7th International Syncope training Event
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Reflex syncope
Diagnosis and treatment

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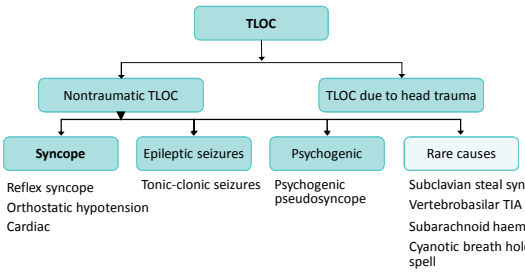
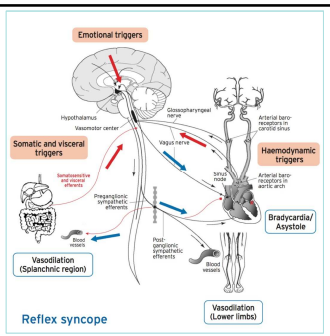
Classification



Pathophysiology

Reflex syncope is TLOC due to a reflex response that encompasses vasodilatation and/or bradycardia (rarely tachycardia), leading to systemic hypotension and cerebral hypoperfusion.



Classification
Reflex (neurally-mediated) syncope

- **Vasovagal:**
  - orthostatic VVS: standing, less common sitting,
  - emotional: fear, pain (somatic or visceral), instrumentation, blood phobia.
- **Situational:**
  - micturition,
  - gastrointestinal stimulation (swallow, defaecation),
  - cough, sneeze,
  - post-exercise,
  - others (e.g. laughing, brass instrument playing).
- **Carotid sinus syndrome.**
- **Non-classical forms** (without prodromes and/or without apparent triggers and/or atypical presentation.

Epidemiology - Frequency of the causes of syncope according to the settings (1)

Setting	Source	Reflex (%)	Orthostatic hypotension (%)	Cardiac (%)	Non syncopal T-LOCs (%)	Un-explained (%)
General population	*Framingham studies*	21	9.4	9.5	9	37
Emergency department	*Range*	35-48	4-24	5-21	8-20	17-33
Syncope Unit (dedicated facility)	*Range*	55-73	1-10	6-37	1-6	5-20

Epidemiology - Frequency of the causes of syncope according to age

Age	Source	Reflex (%)	Orthostatic hypotension (%)	Cardiac (%)	Non syncopal T-LOCs (%)	Un-explained (%)
<40 years	*Olde Nordkamp*	51	2.5	1.1	18	27
40-60 years	*Olde Nordkamp*	37	6	3	19	34
<65 years	*Del Rosso*	68.5	0.5	12	-	19
>60/65 years	*Del Rosso*	52	3	34	-	11
	Ungar	62	8	11	-	14
	Olde Nordkamp	25	8.5	13	12.5	41
>75 years	*Ungar*	36	30	16	-	9

Triggers for syncope.

Typical reflex syncope
Prolonged standing;
Pain/invasive procedures;
Emotion: sight of blood, injury to oneself or to others, stress;
Post-exercise;
Situational syncope
Gastro-intestinal (GI): swallowing, colic, defecation, GI tract instrumentation
Urogenital (UG): micturition, vaginal examination, prostate examination/massage, UG tract instrumentation;
Eyeball pressure;
Respiratory: Cough, sneeze, laugh, wind-instrument paying, singing, weight-lifting, mess trick, stretching

Richard Sutton, Journal of Arrhythmia 2017

Circumstances of the attack

Historical clue	Possible diagnosis
Supine position (awake)	- Cardioinhibitory VVS through pain or fear - Arrhythmia - PPS and PNES
During normal sleep	- Epilepsy - Arrhythmia - If prodrome of VVS causing awakening + syncope thereafter: "sleep syncope"
Sitting	- All causes (including "orthostatic VVS" and classical OH)
Standing for some period	- All causes - If TLOC occurs only while standing: OH, orthostatic VVS
Couple of steps after standing up or straightening from bending or squatting position	Initial OH and classical OH

