Complete Summary

GUIDELINE TITLE

Guidelines on management (diagnosis and treatment) of syncope - update 2004.

BIBLIOGRAPHIC SOURCE(S)

Brignole M, Alboni P, Benditt DG, Bergfeldt L, Blanc JJ, Bloch Thomsen PE, van Dijk JG, Fitzpatrick A, Hohnloser S, Janousek J, Kapoor W, Kenny RA, Kulakowski P, Masotti G, Moya A, Raviele A, Sutton R, Theodorakis G, Ungar A, Wieling W. Guidelines on management (diagnosis and treatment) of syncope--update 2004. Europace 2004 Nov;6(6):467-537. [399 references] PubMed

GUIDELINE STATUS

This is the current release of the guideline.

This guideline updates a previous version: Brignole M, Alboni P, Benditt D, Bergfeldt L, Blanc JJ, Bloch Thomsen PE, van Dijk JG, Fitzpatrick A, Hohnloser S, Janousek J, Kapoor W, Kenny RA, Kulakowski P, Moya A, Raviele A, Sutton R, Theodorakis G, Wieling W. Guidelines on management (diagnosis and treatment) of syncope. Eur Heart J 2001 Aug;22(15):1256-306.

COMPLETE SUMMARY CONTENT

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SCOPE

DISEASE/CONDITION(S)

Syncope

GUIDELINE CATEGORY

Diagnosis
Evaluation
Management
Treatment

CLINICAL SPECIALTY

Cardiology
Family Practice
Internal Medicine

INTENDED USERS

Physicians

GUIDELINE OBJECTIVE(S)

- To provide specific recommendations on the diagnostic evaluation and management of syncope
- To focus on the following main questions:
    - What are the diagnostic criteria for the causes of syncope?
    - What is the preferred approach to the diagnostic work-up in various subgroups of patients with syncope?
    - How should patients with syncope be risk stratified?
    - When should patients with syncope be hospitalized?
    - Which treatments are likely to be effective in preventing syncopal recurrences?

TARGET POPULATION

Patients with syncope

INTERVENTIONS AND PRACTICES CONSIDERED

Diagnosis

1. History, physical examination with orthostatic blood pressure measurements, and 12-lead electrocardiogram
2. Further evaluation including echocardiography, stress testing, and tests for arrhythmia detection such as prolonged electrocardiographic (ECG) and loop (external or implantable loop recorders) monitoring or electrophysiological study
3. Tilt testing, with or without nitroglycerine or isoproterenol/isoprenaline provocation
4. Carotid massage
5. Psychiatric assessment, when applicable
6. Reappraisal of work-up
7. Intravenous injection of adenosine triphosphate (ATP test)
8. Ventricular signal-averaged electrocardiogram (considered, but not recommended routinely)
9. Exercise testing

10. Cardiac catheterization and angiography
11. Neurological evaluation including electroencephalography, computed tomography, magnetic resonance imaging, and carotid Doppler ultrasonography

Treatment

1. Education of patients to avoid trigger events, recognize the symptoms, and manoeuvres to abort episode
2. Modification of hypotensive drug treatment for concomitant conditions
3. Volume expansion through increased salt intake or use of low-dose fludrocortisone
4. Exercise training
5. Tilt-training
6. Beta-blockers (considered but not recommended)
7. Vasoconstrictors
8. Alpha stimulating agents, such as midodrine
9. Cardiac pacemaker therapy
10. Implantable pacemaker cardioverter-defibrillators
11. Anti-arrhythmic agents, particularly class III agents such as amiodarone
12. Surgery, including revascularization or angioplasty
13. Behavior modification
14. Provision of care in a syncope management facility

MAJOR OUTCOMES CONSIDERED

- Accuracy, sensitivity, specificity, and prognostic value of diagnostic tests and procedures
- Syncopal recurrences
- Mortality risk
- Symptom recurrence and associated injuries
- Quality of life
- Complications and adverse effects of diagnostic procedures

METHODOLOGY

METHODS USED TO COLLECT/SELECT EVIDENCE

Searches of Electronic Databases

DESCRIPTION OF METHODS USED TO COLLECT/SELECT THE EVIDENCE

Subgroups of the panel were formed and each was assigned the task of reviewing the literature on specific topics and of developing a draft summarizing the issue. Each subgroup was to perform literature searches on MEDLINE and to supplement the search by documents from their personal collections.

