



TASK FORCE ON SYNCOPE, EUROPEAN SOCIETY OF CARDIOLOGY

Part 2. Diagnostic tests and treatment: summary of recommendations

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The strength of *recommendations* has been ranked as follows:

- Class I, when there is evidence for and/or general agreement that the procedure or treatment is useful. Class I recommendations are generally those reported in the sections labelled as ‘Recommendations’ and in the tables.
- Class II, when usefulness of the procedure or treatment is less well established or divergence of opinion exists among the members of the Task Force.
- Class III, when the procedure or treatment is not useful and in some cases may be harmful.

The strength of *evidence* supporting a particular procedure/treatment option has been ranked as follows:

- Level of Evidence A=Data derived from multiple randomized clinical trials or meta-analyses.
- Level of Evidence B=Data derived from a single randomized trial or multiple non-randomized studies.
- Level of Evidence C=Consensus opinion of experts.

When not expressed otherwise, evidence is of type C.

Diagnostic tests

Carotid sinus massage

Carotid sinus massage is a tool used to disclose carotid sinus syndrome in patients with syncope. Carotid sinus syndrome is diagnosed in patients who are found to have an abnormal response to carotid sinus massage (carotid sinus hypersensitivity) and an otherwise negative work-up for syncope. The relationship between carotid sinus hypersensitivity and spontaneous, otherwise unexplained, syncope is established (level B).

Recommendations

Indications and methodology

Class I

- Carotid sinus massage is recommended in patients over age 40 years with syncope of unknown aetiology after the initial evaluation. In case of risk of stroke due to carotid artery disease, massage should be avoided.
- Electrocardiographic monitoring and continuous blood pressure measurement during carotid massage is mandatory. Duration of massage of a minimum of 5 and a maximum of 10 s is recommended. Carotid massage should be performed with the patient both supine and erect.

Diagnosis

Class I

- The procedure is considered positive if symptoms are reproduced during or immediately after the massage in presence of asystole longer than 3 s and/or a fall in systolic blood pressure of 50 mm of Hg or more. A positive response is diagnostic of the cause of syncope in the absence of any other competing diagnosis.

Tilt testing

Recommendations

Tilt test protocols

Class I

- Supine pre-tilt phase of at least 5 min when no venous cannulation is performed, and at least 20 min when cannulation is undertaken.
- Tilt angle is 60 to 70 degree.
- Passive phase of a minimum of 20 min and a maximum of 45 min.
- Use of either intravenous isoprenaline/isoproterenol or sublingual nitroglycerin for drug provocation if passive phase has been negative. Drug challenge phase duration of 15–20 min.

Table 1 Classification of positive responses to tilt testing

- *Type 1 mixed.* Heart rate falls at the time of syncope but the ventricular rate does not fall to less than 40 bpm or falls to less than 40 bpm for less than 10 s with or without asystole of less than 3 s. Blood pressure falls before the heart rate falls.
- *Type 2A cardioinhibition without asystole.* Heart rate falls to a ventricular rate less than 40 bpm for more than 10 s but asystole of more than 3 s does not occur. Blood pressure falls before the heart rate falls.
- *Type 2B cardioinhibition with asystole.* Asystole occurs for more than 3 s. Blood pressure fall coincides with or occurs before the heart rate fall.
- *Type 3 vasodepressor.* Heart rate does not fall more than 10% from its peak at the time of syncope.
- *Exception 1. Chronotropic incompetence.* No heart rate rise during tilt testing (i.e. less than 10% from the pre tilt rate).
- *Exception 2. Excessive heart rate rise.* An excessive heart rate rise both at the onset of the upright position and throughout its duration before syncope (i.e. greater than 130 bpm).

- For isoprenaline, an incremental infusion rate from 1 up to 3 µgm/min in order to increase average heart rate by about 20–25% over baseline, administered without returning the patient to the supine position.
- For nitroglycerin, a fixed dose of 400 µgm nitroglycerin spray sublingually administered in the upright position.
- The end-point of the test is defined as induction of syncope or completion of the planned duration of tilt including drug provocation. The test is considered positive if syncope occurs (Table 1).

