Νεώτερα Δεδομένα στη Συγκοπή

Στέφανος Αρχοντάκης
Επικουρικός Επιμελητής Β, ΓΝΜΑ ''Ελενα Βενιζέλου''
Επιστημονικός Συνεργάτης ΓΝΑ Ιπποκράτειο

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«Επαθα συγκοπή» - Ημουν κάτω από το νεροχύτη και έστελνα sms στην αστυνομία όταν ο δολοφόνος του Charlie Hebdo ήρθε να πιει νερό

Ο νεαρός γραφίτας Λιλιέν Λεπέρ, που είχε κρυφτεί κάτω από τον νεροχύτη και έδωσε κρίσιμες πληροφορίες στην Αστυνομία, μίλησε για πρώτη φορά στη γαλλική τηλεόραση.
Syncope

"T-LOC (e.g., short duration episode of loss of awareness characterized by amnesia for the period of unconsciousness, abnormal motor control & loss of responsiveness) additionally characterized, by (a) rapid onset, (b) short duration, (c) spontaneous-complete recovery"

"Due to global cerebral hypoperfusion"
Reflex (neurally mediated) syncope

Vasovagal:
- orthostatic VS: standing, less common sitting
- emotional: fear, pain (somatic or visceral), instrumentation, blood phobia

Situational:
- micturition
- gastrointestinal stimulation (swallow, defaecation)
- cough, sneeze
- post-exercise
- others (e.g. laughing, brass instrument playing)

Carotid sinus syndrome

Non-classical forms (without prodromes and/or without apparent triggers and/or atypical presentation)

Syncope due to OH
Note that hypotension may be exacerbated by venous pooling during exercise (exercise-induced), after meals (postprandial hypotension), and after prolonged bed rest (deconditioning).

Drug-induced OH (most common cause of OH):
- e.g. vasodilators, diuretics, phenothiazine, antidepressants

Volume depletion:
- haemorrhage, diarrhoea, vomiting, etc.

Primary autonomic failure (neuropathic OH):
- pure autonomic failure, multiple system atrophy, Parkinson’s disease, dementia with Lewy bodies

Secondary autonomic failure (neuropathic OH):
- diabetes, amyloidosis, spinal cord injuries, auto-immune autonomic neuropathy, paraneoplastic autonomic neuropathy, kidney failure

Cardiac syncope

Arrhythmia as primary cause:
Bradycardia:
- sinus node dysfunction (including bradycardia/tachycardia syndrome)
- atrioventricular conduction system disease

Tachycardia:
- supraventricular
- ventricular

Structural cardiac: aortic stenosis, acute myocardial infarction/ischaemia, hypertrophic cardiomyopathy, cardiac masses (atrial myxoma, tumours, etc.), pericardial disease/tamponade, congenital anomalies of coronary arteries, prosthetic valve dysfunction
Cardiopulmonary and great vessels: pulmonary embolism, acute aortic dissection, pulmonary hypertension

Orthostatic hypotension

COMMON CAUSES OF SYNCOPE

Reflex response to a stimulus ("neurally mediated")

Underlying cardiovascular disease / condition

Syndrome | Ancillary test for diagnosis | Time from upright position to abnormal BP response | Pathophysiology
---|---|---|---
Initial OH | Beat-to-beat BP on active standing test (lying to standing) | 0-15 seconds | Transient mismatch between cardiac output and total peripheral resistance

Classical OH | Active standing test; TTT | <3 minutes | Impaired increase in total peripheral resistance and HR in autonomic failure resulting in pooling of blood; alternately, severe volume depletion

Delayed OH (sometimes followed by reflex syncope) | TTT; active standing test | >3 minutes | Pathophysiology uncertain. Progressive fall in venous return and low cardiac output are likely

Orthostatic vagovagal syncope | TTT | Usually prolonged standing | Vagal reflex due to progressive pooling of blood with final vasodepressor and/or cardiodepressor pathways, often preceded by autonomic activation

POTS | Active standing test; or TTT | <10 minutes | Abnormal HR response

Likely mechanism severe deconditioning, immune-mediated processes, excessive venous pooling and hyperadrenergic state

2018 ESC Guidelines for the diagnosis and management of syncope
Prevalence

- Yearly prevalence resulting in medical evaluation: 9.5 / 1000 inhabitants
- 10% of patients hospitalized
**Prognosis**

- **Severity** related to: (a) **causal risk** (underlying disease), (b) **Consequential risk** of syncope (e.g., physical trauma, work-school activity, QoL, psychological effects, driving)

