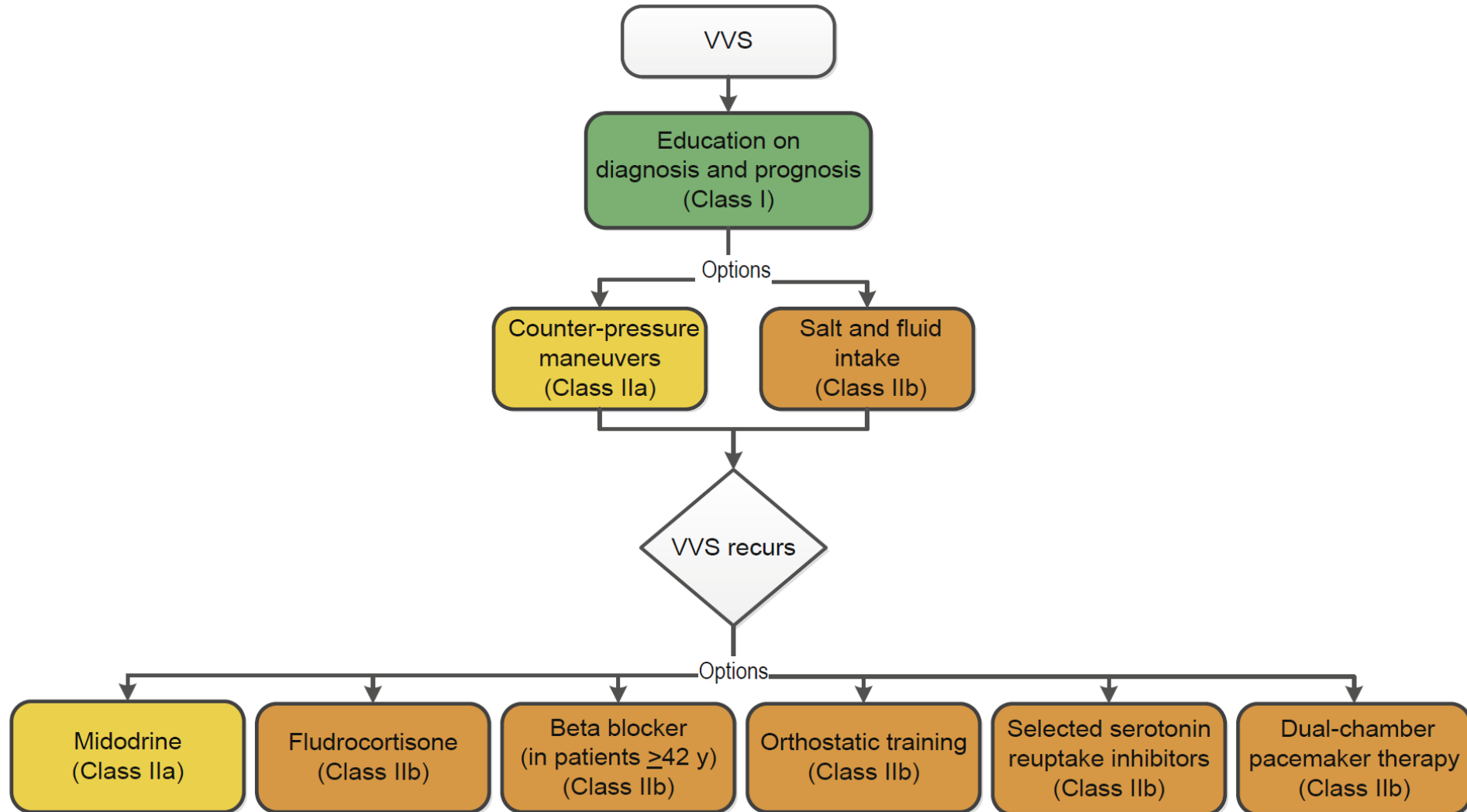
Recommendation for Pacemakers in VVS

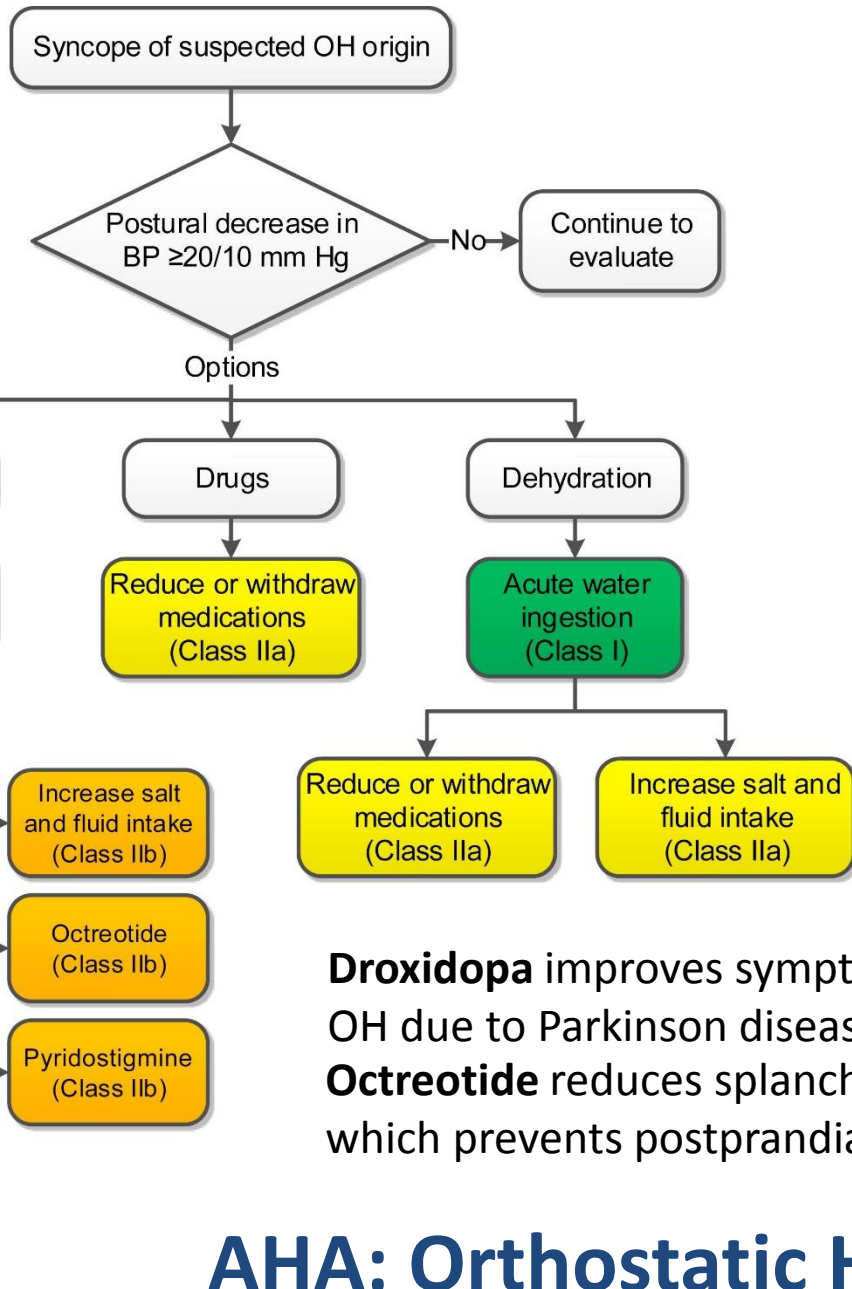
COR	LOE	RECOMMENDATION
IIb	B-R ^{SR}	Recommendations for Carotid Sinus Syndrome
IIa	B-R	Permanent cardiac pacing is reasonable in patients with carotid sinus syndrome that is cardioinhibitory or mixed (267-275).
IIb	B-R	It may be reasonable to implant a dual-chamber pacemaker in patients with carotid sinus syndrome who require permanent pacing (276-279).

ESC: Vasovagal Syncope



AHA: Vasovagal Syncope





Droxidopa improves symptoms of neurogenic OH due to Parkinson disease
Octreotide reduces splanchnic blood flow by which prevents postprandial hypotension

AHA: Orthostatic Hypotension

4. MANAGEMENT OF CARDIOVASCULAR CONDITIONS

See [Online Data Supplements 17 to 24](#) for data supporting Section 4.