Class II

Divergence of opinion exists in the case of induction of pre-syncope.

*Indications**Class I*

Tilt testing is indicated for diagnostic purposes:

- In case of unexplained single syncopal episode in high risk settings (e.g. occurrence of, or potential risk for, physical injury or with occupational implications), or recurrent episodes in the absence of organic heart disease, or, in the presence of organic heart disease, after cardiac causes of syncope have been excluded;
- When it will be of clinical value to demonstrate susceptibility to neurally-mediated syncope to the patient.

Class II

Tilt testing is indicated for diagnostic purposes:

- When an understanding of the haemodynamic pattern of syncope may alter the therapeutic approach;
- For differentiating syncope with jerking movements from epilepsy;
- For evaluating patients with recurrent unexplained falls;
- For assessing recurrent presyncope or dizziness.

Class III

- Assessment of treatment.

- A single episode without injury and not in a high risk setting.
- Clear-cut clinical vasovagal features leading to a diagnosis when demonstration of a neurally mediated susceptibility would not alter treatment.

*Diagnosis**Class I*

- In patients without structural heart disease, tilt testing can be considered diagnostic, and no further tests need to be performed when spontaneous syncope is reproduced.
- In patients with structural heart disease, arrhythmias or other cardiac causes should be excluded prior to considering positive tilt test results as evidence suggesting neurally mediated syncope.

Class II

- The clinical meaning of abnormal responses other than induction of syncope is unclear.

**Electrocardiographic monitoring
(non-invasive and invasive)***Recommendations**Indications**Class I*

- Holter monitoring is indicated in patients with structural heart disease and frequent symptoms or even infrequent when there is a high pre-test probability of identifying an arrhythmia responsible for syncope.
- When the mechanism of syncope remains unclear after full evaluation, External or Implantable Loop

Table 2 Minimal suggested electrophysiological protocol for diagnosis of syncope

- Measurement of sinus node recovery time and corrected sinus node recovery time by repeated sequences of atrial pacing for 30–60 s with at least one low (10–20 beats.min⁻¹ higher than sinus rate) and two higher pacing rates*.
- Assessment of the His–Purkinje system includes measurement of the HV interval at baseline and His–Purkinje conduction with stress by incremental atrial pacing. If the baseline study is inconclusive, pharmacological provocation with slow infusion of ajmaline (1 mg/kg i.v.), procainamide (10 mg/kg i.v.), or disopyramide (2 mg/kg i.v.) is added unless contraindicated.
- Assessment of ventricular arrhythmia inducibility performed by ventricular programmed stimulation at two right ventricular sites (apex and outflow tract), at two basic drive cycle lengths (100 or 120 beats.min⁻¹ and 140 or 150 beats.min⁻¹), with up to two extrastimuli**.
- Assessment of supraventricular arrhythmia inducibility by any atrial stimulation protocol.

Comments:

*When sinus node dysfunction is suspected autonomic blockade may be applied, and measurements repeated.

**A third extrastimulus may be added. This may increase sensitivity, but reduces specificity. Ventricular extrastimulus coupling intervals below 200 ms also reduce specificity.

Recorders are recommended when there is a high pre-test probability of identifying an arrhythmia responsible of for syncope.

Diagnosis

Class I

- ECG monitoring is diagnostic when a correlation between syncope and an electrocardiographic abnormality (brady- or tachyarrhythmia) is detected.
- ECG monitoring excludes an arrhythmic cause when there is a correlation between syncope and sinus rhythm.
- In the absence of such correlations additional testing is recommended with possible exception of:
 - ventricular pauses longer than 3 s when awake;
 - periods of Mobitz II or 3rd degree atrioventricular block when awake;
 - rapid paroxysmal ventricular tachycardia.

Electrophysiological testing

The diagnostic efficiency of the invasive electrophysiological study is highly dependent on the degree of suspicion of the abnormality (pre-test probability), but also on the applied protocol, and the criteria used for diagnosing the presence of clinically significant abnormalities. There are four areas of interest: suspected bradycardia, bundle branch block (impending high degree AV block); suspected supraventricular tachycardia; suspected ventricular tachycardia (Table 2).

