Παρασυμπαθητικοτονική συγκοπή: Εμφύτευση μόνιμου καταγραφέα, βηματοδότη ή τίποτα;

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Παρασυμπαθητικοτονική συγκοπή

- 1-3% νήπια
- First Median 14yo, 60y.o. 42% ♀, 32% ♂
- > 1 VVS syncope
- Σπάνια >40 de novo έναρξη.
- Σε όλα τα ηλικιακά group

ΕΞΕΛΙΚΤΙΚΟ ΦΑΙΝΟΜΕΝΟ?

Heart Rhythm, Vol 12, No 6, June 2015
Reflex syncope
1 στους 4 ανθρώπους θα έχει ένα επεισόδιο τουλάχιστον στη ζωή του

Μόνο όμως 1 στους 20 θα έχει 5 και ακόμα λιγότεροι περισσότερα

>50% of pts with recurrent syncopal episodes do not have recurrences in the following 1 or 2 years and, in those with recur. the burden of syncope decreases by >70%.

- Education/Ressurance
- Trigger avoidance
- Hydration
- Hypotensive drugs avoidance
- Drugs BP raising
- Counterpressure Maneuvers

ESC Guidelines 2018
Reflex syncope

Education, life-style measures (Class I)

Severe/recurrent form

- Low BP phenotype

- Prodromes

- Hypotensive drugs

- Dominant cardioinhibition

Younger

- Fludrocortisone (Class IIb)
- Midodrine (Class IIb)
- Counter-pressure manoeuvre (Class IIa)
- Tilt training (Class IIb)

No or very short

ILR-guided management in selected cases (Class I); See section 4.2.4

Stop/reduce hypotensive drugs (Class IIa)

Older

Cardiac pacing (Class IIa/IIb)
See Figure 10
«Άτυπη Αντανακλ. Συγκοπή» Trigger Ø, Prodromes Ø
Diagnosis: Ατομ. Αναμνηστικό/ Εξ αποκλεισμού

Ανικανότητα/ ποιότ. ζωής/τραυματ./επαγγελ δυσχέρεια

Ηλικιωμένοι σοβαρότεροι τραυματισμοί/ απώλ. αυτοπεποίθησης

Δευτερογενής ψυχολογική επιβάρυνση
<table>
<thead>
<tr>
<th>Parameter Settings</th>
<th>ECG Recording</th>
<th>Duration</th>
</tr>
</thead>
<tbody>
<tr>
<td>Asystole</td>
<td>On</td>
<td>0.0 sec</td>
</tr>
</tbody>
</table>

Sensing

- Sensitivity: 0.035 mV (35 μV)
- Sensing Threshold Decay Delay: 150 ms
2,263 consecutive tilt-table tests in 2,247 patients with syncope

149 asystoles (6.6%) (mean 10 seconds); 11 had asystole for ≥30 sec (max 63 sec)

No pacemaker / conservative management, F.U. median of 42 months

4 had syncope and only 1 had syncope-related injury, suggesting that pacing is not required for all individuals even if they have asystole on the tilt-table test

<table>
<thead>
<tr>
<th>Table I.</th>
<th>Type of Response to Head-Up Tilt Test</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Response to Head-Up Tilt Test</strong></td>
<td><strong>N (%)</strong></td>
</tr>
<tr>
<td>Type 1 Mixed</td>
<td>645 (28.5%)</td>
</tr>
<tr>
<td>Type 2A Cardioinhibitory without asystole (&gt;3 seconds)</td>
<td>52 (2.3%)</td>
</tr>
<tr>
<td>Type 2B Cardioinhibitory with asystole (&gt;3 seconds)</td>
<td>149 (6.6%)</td>
</tr>
<tr>
<td>Type 3 Vasodepressor</td>
<td>389 (17.2%)</td>
</tr>
<tr>
<td>Negative/inconclusive/other</td>
<td>1,028 (45.4%)</td>
</tr>
<tr>
<td>Total</td>
<td>2,263 (100%)</td>
</tr>
</tbody>
</table>

1/3 είχαν ασυστολία μετά την έναρξη της συγκοπής

On the horizontal axis, the start of asystole is shown relative to the start of transient loss of consciousness (TLOC).
**Recommendation for Pacemakers in VVS**

<table>
<thead>
<tr>
<th>COR</th>
<th>LOE</th>
<th>Recommendation</th>
</tr>
</thead>
<tbody>
<tr>
<td>IIb</td>
<td>B-R</td>
<td>Dual-chamber pacing might be reasonable in a select population of patients 40 years of age or older with recurrent VVS and prolonged spontaneous pauses. [404-408,410]</td>
</tr>
</tbody>
</table>

Among patients with a positive tilt-table test, a benefit of pacing for treatment of recurrent syncope was evident as compared with medical or no therapy in open-label trials, but this result must be interpreted with caution because of the possibility of outcome ascertainment bias. In 2 RCTs, there was no statistically significant benefit seen with active pacing. However, in a select population of patients >40 years of age with recurrent syncope and documented spontaneous pauses ≥3 seconds correlated with syncope or an asymptomatic pause ≥6 seconds, dual-chamber pacing reduced syncope recurrence. There was less benefit in patients with a positive tilt-table test that induced a vasodepressor response. [405]
"pts > 40 years recurrent reflex syncope+ asystole in ILR, PACING EFFECTIVE"

2-year estimated syncope recurrence rate
57% PM off and 25% PM on, RR reduction of 57%.