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Circumstances of the attack

During physical exercise	- Cardiac structural- Cardiac arrhythmic: AV block, LQTS1, catecholaminergic VT- May occur in autonomic failure- VVS in very young/teenagers
Directly after cessation of physical exercise	- Post-exercise hypotension in middle-aged and elderly people: autonomic failure - Young people: VVS, particularly in trained athletes
During arm exercise	Steal syndrome (very rare)
Palpitations	- Cardiac tachyarrhythmia Postural tachycardia in VVS, POTS
Strong emotions other than fear (e.g. argument)	- Cataplexy - Arrhythmia: catecholaminergic polymorphic VT; also during exercise, in children and young adults
Startling (e.g. alarm clock)	- LQTS2 - Startle epilepsy
During fever	VVS (more often) - Brugada syndrome
Flashing lights	Epilepsy with photosensitivity
Sleep deprivation	- Epilepsy VVS
Heat/warmth/hot bath	VVS - Classical OH

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Circumstances of the attack

Micturition, defaecation	Situational reflex syncope (note: defaecation and diarrhoea may act as triggers for VVS but also as symptoms of VVS)
Coughing	Situational syncope (usually prolonged intensive coughing, often in smokers with lung disease)
Swallowing	Situational syncope (usually oesophageal disease)
Laughing out loud, telling jokes, unexpectedly meeting an acquaintance	Cataplexy (ask about excessive daytime sleepiness)
Laughter	Situational reflex syncope (very rare)
During and after eating	- All causes (a specific circumstance)- Only during/after eating (15 minutes): postprandial hypotension, particularly in the elderly and with autonomic failure- If preferentially during meals: arrhythmia/Brugada syndrome
Head movements, pressure on the neck, shaving	Spontaneous type of carotid sinus syncope
Fear, pain, instrumentation	Classical VVS

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Classic prodromal phase (VVS)

- **Lightheadedness**
- **A feeling of being warm or cold**
- **Sweating**
- **Palpitations**
- **Nausea or non-specific abdominal discomfort**
- **Visual "blurring" occasionally proceeding to temporary darkening or "white-out" of vision**
- **Diminution of hearing and/or occurrence of unusual sounds (particularly a "whooshing" noise)**
- **Pallor reported by onlookers**

Onset of the attack

Historical clue	Possible diagnosis
Change in vision: seeing dark spots, loss of colour vision (rare).Change in hearing: sounds coming as if from a distance, buzzing or ringing in the ears	Syncope: symptoms of cerebral hypoperfusion, so not related to cause of syncope
Nausea, sweating, pallor	Reflex syncope: autonomic activation
Pain in shoulders and neck ("coat hanger pattern")	Classical OH: ischaemia of local muscles
Shout at onset of attack ("ictal cry")	Epilepsy
Rising sensation from abdomen	- Epileptic aura - Rising abdominal sensation occurs in VVS, not often
Rising sensation from abdomen, unpleasant smell or taste, or other phenomena specific to subject but recurring in attacks	Epileptic aura

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Clinical and ECG features that suggest a reflex (neurally-mediated) syncope

- Long history of recurrent syncope, in particular occurring before the age of 40 years.
- After unpleasant sight, sound, smell, or pain.
- Prolonged standing.
- During meal.
- Being in crowded and/or hot places.
- Autonomic activation before syncope: pallor, sweating, and/or nausea/vomiting.
- With head rotation or pressure on carotid sinus (as in tumours, shaving, tight collars).
- Absence of heart disease.