Suspected bradycardia. The pre-test probability of a transient symptomatic bradycardia as the cause of syncope is relatively high when there is asymptomatic sinus bradycardia (<50 bpm) or sinoatrial block in the absence of negatively chronotropic medications. Sinus

node dysfunction can be demonstrated by a prolonged sinus node recovery time. The prognostic value of a prolonged sinus node recovery time is largely unknown. It is opinion of the panel that, in presence of a SNRT>2 s or CSNRT>1 s, sinus node dysfunction may be the cause of syncope.

Bundle branch block. In patients with syncope and bifascicular block, an electrophysiological study is highly sensitive in identifying patients with intermittent or impending high degree AV block (level B). This block is the likely cause of syncope in most cases, but not of the high mortality rate observed in these patients that seems mainly related to underlying structural heart disease and ventricular tachyarrhythmias (level B). Unfortunately, ventricular programmed stimulation does not seem to be able correctly to identify these patients and the finding of inducible ventricular arrhythmia should therefore be interpreted with caution.

Suspected supraventricular tachycardia. Supraventricular tachycardia presenting as syncope without accompanying palpitations is probably rare. Both non-invasive (transoesophageal) and invasive electrophysiological studies may be used to evaluate the haemodynamic effects of an induced tachycardia.

Suspected ventricular tachycardia. Electrophysiological study with programmed electrical stimulation is an effective diagnostic test in patients with coronary artery disease, markedly depressed cardiac function and unexplained syncope (level B). Its utility is more questionable in patients with non-ischæmic dilated cardiomyopathy (level B). Several studies on patients who underwent implantation of an automatic defibrillator showed a high incidence of spontaneous ventricular arrhythmia requiring device therapy, and suppression of syncope recurrences (level B). However, these results applied to a highly selected, high-risk population that might be not representative of the patients encountered in clinical practice.

Recommendations

Indications

Class I

- An invasive electrophysiological procedure is indicated when the initial evaluation suggests an arrhythmic cause of syncope (in patients with abnormal electrocardiography and/or structural heart disease or syncope associated with palpitations or family history of sudden death).

Class II

- Diagnostic reasons: to evaluate the exact nature of an arrhythmia which has already been identified as the cause of the syncope.
- Prognostic reasons: in patients with cardiac disorders, in which arrhythmia induction has a bearing on the selection of therapy; and in patients with high-risk occupations, in whom every effort to exclude a cardiac cause of syncope is warranted.

Class III

- In patients with normal electrocardiograms and no heart disease and no palpitations an electrophysiological study is not usually undertaken.

Diagnosis

Class I

- Normal electrophysiological findings cannot completely exclude an arrhythmic cause of syncope; when an arrhythmia is likely, further evaluations (for example loop recording) are recommended.
- Depending on the clinical context, abnormal electrophysiological findings may not be diagnostic of the cause of syncope.
- An electrophysiological study is diagnostic, and usually no additional tests are required, in the following cases:
 - sinus bradycardia and a very prolonged CSNRT (as discussed in the text);
 - bifascicular block and:
 - a baseline HV interval of ≥ 100 ms, or
 - 2nd or 3rd degree His–Purkinje block is demonstrated during incremental atrial pacing, or
 - (if the baseline electrophysiological study is inconclusive) high-degree His–Purkinje block is provoked by intravenous administration of ajmaline, procainamide, or disopyramide;
 - previous myocardial infarction and induction of sustained monomorphic ventricular tachycardia;
 - arrhythmogenic right ventricular dysplasia and induction of ventricular tachyarrhythmias;

- induction of rapid supraventricular arrhythmia which reproduces hypotensive or spontaneous symptoms.

Class II

Divergence of opinion exists on the diagnostic value of electrophysiological study in case of:

- HV interval of >70 ms but <100 ms;
- induction of polymorphic ventricular tachycardia or ventricular fibrillation in patients with ischaemic or dilated cardiomyopathy;
- Brugada syndrome.