NUMBER OF SOURCE DOCUMENTS

Not stated

METHODS USED TO ASSESS THE QUALITY AND STRENGTH OF THE EVIDENCE

Weighting According to a Rating Scheme (Scheme Given)

RATING SCHEME FOR THE STRENGTH OF THE EVIDENCE

Levels of Evidence:

A. Data derived from multiple randomised clinical trials or meta-analyses
B. Data derived from a single randomised clnical trial or large nonrandomised studies
C. Consensus of opinion of the experts and/or small studies, retrospective studies, registries

When not expressed otherwise, evidence is of type C.

METHODS USED TO ANALYZE THE EVIDENCE

Systematic Review

DESCRIPTION OF THE METHODS USED TO ANALYZE THE EVIDENCE

Not stated

METHODS USED TO FORMULATE THE RECOMMENDATIONS

Expert Consensus

DESCRIPTION OF METHODS USED TO FORMULATE THE RECOMMENDATIONS

The methodology for writing the guideline document consisted of literature reviews and consensus development by the panel assembled by the European Society of Cardiology (ESC). The ESC guidelines for the management (diagnosis and treatment) of syncope were published in August 2001. Since then, numerous clinical trials and observational studies have been published or presented, some of which alter the recommendations made in the original document.

Therefore, the Task Force on Syncope of the ESC met in August 2002 and developed a comprehensive outline of the issues that needed to be addressed in the document. Subgroups of the panel were formed and each was assigned the task of reviewing the literature on a specific topic and of developing a draft summarizing the issue. The panel reconvened in September 2003, reviewed the draft documents, made revisions whenever appropriate and developed the consensus recommendations. The panel discussed each recommendation and arrived at consensus by obtaining a majority vote. When there was divergence of opinion, this was noted. Since the goal of the project was to provide specific recommendations for diagnosis and management, guidelines are provided even when the data from the literature was not definitive. It must be pointed out that

most of the recommendations are based on consensus expert opinion. All the members of the panel reviewed final drafts and approved the final document.

With respect to the initial document, the following sections (and recommendations) were widely revised in the 2004 update:

- Classification of transient loss of consciousness
- Epidemiological and prognostic considerations
- Initial evaluation and diagnostic flow
- Prolonged electrocardiographic monitoring
- Electrophysiological shock
- Adenosine triphosphate (ATP) test
- Ventricular signal averaged electrocardiogram, T wave alternans
- Exercise testing
- Neurological and psychiatric evaluation
- Treatment of neurally-mediated (reflex) syncope
- Syncope in the older adult
- Syncope in paediatric patients
- Driving and syncope
- Glossary of terms

Furthermore, since the strategies for the assessment of syncope vary widely among physicians and among hospitals in Europe, the Task Force recognized the need to coordinate the evaluation of syncope. They sought to define European Society of Cardiology standards for the management of syncope and they proposed a model of organization for the evaluation of the syncope patient. A new section was thus added to the document on this topic.

RATING SCHEME FOR THE STRENGTH OF THE RECOMMENDATIONS

The strength of recommendations has been ranked as follows:

Class I: Evidence and/or general agreement that a given diagnostic procedure/treatment is beneficial, useful, and effective

Class II: Conflicting evidence and/or a divergence of opinion about the usefulness/efficacy of the treatment

- **Class IIa**: Weight of evidence/opinion is in favour of usefulness/efficacy
- **Class IIb**: Usefulness/efficacy is less well established by evidence/opinion

Class III*: Evidence or general agreement that the treatment is not useful/effective and in some cases may be harmful

*Use of Class III is discouraged by the European Society of Cardiology.

COST ANALYSIS

Patients with syncope are often admitted to hospital and undergo expensive and repeated investigations, many of which do not provide a definite diagnosis. In a study, performed in 1982, patients often underwent multiple diagnostic tests

despite which a cause of syncope was established in only 13 of 121 patients. With the advent of newer diagnostic tests (e.g., tilt testing, wider use of electrophysiological testing, loop monitoring) it is likely that patients are undergoing a greater number of tests at considerably higher cost. In a recent study, based on administrative data from Medicare, there were estimated to be 193,164 syncope hospital discharges in 1993 in the U.S.A. The cost per discharge was calculated as $4,132 and increased to $5,281 for those patients who were readmitted for recurrent syncope. This figure underestimates the true total cost associated with syncope because many patients with syncope are not admitted to hospital for either investigation or therapy. In the UK the overall cost per patient was 611 pounds sterling, with 74% attributed to the costs of hospital stay alone. Cost per diagnosis of patients admitted to hospital was 1,080 pounds sterling.