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**Original Investigation**

**Syncope and Motor Vehicle Crash Risk**

A Danish Nationwide Study

Anna-Karin Numé, MD; Gunnar Gislason, MD, PhD; Christine B. Christiansen, MD, PhD; Deewa Zahr, MB; Mark A. Hafky, MD; Christian Torp-Pedersen, MD, DSc; Martin H. Ruwald, MD, PhD


Published online February 29, 2016.
Prognosis

**Risk of Death** related to the severity of underlying disease (e.g., cardiac: major risk factor for SCD, OH: 2x risk for death, CAD, HF, stroke, vasovagal: excellent prognosis)

**Recurrence** related to the number of episodes in the 1-2 last years. Not associated to mortality but is associated with poor functional status. Associated with minor trauma (29%) or major trauma (4.7%)

Aims in diagnosis

1. Presentation of patient with probable TLOC (may include ambulance or referral data)
   - TLOC present? (history)
     - No TLOC
       - Act as needed
     - Syncope
   - TLOC - non syncopal
     - Initial syncope evaluation (H&P exam, ECG, supine and standing BP)
     - Certain or highly likely diagnosis (see definition in Table of Recommendations)
     - Uncertain diagnosis (see Table 5)
     - Risk stratification (see Table 6)

2. Syncope
   - Reflex syncope
   - Orthostatic hypotension
   - Cardiac

3. TLOC due to head trauma
   - Syncope
   - Epileptic seizures
   - Psychogenic
   - Rare causes
     - Generalized: Tonic, Clonic, Tonic-clonic, Atonic
     - Psychogenic pseudosyncope (PPS)
     - Psychogenic non-epileptic seizures (PNES)
     - Subclavian steal syndrome
     - Vertebrobasilar TIA
     - Subarachnoid haemorrhage
     - Cynoactic breath holding spell

4. Nontraumatic TLOC
   - Early evaluation & treatment
   - Ancillary tests followed by treatment
   - Explanation, no further evaluation

5. TLOC due to head trauma
Use of an implantable loop recorder to increase the diagnostic yield in unexplained syncope: results from the PICTURE registry

Nils Edvardsson1, Viveka Frykman1, Rob van Mechelen1, Peter Mitro4, Afsaneh Mohi-Oskarsson1, Jean-Luc Pasqué6, Hernanth Ramanna1, Frank Schwertheer5, Rodolfo Ventura1, Denzina Voulgaraki10, Claudio Garuti10.

The median number of tests performed per patient was 13 (inter-quartile range 9 - 20)

Table 2 History of diagnostic tests performed before ILR implant

<table>
<thead>
<tr>
<th>Test</th>
<th>Number</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total recruitment</td>
<td>570</td>
<td>100%</td>
</tr>
<tr>
<td>Standard ECG</td>
<td>556</td>
<td>98%</td>
</tr>
<tr>
<td>Echocardiography</td>
<td>490</td>
<td>86%</td>
</tr>
<tr>
<td>Basic laboratory tests</td>
<td>488</td>
<td>86%</td>
</tr>
<tr>
<td>Ambulatory ECG monitoring</td>
<td>382</td>
<td>67%</td>
</tr>
<tr>
<td>In-hospital ECG monitoring</td>
<td>311</td>
<td>55%</td>
</tr>
<tr>
<td>Exercise testing</td>
<td>297</td>
<td>52%</td>
</tr>
<tr>
<td>Orthostatic blood pressure measurements</td>
<td>275</td>
<td>48%</td>
</tr>
<tr>
<td>MRI / CT scan</td>
<td>267</td>
<td>47%</td>
</tr>
<tr>
<td>Neurological or psychiatric evaluation</td>
<td>270</td>
<td>47%</td>
</tr>
<tr>
<td>EEG</td>
<td>222</td>
<td>39%</td>
</tr>
<tr>
<td>Carotid sinus massage</td>
<td>205</td>
<td>36%</td>
</tr>
<tr>
<td>Tilt test</td>
<td>201</td>
<td>35%</td>
</tr>
<tr>
<td>Electrophysiology testing</td>
<td>144</td>
<td>25%</td>
</tr>
<tr>
<td>Coronary angiography</td>
<td>133</td>
<td>23%</td>
</tr>
<tr>
<td>External loop recording</td>
<td>67</td>
<td>12%</td>
</tr>
<tr>
<td>ATP test</td>
<td>15</td>
<td>3%</td>
</tr>
<tr>
<td>Other tests</td>
<td>52</td>
<td>9%</td>
</tr>
<tr>
<td>No tests performed</td>
<td>1</td>
<td>0%</td>
</tr>
</tbody>
</table>

Overall, patients had seen an average of 3 different specialists for their syncope.
“Initial Evaluation”

