# A Review of the State of the Art in the Diagnosis and Treatment of Recurrent Syncope

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## 1. INTRODUCTION

Syncope is the sudden loss of consciousness resulting from a temporary impairment of cerebral blood flow. Although recovery is always rapid, a syncopal attack is also always accompanied by the loss of postural tone, and hence presents a real danger. Accounting for up to 3% of emergency room visits and 6% of hospital admissions [M1], patients with recurrent syncope endure a quality of life comparable to sufferers of rheumatoid arthritis or chronic lower back pain. Appendix A provides an overview of the disease on a single page [O8].

## 2. HISTORICAL BACKGROUND

Syncope has a rich history: having fascinated people for centuries, it has elicited myriad speculations on its causes. Recent history has refined these speculations significantly, and a concise timeline of the events leading up to today's state of the art runs as follows (from [O10] and other sources)[1]:

FIRST PHASE: *Focusing on etiology; the pathophysiology of vasovagal syncope; and the natural history of various entities*

1773: J. Hunter suggests vasodilation plays an important role.

1888: M. Foster deduces that inadequate cerebral blood flow is key.

1907: W. Gowers recognizes the concurrence of vasodilatory and bradycardic components, and then coins the term "vasovagal".

1932: Sir Thomas Lewis extends Gowers' findings while coining the term "vasovagal syncope" [M21].

1940s: Head upright tilt table testing begins to explore the body's responses to changes in position.

WATERSHED: *In the early 1980s, several studies conclude that syncope's cause is often not established [M25].*

SECOND PHASE: *Focusing on pragmatic approaches*

Early 1980s: Subgroups with high mortalities are identified to tackle this new perspective practically.

Mid 1980s: Much electrophysiological testing leads to an understanding of the roles - and limitations - of syncope tests; plus, studies show that syncope in the elderly is often a complicated product of medications, comorbid diseases, and physiological changes.

[1] The division into phases represents the author's interpretation of events and is not corroborated.

1986 to early 1990s: Tilt table testing is proved to be an excellent diagnostic tool for syncope patients.

1990s: Various international symposia are held on the topic of syncope or its subtopics. Panels are convened to aim for consensus on controversial aspects.

1992: The Vasovagal International Study (VASIS) proposes a three-pronged classification scheme for vasovagal syncope [M7A]. This proves popular but minor modifications are suggested [M7B, M7C].

August 2001: An international "Task Force on Syncope" is created by the European Society of Cardiology, which then publishes "Guidelines on management (diagnosis and treatment) of syncope" [M13A].

March 2002: The intent of this report is to summarize today's prevalent techniques.

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# 3. CLASSIFICATION AND PATHOLOGY

Syncope is a symptom rather than a discrete pathological entity; its causes are many. Appendix B lists over 100 causes found in the literature. A useful approach [O10] is to divide these causes into three broad classes, for - in keeping with the philosophy of the "second phase" identified in the previous section - prognostic reasons:

1. Cardiovascular causes (25-30% of patients; usually the most dangerous)
2. Non-cardiovascular causes (20-40%)[2]
3. Unknown causes (30-50%; often more benign)

In many studies, the percentages vary considerably beyond the ranges delineated above, owing to the diverse selection criteria applied to obtain patients. However, it is becoming popular to reduce the percentage of "unknown" causes, as diagnostic methods improve. In particular, tilt testing and carotid sinus massage have proved to be two important techniques in reducing the percentage of "unknown" syncope.

More specific classification schemes subdivide syncope into finer groups; for example, as in the following [M13A]:

1. Neurally mediated reflex syncopal syndromes
2. Orthostatic
3. Cardiac arrhythmias as primary cause
4. Structural cardiac or cardiopulmonary disease
5. Cerebrovascular

There exists a consensus that the etiology of syncope lies in transient cerebral hypoperfusion. It has been shown that 6 to 8 seconds of cessation of cerebral blood flow [M22], or a systolic blood pressure falling below 60 mmHg [M23] are associated with syncope. However, there is still uncertainty regarding the mechanisms behind cerebral hypoperfusion. The following is a brief overview of the suspected etiologies of the most common types of syncope.

## NEURALLY MEDIATED SYNCOPE

Proposed etiologies for various types of neurally mediated syncope are illustrated in Figure 1 [M5]. The second box down on the left lists "head-up tilt" syncope, which other authors consider to be a form of vasovagal syncope. The essential problem in these patients is believed to be hypersensitive cardiac mechanoreceptors. Vasovagal syncope, the most common type of neurally mediated syncope, manifests itself as follows:

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[2] Vasovagal syncope is occasionally considered "cardiovascular", and it stakes a worthy claim to that category. However, it can also be considered "non-cardiovascular", and in fact is more wisely classified as such. Its low mortality rates suit it better to that category than the high-mortality "cardiovascular" group.

1.Person stands or is tilted upright passively.
2.Roughly a quarter of the person's blood is redistributed in response to this orthostatic stress. Venous pooling occurs in the legs.
3.Decreased venous return is an obvious result.
4.Tachycardia, vasoconstriction, and increased inotropy attempt to compensate - as they should. *Everything up to this point represents a more or less normal compensatory reaction to orthostatic stress.*
5.However, in vasovagal patients, the forceful ventricular contractions activate hypersensitive cardiac mechanoreceptors, triggering an afferent pathway consisting of unmyelinated left ventricular vagal C fibres.
6.This problem, known as the Bezold-Jarisch reflex, ultimately reduces sympathetic tone and increases parasympathetic tone.
7.These changes in tone result in vasodilation and bradycardia, to elicit hypotension.
8. When cerebral hypoperfusion falls sufficiently, syncope results.