ATP test

Intravenous injection of adenosine triphosphate (ATP) has recently been proposed as a tool in the investigation of patients with unexplained syncope. In predisposed patients with unexplained syncope, the stimulation of purinergic receptors causes prolonged ventricular pauses due to atrioventricular block, which are considered as possibly responsible for spontaneous attacks (level B).

Recommendations

The test requires the rapid injection of a 20 mg bolus of ATP during electrocardiographic monitoring. Asystole lasting more than 6 s, or AV block lasting more than 10 s, is considered abnormal. ATP testing produces an abnormal response in some patients with syncope of unknown origin, but not in controls. The diagnostic and predictive value of the test remains to be confirmed by prospective studies. In the absence of sufficient hard data, the test may be indicated at the end of the diagnostic work-up (Class II).

Ventricular signal-averaged electrocardiogram

Recommendations

There is general agreement that ventricular signal-averaged electrocardiogram is not diagnostic of the cause of syncope. In patients with syncope and no evidence of structural heart disease, the technique may be useful for guiding the use of electrophysiological studies. Its systematic use is not recommended (Class III).

Echocardiogram

Even if echocardiography alone is only seldom diagnostic, this test provides information about the type and severity of underlying heart disease which may be useful for risk stratification. If moderate to severe structural

heart disease is found, evaluation is directed toward a cardiac cause of syncope. On the other hand, in the presence of minor structural abnormalities detected by echocardiography, the probability of cardiac cause of syncope may not be high, and the evaluation may proceed as in patients without structural heart disease.

Recommendations

Indications

Class I

- Echocardiography is recommended in patients with syncope when cardiac disease is suspected.

Diagnosis

Class I

- Echocardiographic findings may be useful to stratify the risk by assessing the cardiac substrate.
- Echocardiography only makes a diagnosis in severe aortic stenosis and atrial myxoma.

Exercise testing

Syncope occurring during exercise may be cardiac (level B), even if some case reports showed that it might be a manifestation of an exaggerated reflex vasodilatation. By contrast, postexertional syncope is almost invariably due to autonomic failure or to a neurally-mediated mechanism (level B).

Recommendations

Indications

Class I

Patients who experience an episode of syncope during or shortly after exertion.

Class III

Use of exercise testing is not recommended in patients who do not experience syncope during exercise.

Diagnosis

Class I

- Exercise testing is diagnostic when ECG and haemodynamic abnormalities are present and syncope is reproduced during or immediately after exercise.

- Exercise testing is diagnostic if Mobitz II second degree or 3rd degree AV block develop during exercise even without syncope.

Cardiac catheterization and angiography

Recommendations

Indications

Class I

In patients with syncope suspected to be due, directly or indirectly, to myocardial ischaemia, coronary angiography is recommended in order to confirm the diagnosis and to establish optimal therapy.

Class III

Angiography alone is rarely diagnostic for the cause of syncope.

Neurological and psychiatric evaluation

Recommendations

Indications

Class I

- Neurological referral is indicated in patients in whom loss of consciousness cannot be attributed to syncope.
- In case of unequivocal syncope, neurological referral is warranted when syncope may be due to autonomic failure or to a cerebrovascular steal syndrome.
- Psychiatric evaluation is recommended when symptoms suggest psychogenic syncope (somatization disorder) or if the patient has a known psychiatric disorder.

Class III

- In all other patients with syncope, neurological and psychiatric investigations are not recommended.

Treatment

Neurally-mediated reflex syncopal syndromes

Treatment goals: primarily prevention of symptom recurrence and associated injuries; improved quality of life.

Patients who seek medical advice after having experienced a vasovagal faint principally require reassurance and education regarding the nature of the condition. This assumption is derived from the knowledge of the benign nature of the disease. In particular, based on

review of their medical history, patients should be informed of the likelihood of syncope recurrence. Initial advice should also include review of typical premonitory symptoms which may permit many individuals to recognize an impending episode and thereby avert a frank faint. In general, initial 'treatment' of all forms of neurally-mediated reflex syncope comprises education regarding avoidance of triggering events (e.g. hot crowded environments, volume depletion, effects of cough, tight collars, etc.), recognition of premonitory symptoms, and manoeuvres to abort the episode (e.g. supine posture). Additionally, if possible, strategies should address trigger factors directly (for example, suppressing the cause of cough in cough syncope).