Overall diagnostic accuracy of IE: 91%

1. **History**
2. **Physical Examination (including Orthostatic Challenge!)**
3. **ECG**

- Blood Tests
- Carotid Massage
## Syncopal Event

### Low-risk
- Associated with prodrome typical of reflex syncope (e.g., light-headedness, feeling of warmth, sweating, nausea, vomiting)\(^{36,49}\)
- After sudden unexpected unpleasant sight, sound, smell, or pain\(^{36,49,50}\)
- After prolonged standing or crowded, hot places\(^{36}\)
- During a meal or postprandial\(^{51}\)
- Triggered by cough, defaecation, or micturition\(^{52}\)
- With head rotation or pressure on carotid sinus (e.g., tumour, shaving, tight collar)\(^{53}\)
- Standing from supine/sitting position\(^{54}\)

### High-risk

#### Major
- New onset of chest discomfort, breathlessness, abdominal pain, or headache\(^{26,44,55}\)
- Syncope during exertion or when supine\(^{36}\)
- Sudden onset palpitation immediately followed by syncope\(^{36}\)

#### Minor (high-risk only if associated with structural heart disease or abnormal ECG):
- No warning symptoms or short (<10 s) prodrome\(^{36,38,49,56}\)
- Family history of SCD at young age\(^{57}\)
- Syncope in the sitting position\(^{54}\)

## Past Medical History

### Low-risk
- Long history (years) of recurrent syncope with low-risk features with the same characteristics of the current episode\(^{58}\)
- Absence of structural heart disease\(^{27,58}\)

### High-risk
- Severe structural or coronary artery disease (heart failure, low LVEF or previous myocardial infarction)\(^{36,27,55,59}\)

## Physical Examination

### Low-risk
- Normal examination

### High-risk

#### Major
- ECG changes consistent with acute ischaemia
- Mobitz II second- and third-degree AV block
- Slow AF (<40 b.p.m.)
- Persistent sinus bradycardia (<40 b.p.m.), or repetitive sinoatrial block or sinus pauses >3 seconds in awake state and in absence of physical training
- Bundle branch block, intraventricular conduction disturbance, ventricular hypertrophy, or Q waves consistent with ischaemic heart disease or cardiomyopathy\(^{44,56}\)
- Sustained and non-sustained VT
- Dysfunction of an implantable cardiac device (pacemaker or ICD)
- Type 1 Brugada pattern
- ST-segment elevation with type 1 morphology in leads V1–V3 (Brugada pattern)
- QTc >460 ms in repeated 12-lead ECGs indicating LQTS\(^{56}\)

#### Minor (high-risk only if history consistent with arrhythmic syncope)
- Mobitz I second-degree AV block and 1st degree AV block with markedly prolonged PR interval
- Asymptomatic inappropriate mild sinus bradycardia (40–50 b.p.m.), or slow AF (40–50 b.p.m.)\(^{56}\)
- Paroxysmal SVT or atrial fibrillation\(^{56}\)
- Pre-excited QRS complex
- Short QTc interval (<340 ms)\(^{46}\)
- Atypical Brugada patterns\(^{46}\)
- Negative T waves in right precordial leads, epsilon waves suggestive of ARVC\(^{46}\)
Canadian Syncope Risk Score*

For Adults (Age ≥ 18 years) with Syncope and No Serious Condition obvious during ED evaluation

<table>
<thead>
<tr>
<th>Items</th>
<th>Risk of any Serious Adverse Event within 30 days</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Total Score</td>
</tr>
<tr>
<td></td>
<td>-3 to -2</td>
</tr>
<tr>
<td></td>
<td>-1 to 6</td>
</tr>
<tr>
<td></td>
<td>1 - 2</td>
</tr>
<tr>
<td></td>
<td>3</td>
</tr>
<tr>
<td></td>
<td>4 - 5</td>
</tr>
<tr>
<td></td>
<td>6</td>
</tr>
<tr>
<td></td>
<td>7</td>
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<tr>
<td></td>
<td>8</td>
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<tr>
<td></td>
<td>9</td>
</tr>
<tr>
<td></td>
<td>10</td>
</tr>
<tr>
<td></td>
<td>11</td>
</tr>
</tbody>
</table>

12-month mortality

- Score 0 0%
- Score 1 8.9%
- Score 2 19.6%
- Score 3 34.7%
- Score 4 57.1%

San Francisco Syncope Rule

- Cardiac Failure
- Shortness of breath
- SBP < 90 at triage

EGSYS-U Risk Factors

- Abnormal ECG/Cardiopathy (+3)
- Palpitations/dyspnea (+3)
- Syncope in supine position/Effort syncope (+2)
- Age > 64 years (+1)
- No precipitating and predisposing factors (+1)
- No prodromes (+1)
- Blurred vision (-1)
- Neurovegetative symptoms/endpoint phase (-1)
- Precipitating and predisposing factors (-2)

Risk stratification scores may be considered for risk stratification in the ED.
Patients with intermediate risk profiles randomized to the syncope unit in the ED were more likely to be diagnosed in the ED and were less likely to be hospitalized than patients randomized to the standard care group.

