

# Reflex syncope: assessment and management

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## INTRODUCTION

In the era of evidence-based guidelines, updated frequently by various cardiac societies, and numerous very interesting and high-quality review papers published in peer-reviewed journals, writing an article on state of the art on any topic is a difficult task. How not to repeat the guidelines and well-known facts? One solution is to give more personal view, obviously based on objective knowledge, and to provide useful algorithms as well as interesting original tracings.

Assessment and management of reflex syncope is an important topic because it is frequently encountered in the general population (40% of females and 20% of males faint at least once during their life), is usually benign but may significantly decrease the quality of life and may be effectively treated in the majority of subjects.

## DEFINITIONS

Syncope is a transient loss of consciousness (TLOC) due to global cerebral hypoperfusion. Symptoms occur due to a sudden reduction in cardiac output and when systolic blood pressure falls below 60 mm Hg, brain autoregulation fails and syncope occurs. Syncope has to be differentiated from other forms of TLOC such as seizures, pseudopsychogenic pseudo-syncope, stroke, subclavian artery steal syndrome, insufficiency of vertebral arteries, metabolic comas and other causes.

The main three forms of syncope include (1) reflex syncope, known also as neurocardiogenic syncope, (2) orthostatic hypotension and (3) cardiogenic syncope which usually occurs due to cardiac arrhythmia but sometimes also due to structural heart disease which reduces cardiac output. The most frequent form of reflex syncope is vaso-vagal reaction, followed by situational syncope and carotid sinus syndrome (figure 1).

## DIAGNOSIS

Diagnosis of reflex syncope is easy when circumstances leading to TLOC are typical and no other cause of syncope can be detected, like in the vast majority of young people who faint. The diagnostic path should be strictly executed according to the current guidelines in which the first main step is called 'initial evaluation'.<sup>1</sup> It consists of medical history taking, physical examination, standard ECG recording and measuring blood pressure in the supine and erect positions. At this point, diagnosis can be established in typical cases with reflex syncope, whereas in those who have uncertain diagnosis further investigations are needed (figure 2).

Before planning the next diagnostic procedures, a risk assessment has to be made to identify those who are at high risk of serious complications, including death, and those who are at intermediate or low

## Learning objectives

- ⇒ To summarise the key steps in the reflex syncope workup.
- ⇒ To present currently available treatments for reflex syncope.
- ⇒ To underline the role of non-pharmacological therapy in reflex syncope.
- ⇒ To introduce cardioneuroablation as a new emerging therapy for reflex syncope.

risk. High risk usually equals cardiac syncope and further evaluation should be continued rather urgently, often in hospital, whereas low risk usually means reflex syncope and the next diagnostic steps can be performed on an ambulatory basis. The optimal place for further syncope evaluation is the so-called syncope unit where all necessary diagnostic tests can be performed by a dedicated team. Alternately, a syncope unit may consist of one or two physicians who are experts in syncope evaluation and have access to all other specialists and tests required during syncope workup.

In clinical practice, history taking, physical examination and standard ECG are quite often not enough to rule out cardiac disease. Because one of the major issues which should be addressed during 'initial evaluation' is the detection or exclusion of the presence of structural heart disease, which suggests potentially dangerous cardiac syncope, simplified echocardiography may have a role here. It is named focus cardiac ultrasound<sup>2</sup> and is defined as a point-of-care cardiac ultrasound examination, performed according to a standardised, but restricted, scanning protocol. This protocol consists of three basic views of cardiac chambers, without the need for computation of many complicated echocardiographic parameters. It can be performed by a physician who has been trained in echocardiography just for a few weeks. Such important causes of syncope as cardiac tamponade, severe contractility abnormalities due to myocardial ischaemia, valvular disease (ie, aortic stenosis), hypertrophic cardiomyopathy with left ventricular outflow tract obstruction or such rare diseases as atrial myxoma can be detected (figure 2). However, it has to be acknowledged that the early use of simplified echocardiography during diagnostic process has not yet been prospectively tested and has not been included in the current guidelines.<sup>1</sup>

When after initial examination reflex syncope is suspected but not certain, further tests should be performed. They include tilt testing, 3 min active standing, carotid sinus massage (CSM) and other autonomic tests. However, in some patients, other tests are also necessary such as an exercise test in



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**To cite:** Kulakowski P. *Heart* Epub ahead of print: [please include Day Month Year]. doi:10.1136/heartjnl-2022-322031