When a more aggressive treatment strategy is needed, 'volume expanders' (e.g. increased dietary salt/electrolyte intake with fluids [e.g. 'sport' drinks, salt tablets]) or moderate exercise training appear to be among the safest initial approaches (level B). Additionally, in highly motivated patients with recurrent vasovagal symptoms, the prescription of progressively prolonged periods of enforced upright posture (so-called 'tilt-training') may reduce syncope recurrence (level B).

Many drugs have been used in the treatment of vasovagal syncope (beta-blockers, disopyramide, scopolamine, clonidine, theophylline, fludrocortisone, ephedrine, etilefrine, midodrine, clonidine, serotonin reuptake inhibitors, etc.). In general, while the results have been satisfactory in uncontrolled trials or short-term controlled trials long-term placebo-controlled prospective trials have been unable to show a benefit of the active drug over placebo. Beta-adrenergic blocking drugs have failed to be effective in several long-term follow-up controlled studies. Thus the evidence fails to support beta-blocker efficacy (level A). Vasoconstrictor drugs are potentially more effective in orthostatic hypotension caused by autonomic dysfunction than in the neurally-mediated syncopes. Etilefrine proved to be ineffective (level B). Cardiac pacing has been demonstrated to be effective in highly selected patients affected by cardioinhibitory form (level B).

Cardiac pacing appears to be beneficial in carotid sinus syndrome (level B) and is acknowledged to be the treatment of choice when bradycardia has been documented.

Recommendations

It is valuable to assess the relative contribution of cardioinhibition and vasodepression before embarking on specific treatment as there are different therapeutic strategies for the two aspects. Even if evidence of utility of such an assessment exists only for the carotid sinus massage, it is recommended to extend this assessment also by means of tilt testing or implantable loop recorder.

Patients who have syncope in a 'high risk' setting (e.g. commercial vehicle driver, machine operator, pilot, commercial painter, competitive athlete) merit specific

consideration for treatment. There is no information available regarding the efficacy of treatment in this type of patient, and whether it differs from other patients with neurally-mediated faints.

Treatment is not necessary in patients who have sustained a single syncope and are not having syncope in a high risk setting.

Class I

- Explanation of the risk, and reassurance about the prognosis in vasovagal syncope.
- Avoidance of trigger events as much as possible and reducing magnitude of potential triggers when feasible (e.g. emotional upset) and causal situation in situational syncope.
- Modification or discontinuation of hypotensive drug treatment for concomitant conditions.
- Cardiac pacing in patients with cardioinhibitory or mixed carotid sinus syndrome.

Class II

- Volume expansion by salt supplements, an exercise programme or sleeping >10° head-up in posture-related syncope.
- Cardiac pacing in patients with cardioinhibitory vasovagal syncope with a frequency >5 attacks per year or severe physical injury or accident and age >40.
- Tilt training in patients with vasovagal syncope.

Class III

- The evidence fails to support the efficacy of beta-adrenergic blocking drugs. Beta-adrenergic blocking drugs may aggravate bradycardia in some cardioinhibitory cases.

Orthostatic hypotension

Treatment goals: prevention of symptom recurrence and associated injuries; improved quality of life.

Drug-induced autonomic failure is probably the most frequent cause of orthostatic hypotension. The principal treatment strategy is elimination of the offending agent. It is reasonable for all patients to receive advice and education on factors that influence systemic blood pressure, such as avoiding sudden head-up postural change (especially on waking), standing still for a prolonged period of time, prolonged recumbence during daytime, straining during micturition and defaecation, hyperventilation, high environmental temperature, severe exertion, large meals and alcohol.