Some Existing Syncope Management Unit Models

The service model adopted by the Newcastle group is a multidisciplinary approach to referrals with syncope or falls. All patients attend the same facility (with access to cardiovascular equipment, investigations, and trained staff) but are investigated by geriatrician or cardiovascular physician according to the dominant symptom cited in referral correspondence - falls or syncope. Recently, this group showed that activity at the acute hospital at which the day case syncope evaluation unit was based experienced in 1 year 6,116 fewer bed days for the diagnostic categories comprising syncope and collapse, compared with peer teaching hospitals in the UK. This reduction translated into a significant savings in emergency hospital costs (4 million euros). The savings were attributed to a combination of factors - reduced re-admission rates, rapid access to day case facilities for accident and emergency staff and community physicians, and reduced event rates because of effective targeted treatment strategies for syncope and falls.

METHOD OF GUIDELINE VALIDATION

External Peer Review
Internal Peer Review

DESCRIPTION OF METHOD OF GUIDELINE VALIDATION

Not stated

RECOMMENDATIONS

MAJOR RECOMMENDATIONS

The ratings for the class of recommendations (I-III) and level of evidence (A-C) are defined at the end of the "Major Recommendations" field.

Diagnosis

Initial Evaluation

Diagnostic Criteria Based on the Initial Evaluation

Class I:

The results of the initial evaluation (history, physical examination, orthostatic blood pressure measurements, and electrocardiography [ECG]) are diagnostic of the cause of syncope in the following situations:

- Vasovagal syncope is diagnosed if precipitating events such as fear, severe pain, emotional distress, instrumentation, or prolonged standing are associated with typical prodromal symptoms.
- Situational syncope is diagnosed if syncope occurs during or immediately after urination, defaecation, cough, or swallowing.
- Orthostatic syncope is diagnosed when there is documentation of orthostatic hypotension associated with syncope or pre-syncope. Orthostatic blood pressure measurements are recommended after 5 minutes of lying supine, followed by measurements each minute, or more often, after standing for 3 minutes. Measurements may be continued for longer, if blood pressure is still falling at 3 minutes. If the patient does not tolerate standing for this period, the lowest systolic blood pressure during the upright posture should be recorded. A decrease in systolic blood pressure $\geq$20 mmHg or a decrease in systolic blood pressure to <90 mmHg is defined as orthostatic hypotension regardless of whether or not symptoms occur.
- Cardiac ischaemia-related syncope is diagnosed when symptoms are present with ECG evidence of acute ischaemia with or without myocardial infarction, independently of its mechanism. (*Note: In the case of ischaemic syncope, the mechanism can be cardiac [low output or arrhythmia] or reflex [Bezold-Jarish reflex], but management is primarily that of ischaemia.*)
- Arrhythmia-related syncope is diagnosed by ECG when there is:
    - Sinus bradycardia <40 beats/min or repetitive sinoatrial blocks or sinus pauses >3 seconds
    - Mobitz II second- or third-degree atrioventricular (AV) block
    - Alternating left and right bundle branch block
    - Rapid paroxysmal supraventricular tachycardia or ventricular tachycardia
    - Pacemaker malfunction with cardiac pauses.

Diagnostic Work-Up Based on the Initial Evaluation

When the mechanism of syncope is not evident, the presence of suspected or certain heart disease is associated with a higher risk of arrhythmias and a higher mortality at 1 year. In the patients with clincial features suggesting cardiac syncope (listed in the tables below), cardiac evaluation is recommended. Cardiac evaluation consists of echocardiography, stress testing, prolonged ECG monitoring [Holter, external, or implantable loop recorder as appropriate) and electrophysiological study. If cardiac evaluation does not show evidence of arrhythmia as a cause of syncope, evaluation for neurally mediated syncope is recommended in those with recurrent or severe syncope.

In patients without suspected or certain heart disease, evaluation for neurally mediated syncope is recommended for those with recurrent or severe syncope. The tests for neurally mediated syncope consist of tilt testing and carotid massage and, if negative, prolonged ECG monitoring and implantable loop recorder. The

majority of patients with single or rare episodes in this category probably have neurally mediated syncope and tests for confirmation are usually not necessary.