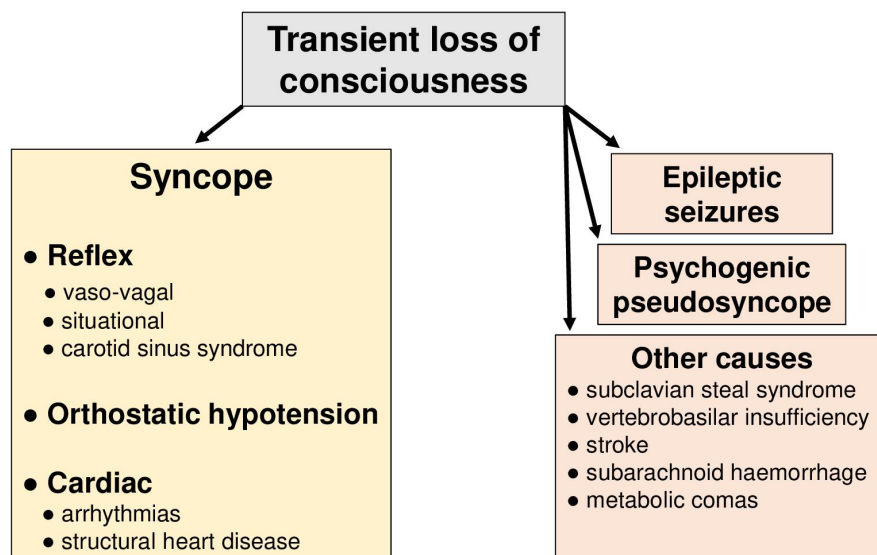


Figure 1 Forms of transient loss of consciousness.

those with exercise-induced syncope or prolonged cardiac rhythm monitoring in those with suspected reflex syncope but inconclusive results of previously mentioned investigations or severe symptoms.

#### Active standing

This 3 min test should be a part of the 'initial examination' when the blood pressure in supine and standing positions is measured; however, in clinical practice it is often performed later during diagnostic workup.<sup>3</sup> It is a basic screening test to detect orthostatic hypotension; however, it may also be useful in some patients with reflex syncope. The definition of a positive result (ie, detection of orthostatic hypotension) is based on changes in blood pressure. Reduction in systolic blood pressure  $>20$  mm Hg, reduction in diastolic blood pressure  $>10$  mm Hg

(normally it should not fall on standing) or very low ( $<90$  mm Hg) values of systolic blood pressure while standing are regarded as an abnormal response. When these changes are accompanied by syncope, the diagnosis is certain. If not, orthostatic hypotension is strongly suspected.

#### Tilt testing

Tilt testing was introduced into clinical practice more than 30 years ago by UK physicians.<sup>4</sup> When I first saw the test performed by Dr James Sneddon at St George's Hospital in London in 1991, my first impression was—what a boring examination and what a waste of time it was. However, it is not true. Tilt testing offers a great opportunity to establish the diagnosis of reflex syncope and to underscore mechanisms leading to TLOC. It can also reassure

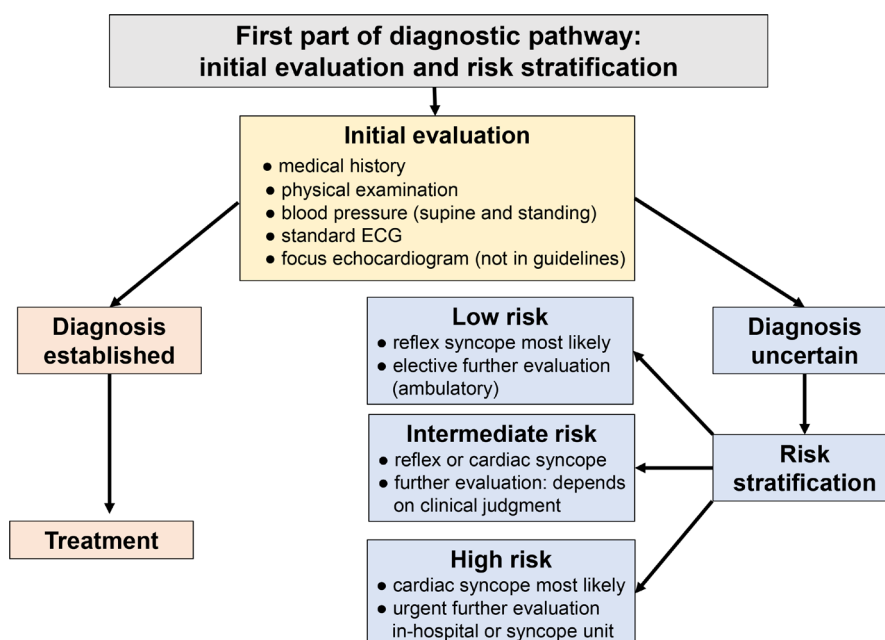


Figure 2 First part of syncope diagnostic workup: initial evaluation and risk stratification.