A syncope unit in the ED, with a multidisciplinary effort and appropriate resources, provides effective and efficient care for a large and challenging group of patients.
Further Evaluation

Echocardiography is indicated for diagnosis and risk stratification in patients with suspected structural heart disease.\(^{235,236}\)

Aortic stenosis, obstructive cardiac tumours or thrombi, pericardial tamponade, and aortic dissection are the most probable causes of syncope when the ECG shows the typical features of these conditions.\(^{237–244}\)

**Indications**

Exercise testing is indicated in patients who experience syncope during or shortly after exertion.

**Diagnostic criteria**

Syncope due to second- or third-degree AV block is confirmed when the AV block develops during exercise, even without syncope.\(^{253–257}\)

Reflex syncope is confirmed when syncope is reproduced immediately after exercise in the presence of severe hypotension.\(^{250–252}\)

Home video recordings of spontaneous events should be considered. Physicians should encourage patients and their relatives to obtain home video recordings of spontaneous events.\(^{206,208}\)

The recording of spontaneous attacks with a video by an eyewitness should be considered for diagnosis of PPS.\(^{116,154}\)

Valsalva manoeuvre should be considered for the assessment of autonomic function in patients with suspected neurogenic OH.\(^{138–143}\)

Deep-breathing tests should be considered for the assessment of autonomic function in patients with suspected neurogenic OH.\(^{142,143,146,147}\)

Diagnostic radiology and laboratory tests such as chest X-ray, brain computed tomography, routine blood haematology, biochemistry, and D-dimer and cardiac markers have a low diagnostic yield, impact on risk stratification of patients with syncope, and should not routinely be used unless specifically suggested by clinical evaluation.

EEG, ultrasound of neck arteries, and computed tomography or magnetic resonance imaging of the brain are not indicated in patients with syncope.\(^{178,435–440}\)

Brain MRI is recommended if neurological examination indicates Parkinsonism, ataxia, or cognitive impairment.

Neurological evaluation is indicated when syncope is due to autonomic failure to evaluate the underlying disease.

Neurological evaluation is indicated in patients in whom TLOC is suspected to be epilepsy.

Cognitive behavioural therapy may be considered in the treatment of PPS if attacks persist after explanation.
ECG-Monitoring
(In-Hospital, 24h Holter, External Loop Recorders, ILR)

**ONLY in high probability of Arrhythmia associated with syncope!**

### ECG classification

<table>
<thead>
<tr>
<th>Type</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Type 1A</td>
<td>Sinus arrest: progressive sinus bradycardia or initial sinus tachycardia followed by progressive sinus bradycardia until sinus arrest (see Web Figure 27)</td>
</tr>
<tr>
<td>Type 1B</td>
<td>Sinus bradycardia plus AV block: progressive sinus bradycardia followed by AV block (and ventricular pauses) with concomitant decrease in sinus rate (see Web Figure 28)</td>
</tr>
<tr>
<td>Type 1C</td>
<td>AV block: sudden onset AV block (and ventricular pause(s)) with concomitant increase in sinus rate (see Web Figures 29 and 30)</td>
</tr>
</tbody>
</table>

### Diagnostic criteria

- Arrhythmic syncope is confirmed when a correlation between syncope and an arrhythmia (bradyarrhythmia or tachyarrhythmia) is detected.

- In the absence of syncope, arrhythmic syncope should be considered likely when periods of Mobitz II second- or third-degree AV block or a ventricular pause >3 s (with the possible exception of young trained persons, during sleep or rate-controlled atrial fibrillation), or rapid prolonged paroxysmal SVT or VT are detected.

- The absence of arrhythmia during syncope excludes arrhythmic syncope.

**Immediate in-hospital monitoring** (in bed or by telemetry) is indicated in high-risk patients (defined in Table 6).

- **Holter monitoring** should be considered in patients who have frequent syncope or presyncope (≥1 episode per week).