Some experiments, including those performed with atropine to suppress vagal tone [L15], challenge this theory, but it currently remains popular.

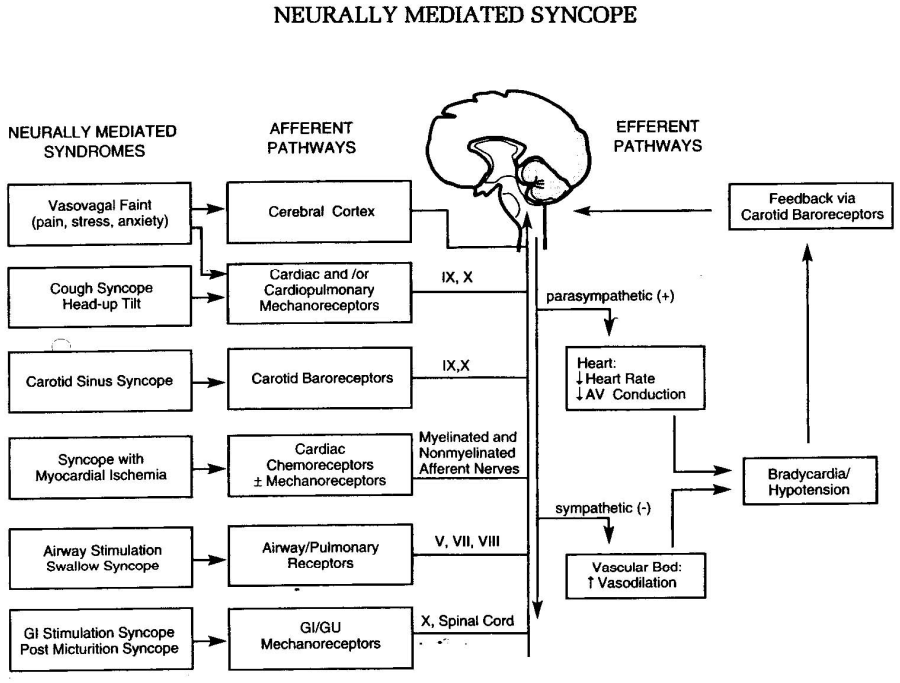


**Figure 1.** *Schematic depicting the most important afferent and efferent pathways and feedback loops for the principal neurally mediated syndromes. Current understanding of these pathways, their multiple interactions, and the involved neurotransmitters remains limited. Roman numerals refer to standard designations for the cranial nerves. A (+) sign means the effect is increased, whereas a (−) sign signifies diminished effect. GI = gastrointestinal; GU = genitourinary.*

ORTHOSTATIC HYPOTENSION

If neurally mediated syncope is caused by an oversensitive autonomic nervous system, orthostatic hypotension often results from a debilitated one. Orthostatic hypotension can be caused by the body's failure to react to the proper extent during step 4 above. (For example, heart rate does not increase to the point required, or more commonly, vasoconstriction does not occur enough.) The patient then "fast-tracks" to step 8 and loses postural tone.

It should now be clear why recurrent syncope in the elderly is most likely to be of the orthostatic type. Elderly patients often suffer from attenuated autonomic nervous systems: for example, altered cerebral autoregulation, volume regulation, and baroreflex sensitivity. Second, many elderly take medications, with the not uncommon side effect of exacerbating orthostatic hypotension. (For instance, anti-hypertension drugs can directly oppose the vasoconstriction attempted in step 4 above.)

Besides **autonomic failure** (primary, secondary, or drugs- or alcohol-related), another cause of orthostatic hypotension is **volume depletion** (haemorrhage, diarrhoea, Addison's disease, etc). Patients with any form of hypovolemia are prone to lower cerebral perfusion for obvious reasons.

## CARDIAC ARRHYTHMIA / STRUCTURAL HEART DISEASE

The etiology of cardiac-related syncope is often multifactorial, although in general, impaired cardiac output prevents the heart from matching the brain's vascular demands at certain times. The individual factors resulting from the cardiac difficulties may include arrhythmia, compromised haemodynamics, and neurally mediated problems. For example, the rate of the arrhythmia, the status of left ventricular function, and the adequacy of vascular compensation - including the potential impact of neural reflex effects - are all important.

Five of the most common cardiac causes of syncope, in no particular order, are [O10]:

- AV conduction system disease / block
- Sinus pauses / bradycardia
- Hypertrophic cardiomyopathy
- Aortic stenosis
- Atrial myxoma

## CEREBROVASCULAR (STEAL SYNDROMES)

In steal syndromes, blood is diverted from its expected path. Steal syndromes occur when the arterial circulation to the arm is clogged, thereby shunting blood through the cerebrovascular system - a system which then necessarily assumes the responsibility of supplying the arm, causing insufficient cerebral perfusion. The most common affliction is subclavian steal, which occurs especially during upper arm exercise. A proposed mechanism is the following:

1. Low pressure exists in the subclavian artery.
2. Retrograde flow occurs in the ipsilateral vertebral artery.
3. Cerebral blood flow is decreased.
4. Syncope occurs.

## CONTROVERSIAL CLASSIFICATIONS

It has become doubtful that vertebro-basilar or carotid TIAs (transient ischaemic attacks) are responsible for true syncope [M13A], but many authors include them as a source [M11A, O10, M14]. Basilar migraines, metabolic problems (such as hypoglycaemia or hyperventilation), intoxication, cataplexy, and psychogenic syncope all have the same problem [M13A, M11A, O10]. Today, few believe that drop attacks or epileptic seizures should be classified as syncopal.