**Table 1** Diagnostic tests in reflex syncope

Test	Indications	Abnormal result	Comments
3 min active standing	<ul style="list-style-type: none"> <li>History of syncope or presyncope, especially when orthostatic hypotension is suspected.</li> </ul>	<ul style="list-style-type: none"> <li>Fall <math>\geq 20</math> mm Hg in SBP, <math>\geq 10</math> mm Hg in DBP or SBP <math>&lt; 90</math> mm Hg.</li> <li>Symptom reproduction—diagnosis certain.</li> <li>Without symptoms—diagnosis likely.</li> </ul>	<ul style="list-style-type: none"> <li>May be performed using standard sphygmomanometer but continuous beat-to-beat non-invasive BP is more accurate.</li> <li>Should be a part of initial evaluation.</li> </ul>
Tilt testing	<ul style="list-style-type: none"> <li>Suspected reflex syncope, OH, POTS, PPS.</li> <li>To educate patients.</li> <li>To differentiate between syncope and seizures.</li> </ul>	<ul style="list-style-type: none"> <li>Reflex syncope: tilt-induced syncope.</li> <li>OH: as above, also detection of delayed OH.</li> <li>POTS: HR increase <math>&gt; 30</math>/min or <math>&gt; 120</math>/min in the absence of OH and symptoms.</li> <li>PPS: patient unresponsive but BP and HR normal, test preferably performed together with EEG or video recording (to exclude seizures).</li> </ul>	<ul style="list-style-type: none"> <li>New possible indication: typical reflex syncope to document prolonged asystole and offer cardioneuroablation in younger patients or pacemaker in elderly.</li> </ul>
Carotid sinus massage	<ul style="list-style-type: none"> <li>Patients <math>&gt; 40</math> years of age with syncope of unknown origin compatible with a reflex mechanism.</li> </ul>	<ul style="list-style-type: none"> <li>Asystole <math>&gt; 3</math> (6) s or fall in SBP <math>&gt; 50</math> mm Hg and symptom reproduction.</li> </ul>	<ul style="list-style-type: none"> <li>To be performed after inconclusive initial evaluation or later using tilting laboratory.</li> <li>In case of asystole, massage should be repeated after atropine to unmask possible vasodepressor component.</li> </ul>
ECG monitoring		For all types of ECG monitoring:	
Holter ECG	Frequent syncope ( $\geq 1$ episode/week).	<ul style="list-style-type: none"> <li>Diagnosis established: spontaneous syncope occurs during ECG monitoring which reveals asystole or rapid paroxysmal tachycardia during event.</li> </ul>	Frequently overused.
External loop recorders	Syncopal episodes $\geq 1$ per 4 weeks.	<ul style="list-style-type: none"> <li>Diagnosis very likely: no syncope during ECG monitoring; however, high-degree AV block, severe bradycardia or rapid paroxysmal tachycardia are recorded.</li> </ul>	Less frequently used in the era of long-term ECG telemetry and wearables.
Ambulatory remote telemetry	Required frequency of syncope not established: depends on telemetry system and patient preferences.		Valuable tool, increasing role when syncope is too rare for Holter/external loop recorder.
ILR	Unexplained syncope but likely arrhythmic or severe asystolic reflex. Episodes too rare to use other forms of ECG monitoring.		<ul style="list-style-type: none"> <li>Should be used at earlier stages of workup than in everyday practice.</li> <li>Additional indications:               <ul style="list-style-type: none"> <li>'drug-resistant epilepsy'.</li> <li>TLOC with jactitation.</li> <li>Unexplained falls.</li> </ul> </li> </ul>
Invasive electrophysiological study	<ul style="list-style-type: none"> <li>When cardiac/arrhythmic cause is suspected but not documented (palpitations preceding syncope or ECG suggestive of arrhythmic cause).</li> <li>No role in detecting reflex syncope.</li> </ul>	<ul style="list-style-type: none"> <li>Inducible VT or SVT with symptom reproduction.</li> <li>HV interval <math>&gt; 70</math> ms or distal third-degree AV block on atrial pacing or pharmacological challenge in patients with bifascicular BBB.</li> <li>cSNRT <math>\geq 525</math> ms in patients with suspected sinus node disease.</li> </ul>	<ul style="list-style-type: none"> <li>Higher diagnostic yield in patients with organic heart disease.</li> <li>Positive result is highly diagnostic, whereas negative result warrants further evaluation.</li> </ul>