- Basic laboratory tests are only indicated if syncope may be due to loss of circulating volume, or if a syncope-like disorder with a metabolic cause is suspected.
- In patients with suspected heart disease, echocardiography, prolonged electrocardiographic monitoring, and, if non-diagnostic, electrophysiological studies are recommended as first evaluation steps.
- In patients with palpitations associated with syncope, electrocardiographic monitoring and echocardiography are recommended as first evaluation steps.
- In patients with chest pains suggestive of ischaemia before or after loss of consciousness, stress testing, echocardiography, and electrocardiographic monitoring are recommended as first evaluation steps.
- In young patients without suspicion of heart or neurological disease and recurrent syncope, tilt testing and, in older patients, carotid sinus massage are recommended as first evaluation steps.
- In patients with syncope occurring during neck turning, carotid sinus massage is recommended at the outset.
- In patients with syncope during or after effort, echocardiography and stress testing are recommended as first evaluation steps.
- In patients with signs of autonomic failure or neurological disease a specific diagnosis should be made.
- In patients with frequent recurrent syncope who have multiple other somatic complaints and initial evaluation raises concerns for stress, anxiety, and possible psychiatric disorders, psychiatric assessment is recommended.
- When the mechanism of syncope remains unclear after full evaluation, an implantable loop recorder is indicated in patients who have clinical or ECG features suggesting an arrhythmic syncope (see tables below titled "Clinical Features Suggestive of Specific Causes of Real or Apparent Loss of Consciousness" and "ECG Abnormalities Suggesting an Arrhythmic Syncope") or a history of recurrent syncopes with injury.

Table: Clinical Features Suggestive of Specific Causes of Real or Apparent Loss of Consciousness
Neurally-mediated Syncope • Absence of cardiological disease • Long history of syncope • After sudden unexpected unpleasant sight, sound, smell, or pain • Prolonged standing or crowded, hot places • Nausea, vomiting associated with syncope • During the meal or in the absorptive state after a meal • With head rotation, pressure on carotid sinus (as in tumours, shaving, tight collars) • After exertion
Syncope due to Orthostatic Hypotension • After standing up • Temporal relationship with start of medication leading to hypotension or changes of dosage

Table: Clinical Features Suggestive of Specific Causes of Real or Apparent Loss of Consciousness
• Prolonged standing especially in crowded, hot places • Presence of autonomic neuropathy or Parkinsonism • After exertion
Cardiac Syncope • Presence of definite structural heart disease • During exertion, or supine • Preceded by palpitation • Family history of sudden death
Cerebrovascular Syncope • With arm exercise • Differences in blood pressure or pulse in the two arms
Syncope-like disorders • Refer to original guideline document

Table: ECG Abnormalities Suggesting an Arrhythmic Syncope
• Bifascicular block (defined as either left bundle branch block or right bundle branch block combined with left anterior or left posterior fascicular block) • Other intraventricular conduction abnormalities (QRS duration $\geq$0.12 seconds) • Mobitz I second degree atrioventricular block • Asymptomatic sinus bradycardia (<50 beats/min), sinoatrial block, or sinus pause $\geq$3 seconds in the absence of negatively chronotropic medications • Pre-excited QRS complexes • Prolonged QT intervals • Right bundle branch block pattern with ST-elevation in leads V1-V3 (Brugada syndrome) • Negative T waves in right precordial leads, epsilon waves and ventricular late potentials suggestive of arrhythmogenic right ventricular dysplasia • Q waves suggesting myocardial infarction

Echocardiogram

Indications

Class I:

- Echocardiography is recommended in patients with syncope when cardiac disease is suspected in order to stratify the risk by assessing the cardiac substrate.

Diagnosis

Class I:

- Echocardiography only makes a diagnosis in severe aortic stenosis and atrial myxoma.

Carotid Sinus Massage

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. If there is a risk of stroke due to carotid artery disease, massage should be avoided.
- Electrocardiographic monitoring and continuous blood pressure measurements during carotid massage is mandatory. Duration of massage of a minimum of 5 and a maximum of 10 seconds is recommended. Carotid massage should be performed with the patient both supine and erect.

Diagnosis

Class I:

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

Tilt Testing

Recommended Tilt Test Protocols

Class I:

- Supine pre-tilt phase of at least 5 minutes when no venous cannulation is performed, and at least 20 minutes when cannulation is undertaken.
- Tilt angle is 60 to 70 degrees.
- Passive phase of a minimum of 20 minutes and a maximum of 45 minutes.
- Use of either intravenous isoproterenol/isoprenaline or sublingual nitroglycerin for drug provocation if passive phase has been negative. Drug challenge phase duration of 15 to 20 minutes.
- For isoprenaline, an incremental infusion rate from 1 up to 3 micrograms/min in order to increase average heart rate by about 20 to 25% over baseline, administered without returning the patient to the supine position.
- For nitroglycerin, a fixed dose of 400 micrograms nitroglycerin spray sublingually administered in the upright position.
- The end-point of the test is defined by induction of syncope or completion of the planned duration of tilt including drug provocation. The test is considered positive if syncope occurs.

Indications

Class I:

Tilt testing is indicated for diagnostic purposes:

- In cases of unexplained single syncope episodes 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 in 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 of 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.