- **External loop recorders** should be considered, early after the index event, in patients who have an inter-symptom interval ≤4 weeks.
Symptom-Rhythm Correlation: ILR Permits both Patient-triggered and Automatic Activation

<table>
<thead>
<tr>
<th>Model</th>
<th>Year</th>
<th>Feature</th>
</tr>
</thead>
<tbody>
<tr>
<td>Reveal</td>
<td>1998</td>
<td>Helps diagnose unexplained syncope</td>
</tr>
<tr>
<td>Reveal Plus</td>
<td>2000</td>
<td>Automatic detection added</td>
</tr>
<tr>
<td>Reveal DX</td>
<td>2007</td>
<td>Longevity and ECG memory increased (to 3 yrs., 49.5 minutes), episode logs, ICD sensing technology, MRI labeling, and remote monitoring added</td>
</tr>
<tr>
<td>Reveal XT</td>
<td>2009</td>
<td>AF detection and long-term trended diagnostics (the Cardiac Compass and AF Summary Reports) added</td>
</tr>
</tbody>
</table>
Use of an implantable loop recorder to increase the diagnostic yield in unexplained syncope: results from the PICTURE registry

Nils Edwardsson¹, Viveka Frykman², Rob van Mechelen³, Peter Mitro⁴, Afsaneh Mohii-Oskarsson⁵, Jean-Luc Pasquié⁶, Hemanth Ramanna⁷, Frank Schwertfeger⁸, Rodolfo Ventura⁹, Despina Youlgaraki¹⁰, Claudio Garutti¹⁰, Pelle Stolz¹¹, and Nicholas J. Linker¹² on behalf of the PICTURE Study Investigators

Costs of unstructured investigation of unexplained syncope: insights from a micro-costing analysis of the observational PICTURE registry

Nils Edwardsson¹, Claudia Wolff², Stelios Tsintzos³, Guido Rieger⁴, and Nicholas J. Linker⁵

Aims

The observational PICTURE (Place of Reveal In the Care pathway and Treatment of patients with Unexplained Recurrent Syncope) registry enrolled 570 patients with unexplained syncope, documented their care pathway and the various tests they underwent before the insertion of an implantable loop recorder (ILR). The aims were to describe the extent and cost of diagnostic tests performed before the implant.

Methods and results

Actual costs of 17 predefined diagnostic tests were characterized based on a combination of data from PICTURE and a micro-costing study performed at a medium-sized UK university hospital in the UK. The median cost of diagnostic tests per patient was £1114 (95% CI £995 – £1233). As many patients received more than the median number of tests, the mean expenditure per patient was higher with £1613 (95% CI £1494 – £1732), and for 10% of the patients the cost exceeded £3539. Tests were frequently repeated, and early use of specific and expensive tests was common. In the 12% of patients with types of tests entirely within the recommendations for an initial evaluation before ILR implant, the mean cost was £710.

Conclusion

Important opportunities to reduce test-related costs before an ILR implant were identified, e.g. by more appropriate use of tests recommended in the initial evaluation, by decreasing repetition of tests, and by avoiding early use of specialized and expensive tests. A structured multidisciplinary approach would be the best model to achieve an optimal outcome.
### Supplementary Data Table 5

Meta-analysis of randomized trials comparing diagnostic yields of an implantable loop recorder strategy versus a conventional strategy in patients with unexplained syncope

<table>
<thead>
<tr>
<th>Study</th>
<th>ILR group, n/N (%)</th>
<th>Control group, n/N (%)</th>
<th>Relative probability</th>
<th>95% CI</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>RAST 2001</td>
<td>14/27 (52)</td>
<td>6/30 (20)</td>
<td>2.6</td>
<td>1.2–5.8</td>
<td>0.01</td>
</tr>
<tr>
<td>EaSyAS 2006</td>
<td>43/101 (43)</td>
<td>7/97 (7)</td>
<td>5.9</td>
<td>2.8–12</td>
<td>0.001</td>
</tr>
<tr>
<td>Da Costa 2013</td>
<td>15/41 (37)</td>
<td>4/37 (11)</td>
<td>3.4</td>
<td>1.2–9.3</td>
<td>0.01</td>
</tr>
<tr>
<td>FRESH 2014</td>
<td>18/39 (46)</td>
<td>2/39 (5)</td>
<td>9.0</td>
<td>2.2–36</td>
<td>0.001</td>
</tr>
<tr>
<td>EaSyAS II 2016</td>
<td>62/125 (50)</td>
<td>21/121 (17)</td>
<td>2.9</td>
<td>1.9–4.4</td>
<td>0.001</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>152/333 (46)</strong></td>
<td><strong>40/324 (12)</strong></td>
<td><strong>3.6</strong></td>
<td><strong>2.45.3</strong></td>
<td><strong>0.001</strong></td>
</tr>
</tbody>
</table>