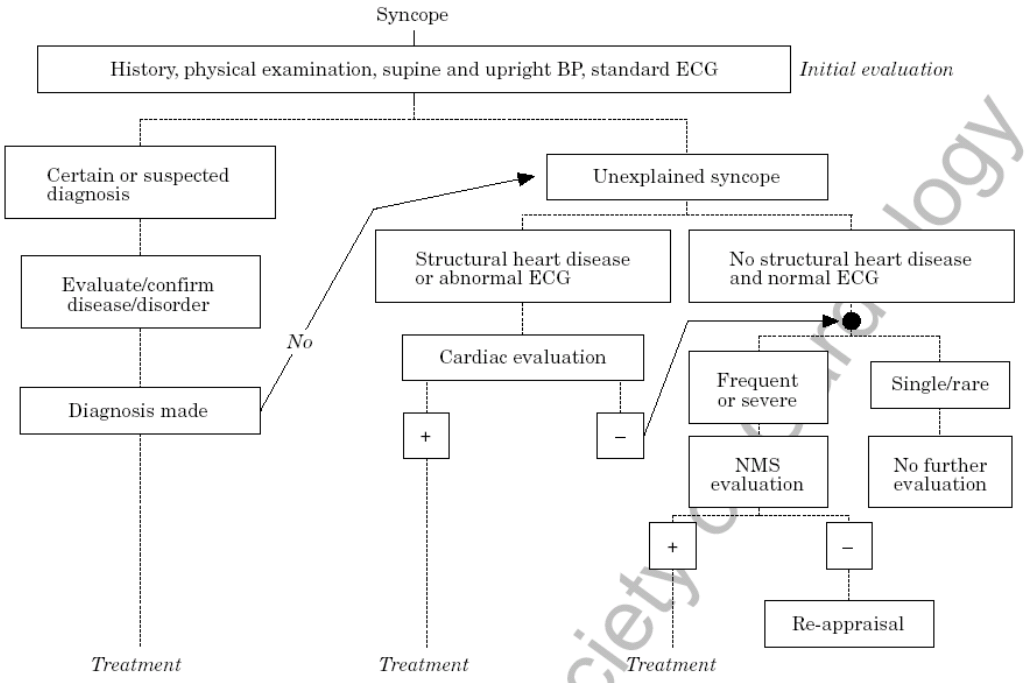


***Figure 2*** **The figure shows the flow diagram proposed by the Task Force on Syncope of an approach to the evaluation of syncope. BP=blood pressure; ECG=electrocardiogram; NMS=neurally mediated syncope.**

| **If the patient has?** | **The first diagnostic step is ?** |
|---|---|
| Suspected heart disease | Echocardiography and prolonged electrocardiographic monitoring (if non-diagnostic, electrophysiological studies should follow) |
| Chest pain suggestive of ischaemia | Stress testing, echocardiography, and electrocardiographic monitoring |
| A young age, without suspicion of heart or neurological disease | Tilt testing |
| Syncope during neck turning | Carotid sinus massage |
| Syncope during effort | Echocardiography and stress testing |

***Table 1: Conditions overriding Figure 2.***

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# 4. DIFFERENTIAL DIAGNOSIS

Numerous flowcharts have been proposed to diagnose the various types of syncope in preparation for treatment. A very recent but generic flowchart was compiled by the Task Force on Syncope [M13A] and appears as Figure 2. Some overriding points to accompany the flowchart are outlined in Table 1. The following is a discussion of the primary diagnostic methods for syncope.

## INITIAL EVALUATION

It is widely accepted that a thorough patient history is the most important component of syncope diagnosis, identifying a potential cause of syncope in nearly half of patients. 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. The results of the initial evaluation are diagnostic in certain situations.

**Vasovagal syncope** is diagnosed if precipitating events such as fear, severe pain, emotional distress, connection to instrumentation, or prolonged standing are associated with typical prodromal symptoms. Tilt table testing can

further classify the type of syncope as Type I, IIA, IIB, or III [M7A], however, in the elderly, "there is no evidence to support the use of head-up tilt studies as part of the initial[3] evaluation" [M13A].

**Situational syncope** is easily diagnosed if syncope occurs during or immediately after urination, defaecation, coughing or swallowing. **Orthostatic syncope** is diagnosed when systolic blood pressure drops >20 mmHg, or falls below 90 mmHg, upon standing after lying for five minutes supine. **Cardiac ischaemia-related syncope** is diagnosed when symptoms are present with ECG evidence of acute ischaemia with or without myocardial infarction. **Arrhythmia-related syncope** is diagnosed by ECG if there exists:

-Sinus bradycardia (<40 beats per min), repetitive sinoatrial blocks, or sinus pauses >3 s
-Mobitz II 2nd or 3rd-degree atrioventricular block
-Alternating left and right bundle branch block
-Rapid paroxysmal supraventricular tachycardia or ventricular tachycardia
-Pacemaker malfunction with cardiac pauses

## ECHOCARDIOGRAPHY

Although echocardiography is useful to ascertain patient risk when information about the type and severity of heart disease can be gleaned, this test actually only makes a final diagnosis in a few cases (e.g. severe aortic stenosis and atrial myxoma).

## CAROTID SINUS MASSAGE

Before performing carotid sinus massage (CSM), baseline measurements of HR and BP should first be taken. Then the right carotid artery is firmly massaged for 5-10 s at the anterior margin of the sternocleo-mastoid muscle at the level of the cricoid cartilage. Two common but different approaches to CSM are:

1.Five seconds of massage in the supine position.
2.Ten seconds of massage supine, then massage while upright if not successful.