ECG Monitoring (Non-invasive and Invasive)

Indications

Class I:

- In-hospital monitoring (in bed or telemetric) is warranted when the patient has important structural heart disease and is at high risk of life-threatening arrhythmias (see section below titled "Need for Hospitalization").
- Holter monitoring is indicated in patients who have the clinical or ECG features suggesting an arrhythmic syncope such as those listed in the tables above titled "Clinical Features Suggestive of Specific Causes of Real or Apparent Loss of Consciousness" and "ECG Abnormalities Suggesting an Arrhythmic Syncope" and very frequent syncopes or presyncopes (e.g., $\geq$1 per week).
- When the mechanism of syncope remains unclear after full evaluation, implantable loop recorder is indicated in patients who have the clinical or ECG features suggesting an arrhythmic syncope (see the tables above titled "Clinical Features Suggestive of Specific Causes of Real or Apparent Loss of Consciousness" and "ECG Abnormalities Suggesting an Arrhythmic Syncope") or a history of recurrent syncope with injury.

Class II:

- Holter monitoring may be useful in patients who have the clinical or ECG features suggesting an arrhythmic syncope such as those listed in the tables above titled "Clinical Features Suggestive of Specific Causes of Real or Apparent Loss of Consciousness" and "ECG Abnormalities Suggesting an Arrhythmic Syncope" in order to guide subsequent examinations (i.e., electrophysiological study).
- External loop recorder may be indicated in patients who have the clinical or ECG features suggesting an arrhythmic syncope such as those listed in the tables above titled "Clinical Features Suggestive of Specific Causes of Real or Apparent Loss of Consciousness" and "ECG Abnormalities Suggesting an Arrhythmic Syncope" and inter-symptom interval $\leq$4 weeks.
- Implantable loop recorder may be indicated:
    - In an initial phase of the work-up instead of completion of conventional investigations in patients with preserved cardiac function who have the clinical or ECG features suggesting an arrhythmic syncope as those listed in the tables above titled "Clinical Features Suggestive of Specific Causes of Real or Apparent Loss of Consciousness" and "ECG Abnormalities Suggesting an Arrhythmic Syncope"
    - To assess the contribution of bradycardia before embarking on cardiac pacing in patients with suspected or certain neurally-mediated syncope presenting with frequent or traumatic syncopal episodes

Class III:

ECG monitoring is unlikely to be useful in patients who do not have the clinical or ECG features suggesting an arrhythmic syncope as those listed in the tables above titled "Clinical Features Suggestive of Specific Causes of Real or Apparent Loss of Consciousness" and "ECG Abnormalities Suggesting an Arrhythmic Syncope," and therefore it should not be performed.

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 no rhythm variation.
- In the absence of such correlations additional testing is recommended with the possible exception of:
    - Ventricular pauses longer than 3 seconds when awake
    - Periods of Mobitz II or third-degree atrioventricular block when awake
    - Rapid paroxysmal ventricular tachycardia.

Class II:

- Presyncope may not be an accurate surrogate for syncope in establishing a diagnosis and, therefore, therapy should not be guided by presyncopal findings.

Electrophysiological Testing

Indications

Class I:

- An invasive electrophysiological procedure is indicated when the initial evaluation suggests an arrhythmic cause of syncope such as those listed in the tables above titled "Clinical Features Suggestive of Specific Causes of Real or Apparent Loss of Consciousness" and "ECG Abnormalities Suggesting an Arrhythmic Syncope" (in patients with abnormal ECG 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 corrected sinus node recovery time (CSNRT)
    - Bifascicular block and:
        - A baseline His-ventricle (HV) interval of $\geq$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
        - Induction of sustained monomorphic ventricular tachycardia
        - Induction of rapid supraventricular arrhythmia which reproduces hypotensive or spontaneous symptoms

Class II:

- The diagnostic value of an electrophysiological study is less well established in case of:
    - His-ventricle interval of >70 ms but <100 ms
    - Induction of polymorphic ventricular tachycardia or ventricular fibrillation in patients with Brugada syndrome, arrhythmogenic right ventricular dysplasia and patients resuscitated from cardiac arrest

Class III:

- The induction of polymorphic ventricular tachycardia or ventricular fibrillation in patients with ischaemic or dilated cardiomyopathy has a low predictive value.