---

2018 ESC Guidelines for the diagnosis and management of syncope

ILR is indicated in an early phase of evaluation in patients with recurrent syncope of uncertain origin, absence of high-risk criteria (listed in Table 6), and a high likelihood of recurrence within the battery life of the device.¹⁷⁵,¹⁷⁶,¹⁸¹–¹⁸⁴,²⁰², Supplementary Data Table 5

ILR is indicated in patients with high-risk criteria (listed in Table 6) in whom a comprehensive evaluation did not demonstrate a cause of syncope or lead to a specific treatment, and who do not have conventional indications for primary prevention ICD or pacemaker indication.¹⁷⁴,¹⁸⁰,¹⁸⁷,¹⁸⁸,¹⁹⁵, Supplementary Data Tables 5 and 6

ILR should be considered in patients with suspected or certain reflex syncope presenting with frequent or severe syncopal episodes.¹⁸⁴–¹⁸⁶

ILR may be considered in patients in whom epilepsy was suspected but the treatment has proven ineffective.¹³⁷,¹⁸⁹–¹⁹¹, Supplementary Data Table 7

ILR may be considered in patients with unexplained falls.¹⁹¹–¹⁹⁴, Supplementary Data Table 8
Non-standardised protocol for angles, time, fasting, hydration, environment
• Use of provocative agents debated
• High specificity/sensitivity in pts with typical VVs **BUT low diagnostic value in pts with Unexplained Syncope**
• (+) CI response during TTT predicts with high probability asystole during syncope **BUT (+) VD response or Mixed response or (-) response does not exclude asystole**  
Electrophysiological Study


- **Invasive method**
Reflex Syncope - Treatment
Reflex Syncope - Treatment

- Reflex syncope
  - Education, life-style measures (Class I)
  - Severe/recurrent form

- Low BP phenotype
- Prodromes
- Hypotensive drugs
- Dominant cardioinhibition

Younger
- Fludrocortisone
- Midodrine (Class IIb)
- Counter-pressure manoeuvre (Class IIa)
- Tilt training (Class IIb)
- ILR-guided management in selected cases (Class I); See Section 3.4
- Stop/reduce hypotensive drugs (Class IIa)

Older
- Cardiac pacing (Class IIa/IIb)
  - See Figure 10

*No or very short
Reflex Syncope - Treatment/ Vaso-vagal syncope

Pacing reduces syncope recurrence!

Pacing does NOT reduce syncope recurrence!

ISSUE 3

International Study on Syncope of Uncertain Etiology 3

Arrhythmia/Electrophysiology

Pacemaker Therapy in Patients With Neurally Mediated Syncope and Documented Asystole

Third International Study on Syncope of Uncertain Etiology (ISSUE-3) A Randomized Trial

Michale Brignole, MD; Carlo Monzelli, MD; Angel Mea, MD; Dietrich Andreasen, MD; Jean Jacques Blanc, MD; Andrew D. Kahan, MD; Wouter Wieling, MD; Xulio Beiras, MD; Jean Claude Deharo, MD; Vitantonio Russo, MD; Marco Tomano, MD; Richard Sutton, DSc; on behalf of the International Study on Syncope of Uncertain Etiology 3 (ISSUE-3) Investigators

Results

- Primary endpoint: Incidence of first syncope recurrence for PPM on vs. off: 25% vs. 57%, p = 0.039
SUP-2 Results

The recurrence rate was similar in the 65 CSM+ (11%), 32 TT+ (7%) and 23 ILR+ (7%) patients.

2013 ESC Guidelines on cardiac pacing and cardiac resynchronization therapy

Compared with the natural history of carotid sinus syndrome, we can expect that the patients who receive a pacemaker will have about a 75% reduction of recurrences. However, syncopal recurrences are still expected to occur in up to 20% of paced patients within 5 years.
Conclusion In patients with neurally mediated syncope, clinical characteristics, outcome, and mechanism of syncope are poorly correlated and not predicted by the results of TT and ATP test. Therefore, these tests are of little or no value in guiding specific therapy.
**Cardiac pacing**

Cardiac pacing should be considered to **reduce syncopal recurrences in patients aged >40 years, with spontaneous documented symptomatic asystolic pause(s) >3 s or asymptomatic pause(s) >6 s due to sinus arrest, AV block, or the combination of the two.**

Cardiac pacing should be considered to **reduce syncope recurrence in patients with cardioinhibitory carotid sinus syndrome who are >40 years with recurrent frequent unpredictable syncope.**

Cardiac pacing may be considered to **reduce syncope recurrences in patients with tilt-induced asystolic response who are >40 years with recurrent frequent unpredictable syncope.**

Cardiac pacing is not indicated in the absence of a documented cardioinhibitory reflex.