AV, atrioventricular; BBB, bundle branch block; BP, blood pressure; cSNRT, corrected sinus node recovery time; DBP, diastolic blood pressure; EEG, electroencephalography; HR, heart rate; HV, His ventricle; ILR, implantable loop recorder; OH, orthostatic hypotension; POTS, postural orthostatic tachycardia syndrome; PPS, psychogenic pseudosyncope; SBP, systolic blood pressure; SVT, supraventricular tachycardia; TLOC, transient loss of consciousness; VT, ventricular tachycardia.

a patient and his/her family that the condition is benign although it may look like something very dangerous (especially when convulsions occur) and may be associated with injury during everyday life.

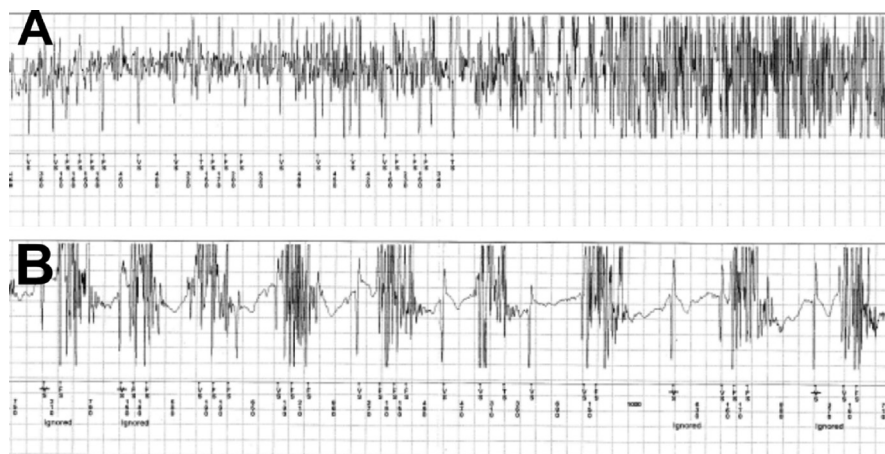
The methodology of tilt testing is beyond the scope of this paper; however, it has to be stressed that adequate interpretation of results requires continuous non-invasive beat-to-beat heart rate and blood pressure measurement. The most often used protocol includes the administration of 300–400  $\mu$ g of sublingual nitroglycerine after a 20 min unmedicated phase; however, it may decrease specificity while increasing sensitivity. In some laboratories, a so-called classical 'Westminster' protocol is still used—a tilt test lasting for 45 min without nitroglycerine challenge.

Current indications for tilt testing are summarised in [table 1](#). In the early days of tilting, we used to perform this test mainly in young people with a typical or almost typical history suggesting reflex syncope. At this initial stage, we all have learnt how long asystole or deep hypotension due to vasodilation can be evoked by tilting in otherwise

healthy persons. Nowadays, tilt testing is more indicated in those with unexplained syncope in whom there is suspicion of reflex mechanism, those in whom other tests, including prolonged ECG monitoring, failed to establish the diagnosis and also to differentiate between reflex syncope and seizures. However, with the advent of new invasive therapies like cardioneuroablation, tilt testing in young people with typical features of reflex syncope again has gained more interest because one needs to document an asystolic form of reflex syncope to propose cardioneuroablation.

### Carotid sinus massage

CSM is another test that quite frequently is not performed in everyday practice mainly due to unnecessary doubts concerning the safety of the test.<sup>3</sup> According to the guidelines,<sup>1</sup> CSM should be performed in all subjects aged  $> 40$  years in whom 'initial diagnosis' did not reveal the cause of TLOC and a reflex mechanism is suspected ([table 1](#)). Massage should be performed while supine and standing for 10 s on the right and then on the left



**Figure 3** Original ECG recording from implantable loop recorder in a patient with epilepsy during seizures. (A) ECG at the beginning and during seizures—artefacts due to clonic-tonic muscle movements are so dense that ECG becomes unreadable. (B) At the end of seizures tonic-clonic movements become less frequent and ECG is now visible, showing normal heart rhythm.

side of the neck at the anterior border of the sternocleidomastoid muscle. If the test has not been already performed before a patient arrived for tilt testing, it is very useful to perform CSM just after tilting using the equipment already available in the tilting room. The use of non-invasive beat-to-beat heart rhythm and blood pressure plethysmographic recordings as well as a tilt table to perform CSM while supine and standing facilitates accurate execution of CSM.