Adenosine Triphosphate (ATP) Test

The test requires the rapid injection of a 20 mg bolus of ATP during electrocardiographic monitoring. Asystole lasting more than 6 seconds, or AV block lasting more than 10 seconds, is considered abnormal. ATP testing produces an abnormal response in some patients with syncope of unknown origin, but not in controls. ATP testing identifies a group of patients with otherwise unexplained syncope with definite clinical features and benign prognosis but possibly heterogeneous mechanism of syncope. Thus, specific treatment should be postponed until a definite mechanism of syncope can be obtained (Class II).

Ventricular Signal-Averaged Electrocardiogram, T Wave Alternans

There is general agreement that ventricular signal-averaged electrocardiogram and T-wave alternans are not diagnostic of the cause of syncope. In patients with syncope and no evidence of structural heart disease, these techniques may be

useful for guiding the use of electrophysiological studies. Their systematic use is not recommended (Class III).

Exercise Testing

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 2 second- or third degree AV block develop during exercise even without syncope.

Cardiac Catheterization and Angiography

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 of the cause of syncope.

Neurological and Psychiatric Evaluation

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 pseudo-syncope or if true syncope is due to psychiatric medication, which may need to be altered.

Class III:

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

Treatment

General Principles

In general, initial treatment (e.g., education and reassurance) is sufficient.

Additional treatment may be necessary in high-risk or high-frequency settings when:

- Syncope is very frequent (e.g., alters the quality of life)
- Syncope is recurrent and unpredictable (absence of premonitory symptoms) and exposes patients at "high risk" of trauma
- Syncope occurs during the prosecution of a "high risk" activity (e.g., driving, machine operator, flying, competitive athletics)

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

It is valuable to assess the relative contribution of cardioinhibition and vasodepression before embarking on 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.

Neurally-Mediated (Reflex) Syncope

Management Recommendations

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 head-up tilt sleeping (>10 degrees) in posture-related syncope
- Tilt training in patients with vasovagal syncope
- Isometric leg and arm counter-pressure manoeuvres in patients with vasovagal 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

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

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

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

Class I:

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

Special Issues in Evaluating Patients with Syncope

Need for Hospitalization

When to Hospitalize a Patient with Syncope

For diagnosis:

- Suspected or known significant heart disease
- Those ECG abnormalities suspected of arrhythmic syncope (see the table above titled "ECG Abnormalities Suggesting an Arrhythmic Syncope")
- Syncope occurring during exercise
- Syncope causing severe injury
- Family history of sudden death
- Other categories that occasionally may need to be admitted:
    - Patients without heart disease but with sudden onset of palpitations shortly before syncope, syncope in supine position, and patients with frequent recurrent episodes
    - Patients with minimal or mild heart disease when there is high suspicion of cardiac syncope

For treatment:

- Cardiac arrhythmias as cause of syncope (see the section titled "Initial Evaluation," above)
- Syncope due to cardiac ischaemia (see the section titled "Initial Evaluation," above)
- Syncope secondary to the structural cardiac or cardiopulmonary diseases (see Table 1.1 titled "Causes of Syncope" in the original guideline document)
- Cardioinhibitory neurally-mediated syncope when pacemaker implantation is planned

Syncope in the Older Adult

Class I:

- Accurate history, where possible, with witness observation and details of medications
- Morning orthostatic blood pressure measurements and supine and upright carotid sinus massage are integral to the initial evaluation unless contraindicated.
- The evaluation of mobile, independent, cognitively normal older adults is as for younger individuals.
- In frailer older adults evaluation should be modified according to prognosis.

Syncope in Paediatric Patients

Class I*:*

- Syncope in childhood is common. The vast majority of episodes are benign and are due to neurally-mediated syncope. Only a minority are due to some potentially life-threatening causes.

- The diagnosis and differentiation of benign from more serious causes is made primarily by the history and standard ECG.
- The mainstay of management of neurally-mediated syncope in childhood includes reassurance, education, behaviour modification, salt, and increased fluid. Even in the instance of cardioinhibitory syncope with an asystolic response, pacemakers should be avoided whenever possible.

Syncope Management Facilities

- A cohesive, structured care pathway-either delivered within a single syncope facility or as a more multi-faceted service-is recommended for the global assessment of the patient with syncope.
- Experience and training in key components of cardiology, neurology, emergency and geriatric medicine are pertinent.
- Core equipment for the facility include surface ECG recording, phasic blood pressure monitoring, tilt table testing equipment, external and internal (implantable) ECG loop recorder systems, 24-hour ambulatory blood pressure monitoring, 24-hour ambulatory ECG, and autonomic function testing.
- Preferential access to other tests or therapy for syncope should be guaranteed and standardized.
- The majority of syncope patients should be investigated as out-patients or day cases.