Method 1 predictably experiences lower positive rates; just ignoring the upright position misses the diagnosis in about a third of cases [M13A.78-9]. The Task Force favours Method 2, and the Falls Clinic's protocol is similar to it as well. Contrasting the Falls Clinic with the recently published **Newcastle protocol** for CSM [J3]:

*Angle of tilt*
J3 recommends that "the patient should lie supine for a minimum of 5 minutes", whereas at the Falls Clinic, CSM is sometimes attempted while upright (70 degrees). J3 recommends performing CSM at a tilted position only after the supine position fails, but recognizes that 30% of subjects will experience a positive response in the latter and not the former.

*Length of time*
J3 recommends 5 seconds of massage, acknowledging that "some authors recommend continuing CSM for seconds if there is no asystole after 5 seconds, but this is not our practice". At the Falls Clinic, CSM lasts more than 5 seconds and sometimes is 10 seconds.

*Post-procedure rest period*
J3 recommends 10 minutes of supine rest following the procedure, which in their experience has "reduced neurological complication rates". At the Falls Clinic, a rest is granted following CSM, but can last much less than 10 minutes.

## HEAD UPRIGHT TILT TABLE TESTING

This technique has excellent specificity and sensitivity when performed correctly. A general outline of a test is:

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[3] The word *initial* is important here, for there is of course ample evidence of the usefulness of head-up tilt testing.

-A passive, supine phase of 20 to 45 minutes
-A tilt to 60 to 70 degrees (some say as high as 80), for about 45 minutes
-The test ends earlier if syncope occurs; patient should then be immediately returned to supine position to recover

Two well-known protocols are the Westminster protocol [M24] and, more recently, the Newcastle protocol [J3]. In general, J3 appears to be in remarkable agreement with the other tilt procedures, but areas of contention do exist, including:

*Fasting*
J2 suggests without explanation that "patients should fast for at least 3 hours before testing, or overnight in preparation for early morning studies". However, the Newcastle protocols disagree: "Patients, in particular those over 60 years old, should be fasted for no more than two hours before the procedure in order to avoid the confounding effects of relative dehydration and hypotension." This is backed by references to Benditt and Grubb.

As J2 and J3 both come from highly respected contributors to the field (Sutton & Bloomfield on one side, vs Kenny et al who then reference Benditt & Grubb), the jury remains "out" on this point. However, interestingly Benditt and Kenny later (in 2001) sat on the international Task Force on Syncope which concluded that "patients should fast for at least 2 h before the test"!

*Drugs*
J3 maintains reasonably that "Where practicable, drugs affecting the cardiovascular and autonomic nervous systems and those likely to affect intravascular volume should be discontinued for at least five half lives before the test...", and a number of other papers betray their aversion to caffeine or nicotine during the test. However, tea is permitted during testing at the Falls Clinic here in Oxford. Perhaps an argument can be made that elderly patients are not affected by tea as much as their medications, but this is uncertain.

Very often, experimenters administer drugs such as isoproterenol or nitroglycerin during a tilt test to increase the rate of positive response. Since this is not the practice at the Falls Clinic, such drugs will not be discussed in detail in this report.

## ELECTROCARDIOGRAPHIC MONITORING

Electrocardiography is of two general types:

*Non-invasive: Holter monitoring, external ECG event monitoring*
When there is a high pre-test probability of identifying an arrhythmia, syncope patients with structural heart disease should undergo Holter monitoring. However, external ECG event monitoring should be used when the mechanism of syncope remains unclear after full evaluation.

*Invasive: ECG event monitoring via an Implantable Loop Recorder*
This is a rapidly growing alternative which helped a recent Miss America win her competition. Olshansky [M10A] suspects value in combining the ILR with measurement of brain activity (electroencephalography), cerebral blood flow, hormonal and blood sugar changes, and, above all, haemodynamic response.

When a correlation between syncope and an electrocardiographic abnormality (brady- or tachyarrhythmia) is detected, ECG monitoring can be considered diagnostic. Second, when there exists a correlation between syncope and sinus rhythm, arrhythmic causes are excluded. In the absence of such correlations, additional testing is usually warranted.

## ELECTROPHYSIOLOGICAL TESTING

Transoesophageal electrophysiological study can screen for supraventricular tachycardia or evaluate sinus node dysfunction. Invasive techniques use endocardial and/or epicardial electrical stimulate-and-record methods to betray abnormalities. Electrophysiological study with programmed electrical stimulation is a good diagnostic

test in patients with coronary artery disease, markedly depressed cardiac function, or simply unexplained syncope. Patients with bifascicular block often benefit from types of electrophysiological study too.

M13A recommends the following protocol as a minimum electrophysiological test when one is needed:

- 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 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 and 140 or 150 beats/min), with up to two extrastimuli.

- Assessment of supraventricular arrhythmia inducibility by any atrial stimulation protocol.

### OTHER TESTS

Other tests include the ATP test (diagnostic value remains to be validated); ventricular signal-averaged electrocardiogram (not recommended by the Task Force); exercise testing (for exertion syncope); cardiac catheterisation and angiography (for suspected myocardial ischaemia); and neurological and psychiatric evaluation.

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## 5. TREATMENT

When deciding on treatment, two important factors to consider are the frequency of syncope occurrence, and the public health risk. In other words, patients who do not suffer from frequent syncope can enjoy minimal treatment, but pilots and truck drivers should be carefully attended to regardless.