---

**Pacing for reflex syncope: decision pathway**

<table>
<thead>
<tr>
<th>Clinical features</th>
<th>Decision Pathway</th>
</tr>
</thead>
<tbody>
<tr>
<td>Severe, recurrent unpredictable syncopes, age &gt;40 years</td>
<td>Pacing not indicated</td>
</tr>
<tr>
<td>Yes</td>
<td>Implant a DDD PM</td>
</tr>
<tr>
<td>Cl-CSST?</td>
<td>Implant a DDD PM &amp; counteract hypotensive susceptibility</td>
</tr>
<tr>
<td>Tilt negative</td>
<td>Implant a DDD PM</td>
</tr>
<tr>
<td>Tilt positive</td>
<td>Implant a DDD PM</td>
</tr>
<tr>
<td>Asystolic tilt testing?</td>
<td>Implant a DDD PM</td>
</tr>
<tr>
<td>Yes</td>
<td>Implant a DDD PM &amp; counteract hypotensive susceptibility</td>
</tr>
<tr>
<td>Asystole?</td>
<td>Implant a DDD PM &amp; counteract hypotensive susceptibility</td>
</tr>
<tr>
<td>Yes</td>
<td>Implant a DDD PM</td>
</tr>
<tr>
<td>Tilt negative</td>
<td>Implant a DDD PM &amp; counteract hypotensive susceptibility</td>
</tr>
<tr>
<td>No</td>
<td>Pacing not indicated</td>
</tr>
</tbody>
</table>

**DDD mode + Rate Drop response!**
Vaso-vagal syncope → PACING ?

VS
Catheter Ablation as a Treatment for Vasovagal Syncope: Long-Term Outcome of Endocardial Autonomic Modification of the Left Atrium

Wei Sun, MD;* Lihui Zheng, MD, PhD;* Yu Qiao, MD; Rui Shi, MD, PhD; Bingbo Hou, MD; Lingmin Wu, MD, PhD; Jinrui Guo, MD; Shu Zhang, MD, PhD; Yan Yao, MD, PhD, FHRS

Background—Autonomic modification through catheter ablation of ganglionated plexi (GP) in the left atrium has been reported previously as a treatment for vasovagal syncope. This study aimed to observe the long-term outcome in a larger cohort.

Methods and Results—A total of 57 consecutive patients (aged 43.2±13.4 years; 35 women) with refractory vasovagal syncope were enrolled, and high-frequency stimulation and anatomically guided GP ablation were performed in 10 and 47 cases, respectively. A total of 127 GP sites with positive vagal response were successfully elicited and ablated, including 52 left superior, 19 left lateral, 18 left inferior, 27 right anterior, and 11 right inferior GPs. During follow-up of 36.4±22.2 months (range 12–102 months), 52 patients (91.2%) remained free from syncope. Prodromes recurred in 16 patients. No statistical differences were found between the high-frequency stimulation and anatomically guided ablation groups in either freedom from syncope (100% versus 89.4%, P=0.348) or recurrent prodromes (50% versus 76.6%, P=0.167). The deceleration capacity, heart rate, and heart rate variability measurements demonstrated a reduced vagal tone lasting for at least 12 months after the procedure, with improved tolerance of repeated head-up tilt testing. No complications were observed except for transient sinus tachycardia that occurred in 1 patient.

Conclusions—Left atrial GP ablation showed excellent long-term clinical outcomes and might be considered as a therapeutic option for patients with symptomatic vasovagal syncope. (J Am Heart Assoc. 2016;5:e003471 doi: 10.1161/...
OH- Treatment

Syncope due to orthostatic hypotension

Education, life-style measures (Class I)  
Adequate hydration and salt intake (Class I)

Stop/reduce vasoactive drugs (Class IIa)

if symptoms persist

Counter-pressure manoeuvres (Class IIa)  
Compression garments (Class IIa)  
Head-up tilt sleeping (Class IIa)  
Midodrine (Class IIa)  
Fludrocortisone (Class IIa)
Cardiac Syncope - Treatment

Syncope due to intrinsic cardiac SND or AV block

ECG-documented bradycardia

- **Symp. SND (Class I)**
  - Established relationship between SB and syncope

- **Asympt. SND (Class IIa)**
  - Non-established relationship between SB and syncope

- **2° and 3° AV block (Class I)**
  - Persistent AVB
  - Paroxysmal AV block (narrow QRS and BBB)
  - AF with slow HR