Comment

This Task Force has the benefit of further publications that are relevant. Data suggest that the risk for car accident related to syncope is low. Repeat tilt testing to assess any therapy probably has no predictive value. There is no evidence that allowing three asymptomatic months to elapse provides any confirmation that attack will not recur. To date, the evidence in favour of drug therapy remains unconvincing. Neurological review in syncopal patients is of little value. Modified disqualifying criteria according to 2004 Syncope Task Force are also reported in table 4.3 in the original guideline document.

Definitions:

Levels of Evidence

A. Data derived from multiple randomised clinical trials or meta-analyses
B. Data derived from a single randomised clinical trial or large nonrandomised studies
C. Consensus of opinion of the experts and/or small studies, retrospective studies, registries

When not expressed otherwise, evidence is of type C.

Classes of Recommendations

The strength of recommendations has been ranked as follows:

Class I: Evidence and/or general agreement that a given diagnostic procedure/treatment is beneficial, useful, and effective

Class II: Conflicting evidence and/or a divergence of opinion about the usefulness/efficacy of the treatment

- **Class IIa**: Weight of evidence/opinion is in favour of usefulness/efficacy.
- **Class IIb**: Usefulness/efficacy is less well established by evidence/opinion.

Class III*: Evidence or general agreement that the treatment is not useful/effective and in some cases may be harmful

*Use of Class III is discouraged by the European Society of Cardiology.

CLINICAL ALGORITHM(S)

An algorithm is provided in the original guideline document for the evaluation of syncope.

EVIDENCE SUPPORTING THE RECOMMENDATIONS

TYPE OF EVIDENCE SUPPORTING THE RECOMMENDATIONS

This document reviews the few randomized-controlled trials that have been reported and studies of non-randomized design.

BENEFITS/HARMS OF IMPLEMENTING THE GUIDELINE RECOMMENDATIONS

POTENTIAL BENEFITS

- Accurate diagnosis of syncope
- In general, treatment of syncope may result in prevention of syncopal recurrences, reduction of mortality risk, prevention of symptom recurrence and associated injuries, and an improved quality of life.

POTENTIAL HARMS

Carotid Sinus Massage

The main complications of carotid sinus massage are neurological. Rarely, carotid massage may elicit self-limited atrial fibrillation of little clinical significance.

Head-up Tilt Test, With or Without Drug Provocation

- Prolonged loss of consciousness
- Atrial fibrillation can be induced during or after a positive tilt test and is usually self-limited.

- Case reports have documented life-threatening ventricular arrhythmias with isoprenaline in the presence of ischaemic heart disease or sick sinus syndrome.
- Minor side effects are common and include palpitations with isoprenaline and headache with nitroglycerin.

Adenosine Triphosphate (ATP) Test

Side effects are generally mild. Facial flush, shortness of breath, and chest pressure are the most frequently reported effects. Lightheadedness or syncope may also occur but are "expected." Rarely, short-duration, self-limiting atrial fibrillation is initiated.

Vasoconstrictors

- Major adverse central nervous system effects
- Hypertension

Volume Expanders

Hypertension

Implanted Devices, Such as Pacemakers

Infrequently, implantable pacing systems have been associated with provoking near-syncope or syncope.

Anti-arrhythmic Agents

Can produce side effects and carry a pro-arrhythmic risk

Subgroups Most Likely to be Harmed

Carotid massage should be avoided in patients with previous transient ischaemic attacks or stroke within the past 3 months or in patients with carotid bruits.

CONTRAINDICATIONS

CONTRAINDICATIONS

Due to possible bronchospastic reactions, the adenosine triphosphate (ATP) test is contraindicated in patients with known asthma. Due to the risk of coronary steal, the test is also contraindicated in patients with significant coronary disease.

QUALIFYING STATEMENTS

QUALIFYING STATEMENTS

- The literature on syncope testing is largely composed of case series, cohort studies, or retrospective analyses of already existing data. The impact of testing on guiding therapy and reducing syncopal recurrences is difficult to discern from these methods of research without randomization and blinding. Because of these issues, the guideline panel performed full reviews of the literature for diagnostic tests but did not use pre-defined criteria for selection of articles to be reviewed. Additionally, the panel did not feel that an evidence-based summary of the literature was possible.
- In assessing treatment of syncope, the guideline document reviews the few randomised-controlled trials that have been reported. For various diseases and disorders with known treatments (e.g., orthostatic hypotension, sick sinus syndrome) those therapies are reviewed and recommendations are modified for patients with syncope. Most studies of treatment have used a non-randomized design and many even lack a control group. The interpretation of these studies is very difficult but their results were used in summary recommendations of treatment.