The use of continuous blood pressure monitoring is very important because the abnormal result of CSM consists of asystole >3 s and sometimes only a fall in the systolic blood pressure values is seen and when the drop exceeds 50 mm Hg compared with baseline, the test is also regarded as positive. Thus, when one uses only a standard blood pressure cuff, rapid changes in blood pressure values may be undiagnosed. When the asystolic response to CSM is seen, the test should be repeated after atropine injection to exclude the vasodepressor (vasodilatation) component of the reflex. The CSM-induced asystole or drop in blood pressure without reproducing symptoms and without a typical history of syncope is called carotid sinus hypersensitivity, and when it is accompanied by symptoms in a person with a history of syncope it is called carotid sinus syndrome.

The CSM is safe and the reported rate of adverse events, mainly transient ischaemic attacks (TIA), is

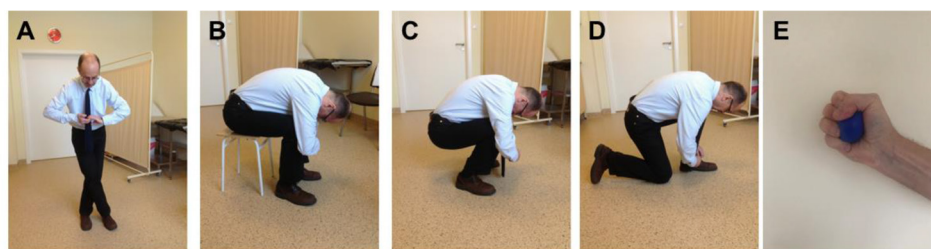
as low as 0.24%.<sup>1</sup> The test should not be performed in patients with a history of stroke or TIA, when there is an audible murmur on the auscultation of carotid arteries or there is known carotid stenosis, for example, >70% on Doppler ultrasonography.

### Prolonged ECG recording

Prolonged ECG monitoring is very useful in establishing the cause of syncope because it records ECG during spontaneous and not test-induced syncope. Although prolonged ECG recording is the main tool to document cardiac arrhythmia as the cause of syncope, it can also be used in patients with suspected reflex syncope.

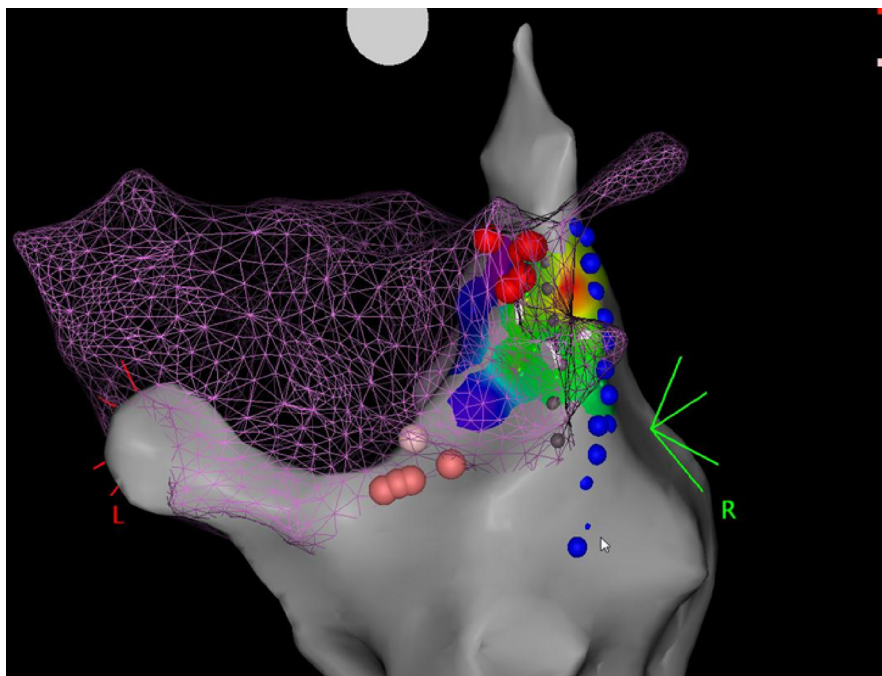
There are several forms of ECG monitoring, ranging from standard 1–7 days Holter ECG to longer monitoring using external loop recorders, ambulatory telemetry transmitted via smartphones, chest adhesive patches or implantable loop recorders (ILR). In recent years, new methods of self-recording ECG such as ECG sticks, handheld monitors, smartphone applications or smartwatches, capable of recording good-quality ECG, have become very popular.