Clinical and ECG features that suggest another cause of syncope

Syncope due to OH
- While or after standing
- Prolonged standing
- Standing after exertion
- Post-prandial hypotension
- Temporal relationship with start or changes of dosage of vasodepressive drugs or diuretics leading to hypotension
- Presence of autonomic neuropathy or parkinsonism

Cardiac syncope
- During exertion or when supine
- Sudden onset palpitation immediately followed by syncope
- Family history of unexplained sudden death at young age
- Presence of structural heart disease or coronary artery disease
- ECG findings suggesting arrhythmic syncope:
  - Bifascicular block (defined as either left or right BBB combined with left anterior or left posterior fascicular block)
  - Other intraventricular conduction abnormalities (QRS duration ≥0.12 s)
  - Mobitz I second-degree AV block and 1° degree AV block with markedly prolonged PR interval
  - Asymptomatic mild inappropriate sinus bradycardia (40–50 b.p.m.) or slow atrial fibrillation (40–50 b.p.m.) in the absence of negatively chronotropic medications
  - Non-sustained VT
  - Pre-excited QRS complexes
  - Long or short QT intervals
  - Early repolarization
  - ST-segment elevation with type 1 morphology in leads V1-V3 (Brugada pattern)
  - Negative T waves in right precordial leads, epsilon waves suggestive of ARVC
  - Left ventricular hypertrophy suggesting hypertrophic cardiomyopathy

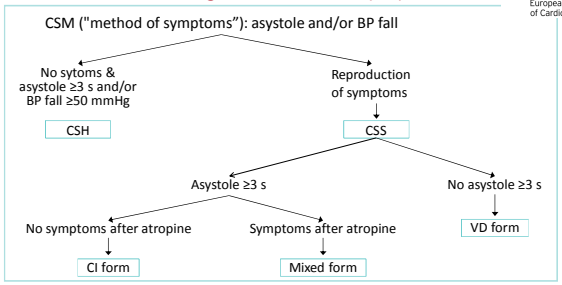
- **The vast majority of patients with reflex syncope do not need further diagnostic evaluation**
- **For patients with suspected reflex syncope after the initial evaluation (atypical presentation), additional testing is used to confirm or exclude the diagnosis.**

Carotid sinus massage

Recommendations	Class	Level
Indication		
1. CSM is indicated in patients >40 years of age with syncope of unknown origin compatible with a reflex mechanism.	I	B
Diagnostic criteria		
2. CSS is confirmed if CSM causes bradycardia (asystole) and/or hypotension that reproduce spontaneous symptoms and patients have clinical features compatible with a reflex mechanism of syncope.	I	B

Carotid sinus massage: "Method of symptoms"

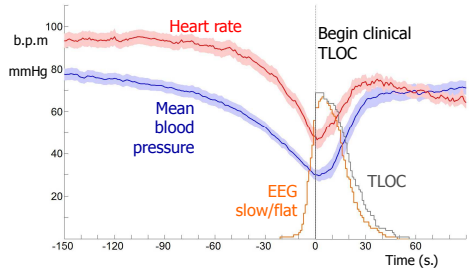
ESC European Society of Cardiology



Tilt testing: **positivity rate**

92%	Typical VVS, emotional trigger (Clom)
78%	Typical VVS, situational trigger (TNG)
73%-65%	Typical VVS, miscellaneous (Clom) (TNG)
56%-51%	Likely reflex, atypical (TNG)
47%	Cardiac syncope (TNG)
45%	Likely tachyarrhythmic syncope (Passive)
36%-30%	Unexplained syncope (TNG) (Clom)
13%-8%	Subjects without syncope (Passive) (Clom) (TNG)

Tilt testing: **Reflex syncope**



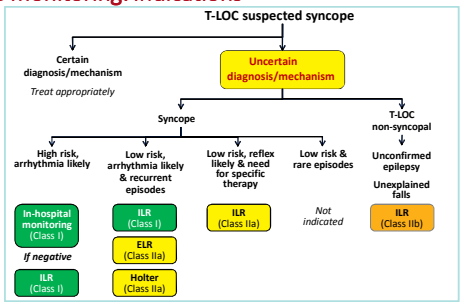
Tilt testing

Recommendations	Class	Level
Indications		
1. Tilt testing should be considered in patients with suspected reflex syncope, OH, POTS, or PPS.	IIa	B
2. Tilt testing may be considered to educate patients to recognize symptoms and learn physical manoeuvres.	IIb	B
Diagnostic criteria		
3. Reflex syncope, OH, POTS, or PPS should be considered likely if tilt testing reproduces symptoms along with the characteristic circulatory pattern of these conditions.	IIa	B