Additional treatment principles, used alone or in combination, are appropriate for consideration on an individual patient basis are chronic expansion of intravascular volume by encouraging a higher than normal salt intake and fluid intake; use of fludrocortisone in low dose; and raising the head of the bed on blocks to permit gravitational exposure during sleep (level B). Midodrine

Table 3 Situations in which ICD therapy is likely to be useful

- Documented syncopal ventricular tachycardia or fibrillation without correctable causes (e.g. drug-induced) (Class I, level A).
- Undocumented syncope likely to be due to ventricular tachycardia or fibrillation:
 - previous myocardial infarction and inducible sustained monomorphic ventricular tachycardia with severe haemodynamic compromise, in the absence of another competing diagnosis as a cause of syncope (Class I, level B).
 - unexplained syncope in patients with depressed left ventricular systolic function in the absence of another competing diagnosis as a cause of syncope (Class II, level B).
 - established long QT syndrome, arrhythmogenic right ventricular dysplasia, or hypertrophic obstructive cardiomyopathy, with a family history of sudden death, in the absence of another competing diagnosis for the cause of syncope (Class II).
 - Brugada syndrome or arrhythmogenic right ventricular dysplasia and inducible ventricular tachyarrhythmias with severe haemodynamic compromise in the absence of another competing diagnosis for the cause of syncope (Class II).

appears to be of particular interest given the rapidly expanding and generally positive experience (level B).

Recommendations

Class I

- Syncope due to orthostatic hypotension should be treated in all patients. In many instances treatment entails only modification of drug treatment for concomitant conditions.

Cardiac arrhythmias as primary cause

Treatment goals: prevention of symptom recurrence, improved quality of life, reduction of mortality risk.

Sinus node dysfunction (including bradycardia-tachycardia syndrome). In general, cardiac pacemaker therapy is indicated and has proved highly effective in patients with sinus node dysfunction when bradyarrhythmia has been demonstrated to account for syncope (Class I, level B).

AV conduction system disease. Pacing is able to improve survival in patients with heart block as well as prevent syncopal recurrences (Class I, level B). Pacing may also be life-saving in patients with bundle branch block and syncope in whom the mechanism of the faint is suspected to be intermittent AV block. However, it is also critical to consider the possibility that ventricular tachyarrhythmias are responsible for loss of consciousness, since many patients who present with varying degrees of conduction system disease have significant concomitant left ventricular dysfunction.

Paroxysmal supraventricular and ventricular tachycardias. Transcatheter ablation has become a very cost-effective treatment option and in paroxysmal supraventricular arrhythmia associated with syncope is probably the treatment of choice (Class I).

In the case of syncope due to ventricular tachycardia, drug therapy may be useful in the setting of normal heart or of heart disease with mild cardiac dysfunction. In patients with depressed cardiac function, the use of implantable pacemaker cardioverter-defibrillators (ICDs) is warranted. Currently, ablation techniques are appropriate first choices in only a few forms of ventricular tachycardia, specifically right ventricular outflow tract tachycardia, bundle-branch reentry tachycardia, and so-called verapamil sensitive left ventricular tachycardias (Table 3).

Recommendations

Class I

- Syncope due to cardiac arrhythmias must receive treatment appropriate to the cause in all patients in whom it is life-threatening and when there is a high risk of injury.

Class II

- Treatment may be employed when the culprit arrhythmia has not been demonstrated and a diagnosis of life-threatening arrhythmia is presumed from surrogate data.
- Treatment may be employed when a culprit arrhythmia has been identified but is not life-threatening or presenting a high risk of injury.

Structural cardiac or cardiopulmonary disease

Structural heart disease can cause syncope when circulatory demands outweigh the impaired ability of the heart to increase its output. More than one pathophysiological factor may contribute to the symptoms. Syncope is not solely the result of restricted cardiac output, but may be in part due to inappropriate neurally mediated reflex vasodilation and/or primary cardiac

arrhythmias. However, the management is primarily that of the underlying disease.

Recommendations

Class I

Treatment is best directed at amelioration of the specific structural lesion or its consequences.

Vascular steal syndromes

Subclavian steal is rare but is the most commonly recognized condition in this group. Direct corrective angioplasty or surgery is usually feasible and effective (Class I).