There are two problems with ECG recording in patients with syncope. The first one is that a patient who faints cannot activate a device and record an ECG during syncope. Therefore, a device has to have a memory loop and store a few minutes (eg,



**Figure 4** Manoeuvres for preventing imminent syncope. (A) Leg crossing, muscle tensing, arm stretching and head down. (B) Sitting with head down and placed between the knees. (C) Squatting down. (D) Kneeling down and pretending that a shoelace is untied. (E) Hand grip using rubber ball.





**Figure 5** Original three-dimensional electroanatomical map of the right (solid fam) and left (mesh fam) atria showing sites of radiofrequency (RF) applications at the area of ganglionated plexi (GP). Red dots indicate right anterior GP; pink dots indicate right inferior GP; blue dots indicate the course of phrenic nerve where RF applications should be avoided.

5–10 min) of ECG when activated manually by a patient after regaining consciousness. Alternatively, these loop recorders can be programmed to automatically store ECG when the heart rate is very slow (say, below 30/min) or very fast (eg, over 160/min). In this way, ECG during the syncopal event can be recorded and analysed. The majority of modern ‘wearables’ such as smartwatches do not have this option; however, it may become available in the nearest future. This is why longer ECG recordings using external loop recorders or remote (home) telemetry are more suitable for syncope evaluation.

The second problem is that syncopal episodes are rather infrequent in the majority of people. The duration of ECG monitoring has to last several months or even a few years which is not possible with standard Holter ECG or even remote ECG monitoring. This is why implantable or insertable loop recorders (ILR) gained popularity. These small ECG recorders of AAA battery size can be very easily inserted subcutaneously in the intercostal space and are capable of almost 60 min ECG storage for up to 4 years of battery life. It has been shown that their diagnostic yield ranges from 33% to 88% (mean 50%) which is much higher than that of other tests.

Current indications for ILR are listed in [table 1](#). Although the main indication for ILR is suspected arrhythmogenic syncope, there is a role of ILR also in patients with suspected reflex syncope when previous tests were inconclusive. Again, as with tilt testing, ILR can be helpful in the identification of patients with asystolic reflex syncope who are candidates for cardioneuroablation.

In addition, ILR is an excellent tool to detect bradycardia or asystole as a cause of syncope in patients with an erroneous diagnosis of epilepsy,

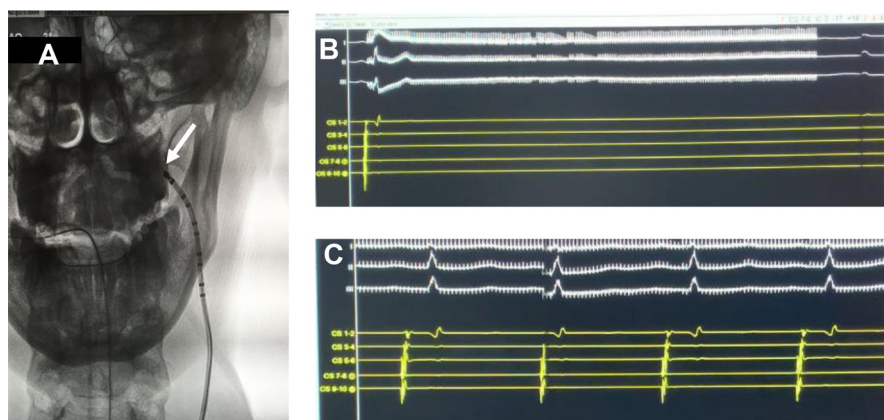
often named by neurologists as ‘drug-resistant epilepsy’. One study showed that in 21% of patients with ‘epilepsy’ the real cause of TLOC was bradycardia (reflex or organic) and not seizures.<sup>5</sup> Of interest, the opposite situation may also happen—in patients with unexplained TLOC with convulsions, ILR may help diagnose true epilepsy. This is because the ECG artefacts during tonic-clonic muscle movements occurring during seizures are very characteristic and when they start to be less frequent at the end of an epileptic attack, a normal cardiac rhythm can be visible. This is proof that TLOC is not due to cardiac arrhythmia ([figure 3](#)).

At this point, it is worth mentioning yet another application of smartphones which is the capability of video recording. Patients’ relatives and friends should be urged to record attacks because it gives additional information on the type of TLOC. Especially, differentiation between reflex syncope with convulsions and true epileptic attack is much easier when an attack is recorded and a syncope specialist or neurologist can evaluate the video.