4.1. Arrhythmic Conditions: Recommendations

4.1.1. Bradycardia: Recommendation

Recommendation for Bradycardia

COR	LOE	RECOMMENDATION
I	C-EO	In patients with syncope associated with bradycardia, GDMT is recommended (169).

4.1.2. Supraventricular Tachycardia: Recommendations

Recommendations for Supraventricular Tachycardia

COR	LOE	RECOMMENDATIONS
I	C-EO	In patients with syncope and supraventricular tachycardia, GDMT is recommended (170).
I	C-EO	In patients with atrial fibrillation, GDMT is recommended (171).

4.1.3. Ventricular Arrhythmia: Recommendation

Recommendation for Ventricular Arrhythmia (VA)

COR	LOE	RECOMMENDATION
I	C-EO	In patients with syncope and VA, GDMT is recommended (169,172-174).

4.2. Structural Conditions: Recommendation

4.2.1. Ischemic and Nonischemic Cardiomyopathy: Recommendations

Recommendation for Ischemic and Nonischemic Cardiomyopathy

COR	LOE	RECOMMENDATION
I	C-EO	In patients with syncope associated with ischemic and nonischemic cardiomyopathy, GDMT is recommended (169,172).

4.2.2. Valvular Heart Disease: Recommendation

Recommendation for Valvular Heart Disease

COR	LOE	RECOMMENDATION
I	C-EO	In patients with syncope associated with valvular heart disease, GDMT is recommended (175).

ESC: Ventricular Arrhythmias

Implantable cardioverter defibrillator indications in patients with unexplained syncope^a and long QT syndrome

Recommendations	Class ^b	Level ^c
ICD implantation in addition to beta-blockers should be considered in LQTS patients who experience unexplained syncope ^a while receiving an adequate dose of beta-blockers. ⁴⁶	IIa	B
Left cardiac sympathetic denervation should be considered in patients with symptomatic LQTS when: <ol style="list-style-type: none"> (1) beta-blockers are not effective, not tolerated, or are contraindicated; (2) ICD therapy is contraindicated or refused; or (3) when patients on beta-blockers with an ICD experience multiple shocks.⁴⁶ 	IIa	C
Instead of an ICD, an ILR should be considered in patients with recurrent episodes of unexplained syncope ^a who are at low risk of SCD based on a multiparametric analysis that takes into account the other known risk factors for SCD.	IIa	C

Implantable cardioverter defibrillator indications in patients with unexplained syncope^a and Brugada syndrome

Recommendations	Class ^b	Level ^c
ICD implantation should be considered in patients with a spontaneous diagnostic type 1 ECG pattern and a history of unexplained syncope. ^{a, 46,353,355,365,366}	IIa	C
Instead of an ICD, an ILR should be considered in patients with recurrent episodes of unexplained syncope ^a who are at low risk of SCD, based on a multiparametric analysis that takes into account the other known risk factors for SCD.	IIa	C

ECG = electrocardiogram; ICD = implantable cardioverter defibrillator; ILR = implantable loop recorder; SCD = sudden cardiac death.

^aUnexplained (or uncertain) syncope is defined as any syncope that does not meet the class I diagnostic criteria defined in section 4. In the presence of clinical features described in this section, unexplained syncope is considered a risk factor for ventricular tachyarrhythmias.

^bClass of recommendation.

^cLevel of evidence.

ARVC

Recommendations for Arrhythmogenic Right Ventricular Cardiomyopathy (ARVC)

COR	LOE	RECOMMENDATIONS
I	B-NR	Implantable cardioverter-defibrillator (ICD) implantation is recommended in patients with ARVC who present with syncope and have a documented sustained VA (177-181).
IIa	B-NR	ICD implantation is reasonable in patients with ARVC who present with syncope of suspected arrhythmic etiology (177,178,180-182).