### NEURALLY MEDIATED REFLEX SYNCOPAL SYNDROMES

An obvious treatment is simply the physician's explaining the risk of the syndrome, and reassuring the patient about the prognosis in the case of vasovagal syncope. Equally obvious is avoidance of trigger events as much as possible (e.g. emotional upset, causal situation in situational syncope, etc.). Reducing or eliminating a hypotensive drug treatment for a concomitant condition can help. Cardiac pacing can help patients with cardioinhibitory or mixed carotid sinus syndrome, as well as those with cardioinhibitory vasovagal syncope with a high frequency, those with severe physical injury, and the elderly. Volume expansion by salt supplements, an exercise programme or head-up tilt sleeping (sleeping at an angle in excess of ten degrees) can assist posture-related syncope. Finally, "tilt training" in patients with vasovagal syncope may be useful.

### ORTHOSTATIC HYPOTENSION

As this is most often caused by drug-induced autonomic failure, an obvious treatment is to eliminate, diminish, or replace the drugs in question. Of course, for some drugs, especially vasodilators and diuretics, this is difficult to do. However, educating the patient on the various circumstances that influence systolic blood pressure (standing, heat, exertion, large meals, etc.), and developing strategies to combat an individual's problems (e.g., encouraging small frequent meals, discussing leg crossing and squatting, etc.) is an easy treatment. Higher salt intake, fluid intake, and the volume-expander fludrocortisone are often advised, while support stockings and abdominal binders can reduce vascular pooling. The newer drug midodrine increases peripheral resistance and reduces gravitational downward displacement of central volume.

CARDIAC ARRHYTHMIAS AS PRIMARY CAUSE

The severity, nature, and setting of the arrhythmia must be considered. Three major cardiac arrhythmias and their corresponding treatments are as follows:

*Sinus node dysfunction:*
Pacemaker therapy is very effective, but where possible, offending drugs (e.g. cardiac glycosides, beta blockers) should be eliminated or replaced.

*AV conduction system disease (e.g., Mobitz type II block):*
Pacemaker therapy is very popular; certain AV blocks merit atropine or isoproterenol.

*Paroxysmal supraventricular and ventricular tachycardias:*
Methods include transcatheter ablation, discontinuing offending drugs, amiodarone, and ICDs (implantable cardioverter-defibrillators).

STRUCTURAL CARDIAC OR CARDIOPULMONARY DISEASE

Treatment is not always possible, especially for patients suffering from primary pulmonary hypertension or restrictive cardiomyopathy. However, when the problem is myocardial ischaemia, pharmacological therapy and revascularization are usually appropriate. For other problems, in general treatment should be aimed directly at improving the specific structural lesion or its consequences.

VASCULAR STEAL SYNDROMES

Direct corrective angioplasty or surgery is ordinarily effective for subclavian steal syndrome.

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# 6. CONCLUSION AND RELATION TO THE SOFTWARE MONITOR

As of March 2002, the classification of the various types of syncope is possibly reaching a sort of maturity. This represents a significant improvement over the situation a mere twenty years ago, when classification schemes were still inchoate.

The diagnosis and treatment of recurrent syncope remains a controversial endeavour, although recent attempts to form consensus have helped streamline such procedures to a certain extent. Moreover, updates on the 2001 Task Force are scheduled for later this year.

The Software Monitor has the potential to uncover new etiological pathways or, alternatively, to pioneer a novel treatment strategy. The current model monitors the following vital signs: ECG, blood pressure (sphygmomanometer cuff), beat-by-beat blood pressure (Finapres), oxygen saturation, and respiration.[4] The state-of-the-art syncope diagnostic protocols often involve the first two or three of these (ECG and blood pressure). Hence, out of the five types of syncope enumerated on page 2, the Software Monitor can assist with the diagnosis of the first three.

In addition to simply measuring primary parameters, the Software Monitor can also derive secondary parameters, including pulse transit time and various heart rate variability indices (the LF/HF ratio, sympathetic vs parasympathetic coefficients of the deBoer model, cross-correlation between blood pressure and heart rate, non-linear indicators, and so on). This added intelligence is a major advantage of the instrument, and will play a key role as the Software Monitor tackles the problem of recurrent syncope.