Tilt testing – Diagnostic use

- Patients with recurrent unexplained syncopal episodes
  - in the absence of organic heart disease,
  - or in the presence of organic heart disease after cardiac causes have been excluded.
- Patients in whom it is of clinical value to demonstrate susceptibility to reflex syncope.
- Patients in whom both reflex syncope and orthostatic hypotension syncope are being considered.

ECG monitoring: indications



ECG monitoring: Indications (2)

Recommendations	Class	Level
Implantable loop recorder		
4. ILR is indicated in an early phase of evaluation in patients with recurrent syncope of uncertain origin, absence of high-risk criteria (listed in *Table 6*), and a high likelihood of recurrence within the battery life of the device.	I	A
5. ILR should be considered in patients with suspected or certain reflex syncope presenting with frequent or severe syncopal episodes.	IIa	B
6. ILR may be considered in patients in whom epilepsy was suspected but the treatment has proven ineffective.	IIa	B
7. ILR may be considered in patients with unexplained falls.	IIb	B

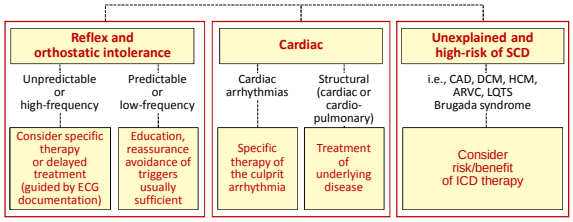
Prolonged monitoring – Diagnostic use

Patients with suspected reflex syncope

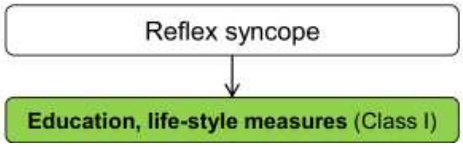
- to exclude primary cardiac causes
- in an attempt to document the heart rhythm during an event

Treatment of syncope: General principles

Diagnostic evaluation



Treatment of Reflex syncope



Treatment of syncope: General principles

Recurrence of syncope in untreated patients in RCT

Reference	Aetiology	Syncopes before evaluation	Syncopes after evaluation (%)
VPS I	VVS -Tilt +	6 (3–40) last 1 year	70% at 1 year
PC-Trial	VVS	3 (2–5) last 2 years	51% at 14 months
VASIS-Etilefrine	VVS -Tilt		24% at 1 year
POST	VVS - Ti		35% at 1 year
Madrid *et al*	VVS - Ti		46% at 1 year
VPS II	VVS - Ti		40% at 6 months
SYNPACE	VVS - Ti		44% at 1 year
VASIS	Reflex -		50% at 2 years
SPAIN	Reflex –		46% at 2 years
ISSUE 3	Reflex	5 (3–6) last 2 years	57% at 2 years
ATP Study	Unexplained – ATP +	Na	69% at 2 years
PRESS	Cardiac – BBB	1 last 6 months	14% at 2 years
THEOPACE	Sick sinus syndrome	3.2 ± 4.3	30% at 4 years

« No treatment » recurrence rate - 50% at 1-2 years

Explain, reassure, educate

What is reflex syncope?

Reflex syncope is the commonest cause of syncope and is due to a temporary, intermittent dysfunction of part of the nervous system, called the autonomic nervous system. The autonomic nervous system controls the heart rate and blood pressure, and can be prone to episodes of over- or under-activity, leading to a slowing of the heart rate or a fall in the blood pressure. Being upright, food, heat, exercise, sight of blood, and emotional stress can sometimes bring on episodes. Patients commonly experience these symptoms for several minutes before losing consciousness and tend to recover fairly quickly afterwards (whereas after an epileptic seizure the person may be quite confused and sleepy for some time). During reflex syncope, the person can also experience some short-lived shaking (similar to that seen in a seizure), as well as incontinence.