## TREATMENT

### Non-pharmacological

Education and lifestyle modifications are effective in 40%–50% of subjects.<sup>1</sup> Several pieces of advice should be given to a patient. First, situations leading to syncope like prolonged standing in a hot environment or collecting blood pressure while sitting should be avoided if possible. Second, proper fluid intake and no reduction in salt in subjects without heart failure or hypertension should be advocated. The amount of fluid should exceed 3–4 L/day to expand intravascular blood volume and improve



**Figure 6** Original example of high-frequency extracardiac vagal stimulation used to confirm cardioneuroablation-induced vagal nerve inhibition. (A) Fluoroscopic image showing pacing electrode (arrow) introduced into the left internal jugular vein and used for stimulation of adjacent vagal nerve. (B) Before procedure, vagal nerve stimulation causes sinus arrest lasting for the whole period of pacing. (C) After procedure, vagal nerve stimulation has no effect on heart rhythm, confirming cardioneuroablation-induced vagal denervation. I, II and III refer to ECG limb leads. CS1–CS10 refer to recordings from electrode in the coronary sinus.

cardiac output. Third, sleeping with the head slightly elevated (additional pillow or bedside elevation) may help because this manoeuvre prevents nocturnal secretion of natriuretic hormones which increase diuresis and cause depletion in the intravascular fluid volume. Fourth, support stockings may prevent syncope recurrences, especially in those with orthostatic hypotension or vasovagal syncope with a dominant vasodepressor reflex. Fifth, exercising should not be forbidden except for those who have exercise-induced syncope. Finally, tilt training may be prescribed which consists of standing against the wall for 5 min twice daily during the first week and gradually extending the duration of standing up to 30 min twice daily. This therapy is aimed to train reflexes to act properly during standing. The results of tilt training are variable mainly because only about 30% of people are willing to continue the training. Thus, it should be prescribed only for highly motivated subjects. The optimal protocol of tilt training and how long it should be continued have not been established.

The next piece of advice that a physician has to give to a patient is how to avoid fainting when prodromal symptoms occur. All these manoeuvres have to be demonstrated and a patient has to learn how to perform them. The best way to avoid impending reflex syncope is to lie down. However, very often it cannot be safely done like in public places or transport. In such a situation, increasing venous return and reducing blood pooling in the legs and abdomen may help. This can be achieved by crossing the legs and repeated tensions of leg, abdominal and buttock muscles with concomitant slight head tilting. Alternatively, sitting with the head down and placed between the knees, squatting down or kneeling and pretending that a shoelace is untied have been shown to reduce symptoms.

Another mechanism that may prevent upcoming syncope is hand grip or arm stretching counterpressure manoeuvres which increase adrenergic tone and vasoconstriction, leading to a rise in blood

pressure. All these manoeuvres are presented in figure 4.

### Pharmacological therapy

In patients with orthostatic hypotension or reflex syncope with dominant vasodepressor, component drugs which increase intravascular fluid volume such as fludrocortisone or agents which increase peripheral vascular resistance via alpha receptor activation such as midodrine can be helpful. However, their efficacy is limited and reaches 58% in the case of midodrine<sup>6</sup> and 56% when fludrocortisone is used.<sup>7</sup> Beta blockers have been proposed by the US guidelines<sup>8</sup> in those <42 years of age; however, European guidelines did not back up this recommendation.<sup>1</sup> Theophylline, a non-selective adenosine receptor antagonist, is another promising agent in patients with low-adenosine phenotype of reflex syncope, especially in those with functional atrioventricular block.<sup>9</sup> However, side effects, although usually benign, are frequent and 39% of patients discontinue this therapy. The drug has no class recommendation in the guidelines. Other treatments such as selective serotonin reuptake inhibitors or norepinephrine transport inhibitors are rarely used in clinical practice.

### Permanent pacing

In patients with prolonged asystole pacemaker implantation is recommended, however, only in those aged >40 years with documented spontaneous cardioinhibitory vasovagal syncope and severe symptoms.<sup>1</sup> Permanent pacing is effective in as much as 75%–88% of patients.<sup>10 11</sup> The main problem is that reflex syncope occurs predominantly in young persons in whom permanent pacing should be avoided as much as possible. Permanent pacing is associated with small but not negligible long-term risk of complications due to repeated battery replacement procedures, infection and thromboembolic risk due to the presence of pacing leads in the venous system and the heart. There

## Key messages

- ⇒ Diagnostic workup in syncope is well defined and includes 'initial evaluation' as the first step, 'risk stratification' as the second step if diagnosis is uncertain after 'initial evaluation' and a bunch of autonomic tests as well as prolonged ECG monitoring which enable to establish diagnosis in the majority of patients.
- ⇒ Non-pharmacological approach is the key element in the treatment of reflex syncope.
- ⇒ Pharmacological therapy is of limited value in reflex syncope.
- ⇒ Permanent pacing may be offered and is effective in older patients with reflex syncope.
- ⇒ Cardioneuroablation is a new promising therapy in younger patients with asystolic reflex syncope.