Arrhythmogenic right ventricular cardiomyopathy		
3. ICD implantation may be considered in patients with ARVC and a history of unexplained syncope.	IIb	C
4. Instead of an ICD, an ILR should be considered in patients with recurrent episodes of unexplained syncope with systolic impairment but without a current indication for ICD.	IIa	C

Long QT Syndrome

Recommendations for Long-QT Syndrome (LQTS)

COR	LOE	RECOMMENDATIONS
I	B-NR	Beta-blocker therapy, in the absence of contraindications, is indicated as a first-line therapy in patients with LQTS and suspected arrhythmic syncope (207-209).
IIa	B-NR	ICD implantation is reasonable in patients with LQTS and suspected arrhythmic syncope who are on beta-blocker therapy or are intolerant to beta-blocker therapy (208,210-214).
IIa	C-LD	Left cardiac sympathetic denervation is reasonable in patients with LQTS and recurrent syncope of suspected arrhythmic mechanism who are intolerant to beta-blocker therapy or for whom beta-blocker therapy has failed (215-217).

Long QT syndrome

1. ICD implantation in addition to beta-blockers should be considered in LQTS patients who experience unexplained syncope while receiving an adequate dose of beta-blockers.	IIa	B
2. Left cardiac sympathetic denervation should be considered in patients with symptomatic LQTS when: <ul style="list-style-type: none"> (a) beta-blockers are not effective, not tolerated, or are contraindicated; (b) ICD therapy is contraindicated or refused; or (c) when patients on beta-blockers with an ICD experience multiple shocks. 	IIa	C
3. Instead of an ICD, an ILR may be considered in patients with recurrent episodes of unexplained syncope with systolic impairment but without a current indication for ICD.	IIa	C

Syncope and Driving

Recommendation for Driving and Syncope

COR

LOE

RECOMMENDATION

IIa

C-EO

It can be beneficial for healthcare providers managing patients with syncope to know the driving laws and restrictions in their regions and discuss implications with the patient.

Advice for Driving in Patients with Syncope

Disorder causing syncope	Group 1 (private drivers)	Group 2 (professional drivers)	
Cardiac arrhythmias			
Untreated arrhythmias	Unfit to drive	Unfit to drive	
Cardiac arrhythmia life-threatening, treatment	Disorder causing syncope	Group 1 (private drivers)	Group 2 (professional drivers)
	Reflex syncope		
	Single/mild	No restrictions unless it occurred during driving.	No restriction unless it occurred during driving or without prodromes.
	Recurrent and severe	After successful treatment is established.	After successful treatment is established. Particular caution if it occurred during driving or without prodromes.
	Pacemaker implanted		
Unexplained syncope			
	No restrictions unless absence of prodrome, occurrence during driving, or presence of severe structural heart disease. If yes, after diagnosis and appropriate therapy is established.	After diagnosis and appropriate therapy is established.	

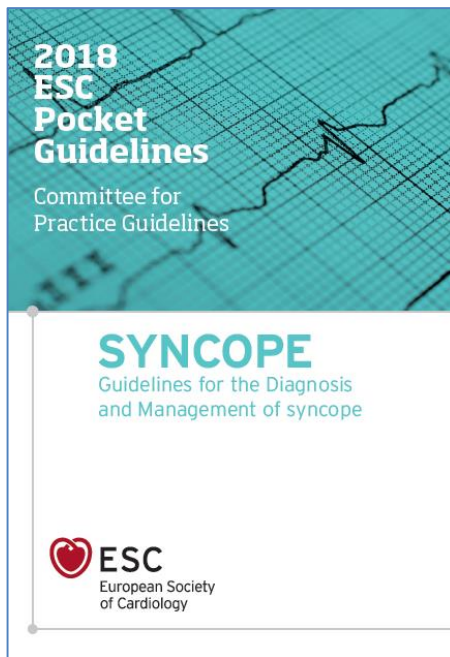
ESC: Video Recording

Recommendations	Class	Level
1. Home video recordings of spontaneous events should be considered. Physicians should encourage patients and their relatives to obtain home video recordings of spontaneous events.	IIa	C
2. Adding video recording to tilt testing may be considered in order to increase reliability of clinical observation of induced events.	IIb	C

Recommendation for History and Physical Examination

COR	LOE	Recommendation
I	B-NR	A detailed history and physical examination should be performed in patients with syncope. ^{58–66}

Help with the Guidelines



Available on
[www.escardio.org/
Guidelines](http://www.escardio.org/Guidelines)