Bifascicular BBB (ECG-undocumented bradycardia)

- Ejection fraction >35%

  - **Consider EPS (Class IIa)**
    - Appropriate therapy
    - (if negative)
      - **Implant ILR (Class I)**
        - Appropriate therapy
        - (if negative)
          - Clinical follow-up

  - **Empirc PM (Class IIb)**

Cardiac tachyarrhythmia syncope

- SVT
  - **Catheter ablation (Class I)**
  - **AA drugs (Class IIa)**

- VT
  - **Catheter ablation (Class I)**
  - **ICD (Class I Class IIa)**
  - **AA drugs (Class IIa)**

- **HV >70ms or induced AV block**
- **Sympt. pause >3''**
- **Asympt. pause >6''**
# Consensus Statement 5—Quality indicators

<table>
<thead>
<tr>
<th>Quality indicator</th>
<th>Process indicator</th>
<th>Desirable outcome target</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. SU</td>
<td>To reduce the rate of unexplained T-LOC</td>
<td>At least 70% of patients receive a definite diagnosis (according to ESC guidelines definitions)</td>
<td>Absolute rate of unexplained T-LOC ≤ 20%</td>
</tr>
<tr>
<td></td>
<td>To reduce the rate of hospitalization (in patients at intermediate–high risk from ED)</td>
<td>At least 20% of patients with unexplained syncope after initial ED evaluation have fast-track access to SU for early assessment</td>
<td>≤ 20% of patients with unexplained T-LOC admitted after ED initial evaluation (according to ESC guidelines definition)</td>
</tr>
<tr>
<td></td>
<td>To reduce costs per patient</td>
<td>At least 20% reduction in costs relative to usual local practice</td>
<td>Applies to new services</td>
</tr>
<tr>
<td></td>
<td>To improve the outcome</td>
<td>Less than 5% re-admissions for syncope recurrence in patients with an established and successfully treated diagnosis (according to ESC guidelines definitions)</td>
<td>Less than 20% of paced patients have recurrence of syncope at 1 year</td>
</tr>
</tbody>
</table>

## 2. Personnel

**Leadership**

- One physician leading the SU

**Staff**

- A dedicated trained staff (specifics for training should map the T-LOC diagnoses and treatments)

**Training**

- Syncope Specialist and Staff attend regular training programme and conferences in addition to accreditations programme

**3. Operations**

**Number of patients**

- At least 100 new cases per year per SU

This is the minimum number necessary in order to develop and maintain expertise for one syncope specialist and one staff personnel and for the SU to be cost-efficient.
A facility featuring a standardized approach to risk stratification, diagnosis, management and follow-up of T-LOC & related symptoms.

**Goal:** Better management of T-LOC/ reduce cost through reduction of unnecessary tests and hospitalizations

**Deliver most care to outpatients in addition to ED and inpatients**

- **Syncope specialist**
- **SU clinical nurse specialist**
- **Standardized internal Protocol**

**Access to specialist consultancies:**
- Cardiology
- Neurology/Neuroimaging tests
- Internal Medicine
- Geriatric
- Psychology
- Autonomic Function Tests

**Equipped with or access to:**
- Echocardiogram
- Stress test
- ECG Holter/ELR
- 24-h BP monitoring
- Tilt-table-test
- ILR/ follow-up of ILR
- EPS
- Coronary angiography
- Blood tests

**Equipped with:**
- 12-lead ECG
- ECG monitoring
- Beat-to-beat BP monitor

- Referrals from GPs, ED, in-hospital and out-hospital services, self referrals
- Provide minimum core treatments for reflex syncope and OH, and treatments or preferential access for cardiac syncope, falls, PPS, and epilepsy
- Training & Education of healthcare professionals
- Employ quality indicators and desirable outcome targets
Management of syncope: clinical and economic impact of a Syncope Unit

Fabrizio Ammirati¹, Roberto Colaceci¹, Antonio Cesario¹, Stefano Strano², Alberto Della Scala³, Irene Colangelo³, Tiziana De Santo³, Elena Toscano³, Renato Ricci⁴, and Massimo Santini⁴

¹Department of Cardiology, G.B. Grassi Hospital, Via Passeroni 28, Ostia Lido, Roma, Italy; ²Center for the Study of Syncope, Policlinico Umberto I, Roma, Italy; ³Medtronic Italia SpA, Sesio S. Giovanni, MI, Italy; and ⁴Department of Cardiology, S. Filippo Neri Hospital, Roma, Italy

After Syncope Unit evaluation, diagnosis was obtained in 82% of patients.

Analysis indicated an 85% reduction of hospital costs in the follow-up period.
Ευχαριστώ!