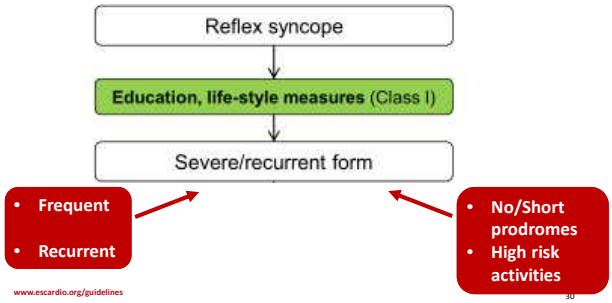
Web addenda

ESC information sheet for patients affected by reflex syncope (1)

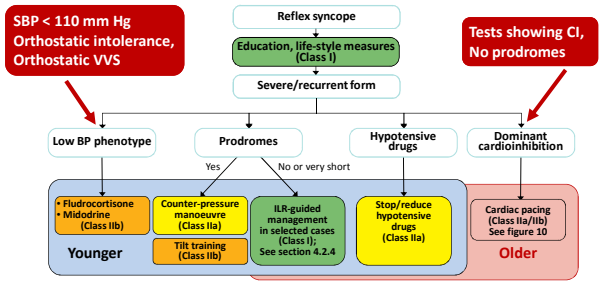
Actions to take to avoid an impending attack of reflex syncope

- When you feel symptoms of syncope coming on, the best response is to lie down. If this is not possible, then sit down and do counter manoeuvres. The final warning symptom is when everything goes dark and you lose vision: then you *only have seconds in which to prevent syncope*.
- Your doctor will have shown you how to do the counter manoeuvres. They all concern tensing large muscles in the body. One way is to press the buttocks together and straighten the knees forcefully; another is to cross your legs and press them together over their entire length. Others make fists and tense the arm muscles.
- Drink around 2 litres of fluid a day and do not use salt sparingly (unless there are medical reasons not to!). A simple way to tell your fluid intake is high enough is to *check the colour of your urine*: if it is dark yellow there is little fluid in your body, so try to keep it very lightly coloured.
- Inform those in your immediate surroundings what to do during a spell: in typical spells there is *no need to call a doctor or an ambulance*. Of course, if you hurt yourself in the fall, this may change.

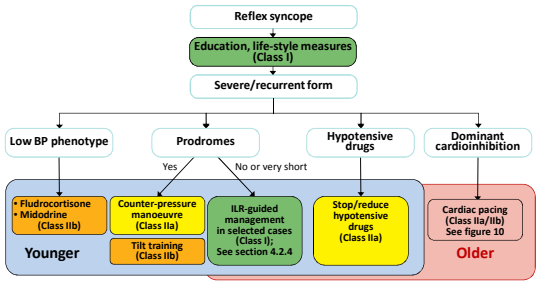
Treatment of Reflex syncope



Treatment of **Reflex syncope**



Treatment of **Reflex syncope**



Treatment syncope: **Counterpressure manoeuvres**

2018 ESC Guidelines on Syncope – Michele brignole & Angel Moya
EHJ Doi:10.1093/eurheartj/ehy037

Treatment of **Reflex syncope (I)**

Recommendations	Class	Level
Education and life-style modification		
1. Explanation of the diagnosis, provision of reassurance, explanation of risk of recurrence, avoidance of triggers and situations are indicated in all patients.	I	B
Discontinuation/reduction of hypotensive therapy		
2. Modification or discontinuation of hypotensive drug regimen should be considered in patients with vasodepressor syncope, if possible.	IIa	B
Physical manoeuvres		
3. Isometric PCM should be considered in patients with prodromes who are less than 60 years of age.	IIa	B
4. Tilt training may be considered for the education of young patients.	IIb	B