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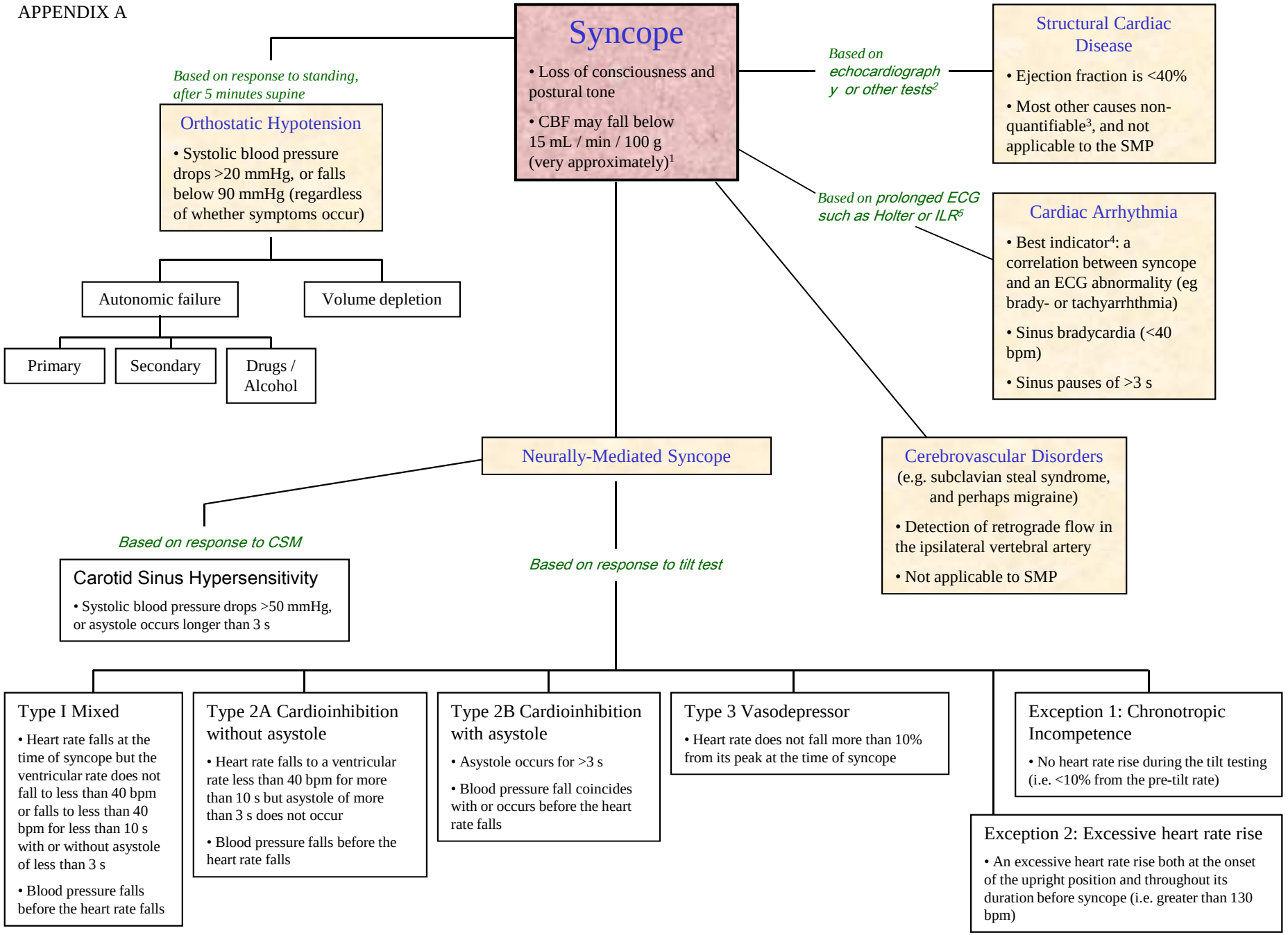
[4] Within the medium-term future, near-infrared spectroscopy will be added to permit the monitoring of cerebral blood flow and cerebral blood volume.

APPENDIX A


Syncope
• Loss of consciousness and postural tone
• CBF may fall below 15 mL / min / 100 g (very approximately)[1]
Based on response to standing, after 5 minutes supine
Orthostatic Hypotension
• Systolic blood pressure drops >20 mmHg, or falls below 90 mmHg (regardless of whether symptoms occur)
Autonomic failure
Volume depletion
Primary
Secondary
Drugs / Alcohol
Based on echocardiography or other tests[2]
Structural Cardiac Disease
• Ejection fraction is <40%
• Most other causes non-quantifiable[3], and not applicable to the SMP
Based on prolonged ECG such as Holter or ILR[5]
Cardiac Arrhythmia
• Best indicator[4]: a correlation between syncope and an ECG abnormality (eg brady- or tachyarrhthmia)
• Sinus bradycardia (<40 bpm)
• Sinus pauses of >3 s
Neurally-Mediated Syncope
Cerebrovascular Disorders
(e.g. subclavian steal syndrome, and perhaps migraine)
• Detection of retrograde flow in the ipsilateral vertebral artery
• Not applicable to SMP
Based on response to CSM
Carotid Sinus Hypersensitivity
• Systolic blood pressure drops >50 mmHg, or asystole occurs longer than 3 s
Based on response to tilt test
Type I 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 >3 s
• Blood pressure fall coincides with or occurs before the heart rate falls
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 the tilt testing (i.e. <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)

# APPENDIX B: Causes of Syncope

*Each time a cause of syncope was encountered during the author's literature review, it was recorded here. Hence, this appendix aims for comprehensiveness but not comprehensibility!*

***It is optional reading.***

## 1. CARDIOVASCULAR (perhaps 30% of patients; 30% mortality after 1a)

1.1 CARDIAC

**1.1.1 Arrhythmia**

- o Bradyarrhythmia / sinus pauses / marked sinus bradycardia / sick sinus syndrome / tachy-brady syndrome
- o Tachyarrhythmia (ventricular or supraventricular)
- o Myocardial infarction (with resulting brady- or tachycardia)
- o The long QT interval syndrome
- o Brugada Syndrome (episodes of rapid polymorphic VT in East Asians with an ECG pattern of right bundle branch block and ST segment elevation in leads V1 to V3)
- o Heart block (see below for causes)
  - o AV block (or Stokes-Adams attack)
  - o Sinoatrial block
  - o Diseases in the His-Purkinje system:
    - o Left anterior hemiblock
    - o Left bundle branch block
    - o Tri/bifascicular block (fascicle is a bundle)
  - o CAUSES OF HEART BLOCK:
    - o Amyloid heart disease (amyloid is a hard waxy deposit consisting of protein and polysaccharides that results from the degeneration of tissue)
    - o Ankylosing spondylitis (ank. is the stiffening and immobility of a joint as the result of disease, trauma, surgery, or abnormal bone fusion; sp. is the inflammation of vertebrae)
    - o Collagen vascular diseases (rheumatoid arthritis, systemic lupus erythematosus, periarteritis nodosa, scleroderma, dermatomyositis, and polyarteritis nodosa)
    - o TB, syphilis, etc.
    - o Tumours (primary or secondary)
    - o Muscular dystrophy
    - o Parasitic infections, lyme disease ( <-- rare)
    - o Rheumatic fever, diphtheria ( <-- developing countries)
- o NOT ARRHYTHMIA
  - - atrial fibrillation (unless ventricular rate is exceedingly fast or slow);
  - - ventricular bigeminy;
  - - ventricular pacing (unless the pacemaker fails or there is malignant neurocardiogenic syncope)