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is ongoing discussion that the age limit for pacemaker implantation should probably be higher, for example, >60 years of age.

If permanent pacing has been chosen, the best results have been obtained using the 'close loop stimulation' system where the sensor analysing changes in myocardial contractility is located at the tip of the pacing lead.<sup>11</sup> Thanks to this advent, the pacing starts at the early stage of the vasovagal reflex and prevents syncope better than other pacing modalities which are triggered by heart rate slowing which is the last part of the vasovagal reaction.

In summary, although permanent pacing has many disadvantages, particularly in young, it is currently the only invasive therapy which has a well-established value in the treatment of asystolic reflex syncope, especially in older patients.

**Cardioneuroablation**

This is a relatively new technique for the treatment of reflex asystolic syncope, introduced by Pachon *et al* in 2005.<sup>12</sup> It uses radiofrequency ablation, the same method as for ablation of various cardiac arrhythmias, to modify autonomic drive to the heart, mainly to diminish parasympathetic activity. It can be accomplished by ablating so-called ganglionated plexi, located in the epicardial fat around the atria. Contrary to the sympathetic part of plexi, parasympathetic endings barely regenerate after ablation and therefore the net result is marked attenuation of the inhibitory effects of the vagus nerve on the sinus node rate and atrioventricular conduction. Following cardioneuroablation, heart rate speeds up and atrioventricular conduction

improves which prevents the development of asystolic pause during the vasovagal reaction.

The method is new, has no recommendation yet in the guidelines and many important issues such as technical aspects, methodology and indications have not yet been properly addressed. Therefore, it should be regarded as an experimental approach. Data in literature confirming efficacy and safety of cardioneuroablation are scarce. One meta-analysis<sup>13</sup> and one small randomised prospective study<sup>14</sup> have suggested that the efficacy of cardioneuroablation was as high as 90% during a 2-year follow-up without significant complications. The procedure is similar to standard ablation for atrial fibrillation although much shorter and less atrial tissue has to be ablated. Thus, in the hands of an experienced electrophysiologist cardioneuroablation is effective and safe.

Currently, the main indication for cardioneuroablation is asystolic (sinus arrest or atrioventricular block) reflex syncope, especially in young people in whom the non-pharmacological approach fails and who are not willing to try pharmacotherapy. The atropine test (2 mg of atropine administered intravenously) is a screening tool to select the proper candidates with functional rather than intrinsic sinus bradycardia or atrioventricular block. An increase in sinus rate by at least 30% (the higher the better) is used to identify those who are likely to favourably respond to cardioneuroablation.

The long-term safety of cardioneuroablation is not known. The most common undesired effect of cardioneuroablation is inappropriate sinus tachycardia following the procedure, occurring in a few per cent of patients. However, in the vast majority it disappears over months due to slight parasympathetic reinnervation. In very symptomatic patients, beta blockers and/or ivabradine to attenuate fast heart rate caused by this procedure may be used,<sup>15-17</sup> although in some cases this treatment may not be fully effective. Other possible unwanted long-term effects of diminishing parasympathetic control of cardiac rhythm and increased adrenergic tone have not yet been reported but theoretically are possible. Therefore, long-term follow-up data are needed before cardioneuroablation could be regarded as safe procedure.

An original example of the cardioneuroablation procedure is shown in figure 5 and an example of extracardiac vagal stimulation before and after the procedure is shown in figure 6.

**SUMMARY**

Evaluation of reflex syncope is often a difficult but fascinating task. It requires a physician to understand the physiological mechanisms of autonomic control of the cardiovascular system, knowledge of cardiac disorders which may lead to syncope and cooperation with other specialists, preferably as a team in a syncope unit. A diagnostic path is easier to carry out when it is done strictly according to the guidelines. New devices allowing for long-term ECG monitoring increase diagnostic yield.

Treatment is still suboptimal but pacing in older patients is effective and cardioneuroablation in young is very promising.

**Contributors** PK is the only author of this paper.

**Funding** The authors have not declared a specific grant for this research from any funding agency in the public, commercial or not-for-profit sectors.

**Competing interests** None declared.

**Patient consent for publication** Not applicable.

**Provenance and peer review** Commissioned; internally peer reviewed.

**Author note** References which include a \* are considered to be key references.

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