2018 ESC Guidelines on Syncope – Michele brignole & Angel Moya
EHJ Doi:10.1093/eurheartj/ehy037

Treatment of Reflex syncope (2)

Recommendations	Class	Level
Pharmacological therapy		
5. Fludrocortisone may be considered in young patients with the orthostatic form of VVS, low-normal values of arterial BP, and absence of contraindication to the drug.	IIb	B
6. Midodrine may be considered in patients with the orthostatic form of VVS.	IIb	B
7. Beta-adrenergic blocking drugs are not indicated.	III	B

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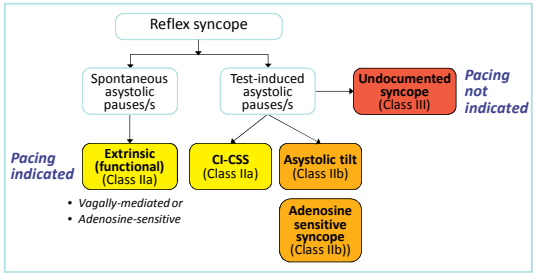
EHJ Doi:10.1093/eurheartj/ehy037

Pacing for reflex syncope



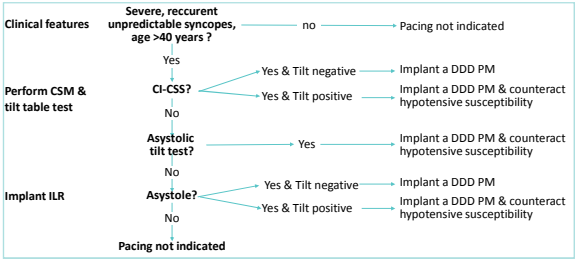
Treatment of syncope: **General principles**

Cardiac pacing in different clinical settings

Expected 2-year syncope recurrence rate	Clinical setting	
High efficacy (≤5% recurrence rate)	Established bradycardia	no hypotensive mechanism
Moderate efficacy (5% to 25% recurrence rate)	Established bradycardia	*and* hypotensive mechanism
Low efficacy (>25% recurrence rate)	Suspected bradycardia	*and* hypotensive mechanism

Tilt test response is the strongest predictor of pacemaker efficacy.

Pacing for reflex syncope: decision pathway



Treatment of syncope: **Reflex syncope (2)**

Recommendations	Class	Level
Cardiac pacing		
1. Cardiac pacing should be considered to reduce syncopal recurrences in patients aged >40 years, with spontaneous documented symptomatic asystolic pause/s >3 seconds or asymptomatic pause/s >6 seconds due to sinus arrest or AV block or the combination of the two.	IIa	B
2. Cardiac pacing should be considered to reduce syncope recurrence in patients with cardioinhibitory carotid sinus syndrome who are >40 years with recurrent frequent unpredictable syncope.	IIa	B
3. Cardiac pacing may be considered to reduce syncope recurrences in patients with tilt-induced asystolic response who are >40 years with recurrent frequent unpredictable syncope.	IIb	B
4. Cardiac pacing may be considered to reduce syncope recurrences in patients with the clinical features of adenosine-sensitive syncope.	IIb	B
5. Cardiac pacing is not indicated in the absence of a documented cardioinhibitory reflex.	III	B

Conclusion

- **Clinical features may be diagnostic but they may sometimes be absent or difficult to correlate to the syncopal episode, particularly in older adults**
- **Initial evaluation is diagnostic in general:**
  - **comprehensive history**
  - **physical examination (which may include carotid sinus massage in older patients),**
  - **ECG**
- **Additional diagnostic evaluation is rarely needed**
- **Education and lifestyle measures are sufficient in the far majority of the patients**
- **When a treatment is considered, the choice relies mainly on clinical features (low BP, prodromes, hypertension drugs, cordioinhibition) and age**
- **Apart from its diagnostic usefulness, the HUT is a predictor of hypotensive susceptibility**