**1.1.2 Vasovagal syncope** *(or simple faint / common syncope / emotional syncope / neurocardiogenic* syncope)*

- o Type I, IIA, or IIB
- o Not Type III - that can be classified as non-cardiovascular for prognostic reasons
- o SOME CAUSES OF VASOVAGAL SYNCOPE
  - o Hypovolemia
  - o Increased venous pooling
  - o Increased beta-adrenergic sensitivity
  - o Baroreceptor over-activity

| |
|---|
| * - The term "neurocardiogenic syncope" is also less frequently used as a synonym for "neurally mediated syncope", or "neurally mediated syncopal syndrome", or "neurally mediated reflex syncopal syndrome", or just "reflex syncope". This is a broader class of syncope which includes vasovagal syncope, carotid sinus syndrome, and post-micturition syncope, but vasovagal syncope is by far the most commonly occurring. NB: See the Reflex Syncope section under "non-cardiovascular" syncope. |
| |
| **1.1.3 Other cardiac causes** |
| o Myocardial infarction (with reduced ejection fraction) |
| o Cardiac tamponade (accumulations of fluids in pericardium, decreasing cardiac output) |
| |
| 1.2 VASCULAR |
| |
| **1.2.1 Orthostatic hypotension** |
| |
| o Primary reasons |
| o Pure autonomic failure (idiopathic O.H.) |
| o Autonomic failure with multiple system atrophy (Shy-Drager syndrome) |
| o Autonomic failure with Parkinson's disease |
| |
| o Secondary reasons |
| o General medical disorders |
| o Diabetes |
| o Amyloid |
| o Alcoholism |
| o Autoimmune disease |
| o Acute and subacute dysautonomia |
| o Guillian-Barre syndrome (acute inflammatory demyelinating polyneuropathy / Landry's ascending paralysis) (An inflammatory disorder of the peripheral nerves, those outside the brain and spinal cord) |
| o Mixed connective tissue disease (synonymous or related to Overlap Syndrome and Undifferentiated Mix Connective Tissue Disorder) (A group of symptoms like those in collagen vascular diseases; not a cause in itself) |
| o Rheumatoid arthritis |
| o Eaton-Lambert syndrome (a neuromuscular disorder; major symptoms include muscle weakness and fatigue especially of the pelvic and thigh muscles) |
| o systemic lupus erythematosus |
| o Carcinomatous autonomic neuropathy (carcinoma is an invasive malignant tumor derived from epithelial tissue that tends to metastasize to other areas of the body) |
| o Metabolic disease |
| o Porphyria (large amounts of porphyrins in the blood and urine) |
| o Fabry's disease (a hereditary fat storage disorder caused by a deficiency of an enzyme involved in the biodegradation of lipids) |
| o Tangier disease (a genetic disorder of cholesterol transport) |
| o B12-deficiency |
| o Hereditary sensory neuropathies (dominant or recessive) (distal wasting of the lower limb muscles) |
| o Infections of the nervous system |
| o Syphilis |
| o Chagas' disease (from a flagellate protozoan parasite in the Americas) |
| o HIV infection |
| o Botulism |
| o Herpes zoster |
| o Central brain lesions |
| o Vascular lesions or tumours involving the hypothalamus and midbrain (e.g. craniopharyngioma) |
| o Multiple sclerosis |
| o Wernicke's encephalopathy (thiamine deficiency, causing acute mental confusion, ataxia and opthalmoplegia) |
| o Spinal cord lesions |