IMPLEMENTATION OF THE GUIDELINE

DESCRIPTION OF IMPLEMENTATION STRATEGY

An implementation strategy was not provided.

IMPLEMENTATION TOOLS

Clinical Algorithm
Foreign Language Translations
Personal Digital Assistant (PDA) Downloads
Pocket Guide/Reference Cards
Slide Presentation

For information about availability, see the "Availability of Companion Documents" and "Patient Resources" fields below.

INSTITUTE OF MEDICINE (IOM) NATIONAL HEALTHCARE QUALITY REPORT CATEGORIES

IOM CARE NEED

Getting Better
Living with Illness

IOM DOMAIN

Effectiveness
Patient-centeredness

IDENTIFYING INFORMATION AND AVAILABILITY

BIBLIOGRAPHIC SOURCE(S)

Brignole M, Alboni P, Benditt DG, Bergfeldt L, Blanc JJ, Bloch Thomsen PE, van Dijk JG, Fitzpatrick A, Hohnloser S, Janousek J, Kapoor W, Kenny RA, Kulakowski P, Masotti G, Moya A, Raviele A, Sutton R, Theodorakis G, Ungar A, Wieling W. Guidelines on management (diagnosis and treatment) of syncope--update 2004. Europace 2004 Nov;6(6):467-537. [399 references] PubMed

ADAPTATION

Not applicable: The guideline was not adapted from another source.

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2001 Aug (revised 2004 Nov)

GUIDELINE DEVELOPER(S)

European Society of Cardiology - Medical Specialty Society

SOURCE(S) OF FUNDING

European Society of Cardiology

GUIDELINE COMMITTEE

Task Force on Syncope

European Society of Cardiology (ESC) Committee for Practice Guidelines

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FINANCIAL DISCLOSURES/CONFLICTS OF INTEREST

The European Society of Cardiology (ESC) Committee for Practice Guidelines (CPG) supervises and coordinates the preparation of new Guidelines and Expert Consensus Documents produced by Task Forces, expert groups or consensus panels. The chosen experts in these writing panels are asked to provide disclosure statements of all relationships they may have which might be perceived as real or potential conflicts of interest. These disclosure forms are kept on file at the European Heart House, headquarters of the European Society of Cardiology. The Committee is also responsible for the endorsement of these Guidelines and Expert Consensus Documents or statements.

GUIDELINE STATUS

This is the current release of the guideline.

This guideline updates a previous version: Brignole M, Alboni P, Benditt D, Bergfeldt L, Blanc JJ, Bloch Thomsen PE, van Dijk JG, Fitzpatrick A, Hohnloser S, Janousek J, Kapoor W, Kenny RA, Kulakowski P, Moya A, Raviele A, Sutton R, Theodorakis G, Wieling W. Guidelines on management (diagnosis and treatment) of syncope. Eur Heart J 2001 Aug;22(15):1256-306.

GUIDELINE AVAILABILITY

Electronic copies: Available from the European Society of Cardiology (ESC) Web site.

Print copies: Available from Elsevier Publishers Ltd. 32 Jamestown Road, London, NW1 7BY, United Kingdom. Tel +44.207.424.4200/ Tel: +44 207 424 4389; Fax: +44 207 424 4433; e-mail: gr.davies@elsevier.com; Web site: www.escardiocontent.org.

AVAILABILITY OF COMPANION DOCUMENTS

The following is available:

- Brignole M, Alboni P, Benditt DG, Bergfeldt L, Blanc JJ, Bloch Thomsen PE, Gert van Dijk J, Fitzpatrick A, Hohnloser S, Janousek J, Kapoor W, Anne Kenny R, Kulakowski P, Masotti G, Moya A, Raviele A, Sutton R, Theodorakis G, Ungar A, Wieling W. Guidelines on management (diagnosis and treatment) of syncope - update 2004. Executive summary. Eur Heart J. 2004 Nov;25(22):2054-72. Electronic copies: Available in Portable Document Format (PDF) from the European Society of Cardiology (ESC) Web site.
- Management of syncope. Pocket guidelines. Available in English, Spanish, and Italian. An order form for ESC pocket guidelines is available in Portable Document Format (PDF) from the European Society of Cardiology (ESC) Web site. Also available for PDA download from the ESC Web site.
- Management of syncope. Slide set. Available from the European Society of Cardiology (ESC) Web site.

PATIENT RESOURCES

None available

NGC STATUS

This NGC summary was completed by ECRI on April 2, 2002. This NGC summary was updated by ECRI on March 4, 2005. The updated information was verified by the guideline developer on July 20, 2005.

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