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| o Familial dysautonomia |
| o Familial hyperbradykininism |
| o Renal failure |
| o Dopamine B-hydroxylase deficiency |
| o Aging |
| o Fluid depletion |
| o Bed rest, illness |
| |
| o Drug reasons |
| o Selective neurotoxic drugs; alcoholism |
| o Tranquilizers (phenothiazines, barbiturates) |
| o Antidepressants (tricyclics, monoamine oxidase inhibitors) |
| o Vasodilator hypotensive drugs (prazosin, hydralazine) |
| o Centrally acting hypotensive drugs (methyldopa, clonidine) |
| o Adrenergic neurone blocking drugs (guanethidine) |
| o Adrenergic blocking drugs (phenoxybenzamine, labetalol) |
| o Ganglion blocking drugs (hexamethonium, mecamylamine) |
| o Angiotensin-converting enzyme inhibitors (captopril, enalapril, lisinopril) |
| |
| **1.2.2 Obstructive valvular lesions** |
| o Mitral valve obstruction |
| o Dissecting aortic aneurysm |
| o Subclavian steal syndrome (or vertebral-basilar artery disease, or carotid artery occlusive syndrome) (stenosis or obstruction of subclavian artery near its origin) |
| o Atrial myxoma (benign tumour of connective tissue embedded in mucus) |
| o Hypertrophic cardiomyopathy |
| o Aortic stenosis |
| |
| **1.2.3 Other vascular reasons** |
| o (Systemic) mastocytosis (episodic release of mast cell mediators) |
| o ((Obstructive) multivessel) cerebrovascular disease (e.g. stroke, TIA, intrinsic atherosclerotic disease, embolic disease) |
| o Pulmonary hypertension |
| o Pulmonary embolus |
| o Cerebral embolus |
| o A169Hypertensive encephalopathy |
| |
| **2. NON-CARDIOVASCULAR** (perhaps 20-30% of patients; >10% mortality after 1a) |
| |
| 2.1 NEUROLOGICAL |
| |
| **2.1.1 Cerebral** *(all these reasons are denied as syncope causes by the Task Force)* |
| o Seizures (but not absence seizures) (if borderline, usu. NCS or "convulsive syncope") (akinetic seizures, usu. in 2- to 5-year-olds, are just like syncope) |
| o Narcolepsy (defective REM timing) |
| o TIAs (these can be considered cardiovascular too) |
| o Basilar migraine (sometimes w/ ataxia [inability to control muscle movement] and paresthesias [skin |
| o Psychogenic causes |
| o Psychogenic unresponsiveness |
| o Hysteria |
| o Panic disorder |
| o Anxiety disorder |
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| **2.1.2 Reflex Syncope** *(or situational syncope / Gower Syndrome / vasodepressor syncope / any of the synonyms for vasovagal syncope mentioned previously in the CV section). A hypersensitive autonomic response; all below are related to an abrupt change in autonomic tone or intravascular volume)* |
| o Vasovagal syncope (see previous note on neurocardiogenic syncope, within the cardiovascular section; note that the best type of vasovagal syncope to be classified here - under "non-cardiovascular causes" - is Type III, although all types are eligible for both CV and non-CV classification) |
| o Carotid sinus {hypersensitivity / syncope / syndrome} |
| o Head-up tilt syncope / gravitational syncope / postural syncope |
| o Drug-induced syncope |
| o Nitroglycerin |
| o Isoproterenol |
| o Sympatholytic agents (bretylium, guanethidine, etc.) |
| |
| o **Situational syncope** *(NB: occasionally this term is extended to the whole category of "reflex syncope")* |
| o From increased intrathoracic pressure |
| o (Post-) tussive syncope / cough syncope (common in chronic obstructive pulmonary disease) |
| o Sneeze syncope |
| o Trumpet player's syncope / Wind instrument player's syncope |
| o Weight lifter's syncope (hyperventilation before lifting causes hypocapnia, cerebral vasoconstriction, and peripheral vasodilation; the Valsalva maneuver of lifting decreases venous return and cardiac output, and squatting further impedes venous return and potentiates the systemic vasodilation and decreased BP.) |
| o Mess Trick syncope (Valsalva during hyperventilation; see Howard P, Leathart GL, Dornhorst AC, Sharpey-Schafer EP. The "mess-trick" and the "fainting lark". Br Med J 1951; p382-4.) |
| o Valsalva-induced syncope |
| o GI stimulation syncope |
| o Rectal examination |
| o GI instrumentation |
| o Defecation syncope |
| o Esophageal/nasopharyngeal stimulation |
| o {Deglutition / glossopharyngeal / swallow} syncope / airway stimulation |
| o Glossopharyngeal neuralgia (a deep stabbing pain in one side of the throat, caused by arterial pressure on a nerve) |
| o Oropharyngeal (the part of the pharynx between the soft palate and the epiglottis), esophageal |
| o Urogenital |
| o (Post-) micturition syncope |
| o Urogenital tract instrumentation |
| o Prostatic massage |
| o Postprandial syncope |
| o Ocular syncope |
| o Special situations causing syncope |
| o High altitude |
| o Diving (causes 'diving reflex') |
| o Prolonged exercise |
| o Exposure to G-forces |
| o Structural and anatomical causes of syncope |
| o Arnold-Chiari Malformations |
| o Tumours of the third ventricle |
| o Stretch syncope |
| |
| 2.2 NON-NEUROLOGICAL |
| |
| o Recreational drug use |
| o Alcohol |
| o Methamphetamine |
| o Ecstasy (MDMA) |

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| o Hyperventilation Syncope *(NB: sometimes merely a symptom of arrhythmia, and not recognized by all as a cause of syncope) (H.S. is attributed to respiratory alkalosis; hypocapnia-induced vasoconstriction reduces cerebral blood flow.)* |
| o Metabolic causes *(not universally recognized as a cause of syncope)* |
| o Hypoglycemia |
| o Hypoxia |
| o Meningitis |
| o Encephalitis |
| o Sepsis |
| |
| **3. SUO (SYNCOPE OF UNEXPLAINED ORIGIN)** (perhaps 50% of patients; 6 - <10% mortality after 3a) |
| |
| o Unknown cause |
| |
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| **Notes on classification schemes:** |
| It is possible to reconcile this categorization with that of the Task Force [M13A], which comprises five areas: |
| 1. Neurally-mediated reflex syncopal syndromes -> 2.1.2, 1.1.2 |
| 2. Orthostatic -> 1.2.1 |
| 3. Cardiac arrhythmias as primary cause -> 1.1.1 |
| 4. Structural cardiac or cardiopulmonary disease -> 1.1.3, 1.2.2 (minus steal), 1.2.3 |
| 5. Cerebrovascular -> 1.2.2 (subclavian steal only) |
| |
| Non-syncope: 2.1.1, 2.2 (not sure where to put recreational drug use though) |

# REFERENCES

Key: J = James and others; L = Lionel; M = Mark; O = Other resource (i.e., not a scientific paper)

Suffix letters group related items (e.g. M11A and M11B are related)

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