As the average age 63 years and only 56 % had typical vasovagal, Sinus Node Dysfunction?

"Μη αξιολόγηση rate drop response algorithm used"

Recurrence not Syncope Burden

Circ Arrhythm Electrophysiol. 2014;7:10-16
reflex syncope

VS

1. delayed orthostatic hypotension,
2. POTS
3. psychogenic pseudosyncope

Figure 1  Tilt-testing positivity rate in different clinical conditions. The studies reported in the figure used the Westminster protocol for passive tilt, the Italian protocol for glyceryltrinitrate tilt, and the clomipramine protocol for a total of 1453 syncope patients and 407 control subjects without syncope. Studies using other tilt protocols, e.g. isoproterenol challenge, were not included. VVS, vasovagal syncope; clom, clomipramine; TNT, glyceryltrinitrate.
# Treatment of reflex syncope

## 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.\(^{184,185,200,292}\)

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.\(^{292,297,298,303}\)

Cardiac pacing may be considered to reduce syncope recurrences in patients with the clinical features of adenosine-sensitive syncope.\(^5,227,286\)

Cardiac pacing is not indicated in the absence of a documented cardioinhibitory reflex.\(^{299,300}\)

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ILR should be considered in patients with suspected or certain reflex syncope presenting with frequent or severe syncopal episodes.\(^{184–186}\)
• TILT NEGATIVE, TRIGGER NEG., PRODROME NEG., ASYSTOLIC SYNCOPE IS VVS ONLY BY EXCLUSION

• ATP SENSITIVE SYNCOPE?

• EARLY ANF OR CONDUCTION SYSTEM DISEASE?
ΣΥΜΠΕΡΑΣΜΑΤΑ

• Υποστηρικτικά μέτρα και εφησυχασμός είναι ο βασικός πυλώνας στην αντιμετώπιση της VVS ιδίως σε νεαρά άτομα

• Στον περίστ. ασθενή >40 χρ με απρόσμενη, σοβαρή και υποτροπιάζουσα συγκοπή ILR ενδείκνυται (PM)

• Σε αυτά τα περιστατικά ο βηματοδότης μπορεί να μειώσει την συχνότητα (μόνο) των συγκοπικών επεισοδίων

• Η ασυστολία στο Tilt Test δεν είναι ένδειξη βηματοδότησης
Pacing for reflex syncope: decision pathway

Clinical features

Severe, recurrent unpredictable syncopes, age >40 years?

Yes

CI-CSS?

Yes & Tilt negative

Implant a DDD PM

Yes & Tilt positive

Implant a DDD PM & counteract hypotensive susceptibility

No

Asystolic tilt testing?

Yes

Implant a DDD PM & counteract hypotensive susceptibility

No

Asystole?

Yes & Tilt negative

Implant a DDD PM

Yes & Tilt positive

Implant a DDD PM & counteract hypotensive susceptibility

No

Pacing not indicated

Perform CSM & tilt table test

Rec pm cont

1 y 9 22

2 15 37

3 20 43

Implant ILR
Table 9  Expected syncope recurrence rates with a permanent pacemaker in different clinical settings (for more details see Supplementary Data  Table 9).

<table>
<thead>
<tr>
<th>Clinical setting</th>
<th>Expected 2-year syncope recurrence rate with cardiac pacing</th>
</tr>
</thead>
<tbody>
<tr>
<td>Syncope due to established bradycardia and absence of hypotensive mechanism</td>
<td>High efficacy (&lt;5% recurrence rate)</td>
</tr>
<tr>
<td>Syncope due to established bradycardia and associated hypotensive mechanism</td>
<td>Moderate efficacy (5–25% recurrence rate)</td>
</tr>
<tr>
<td>Syncope due to suspected bradycardia and associated hypotensive mechanism</td>
<td>Low efficacy (&gt;25% recurrence rate)</td>
</tr>
</tbody>
</table>
Reflex syncope

- Spontaneous asystolic pauses/s
  - Extrinsic (functional) (Class IIa)
    - Vagally-mediated or Adenosine-sensitive
  - CI-CSS (Class IIa)
  - Asystolic tilt (Class IIb)
  - Adenosine sensitive syncope (Class IIb)

- Test-induced asystolic pauses/s
  - No
    - Undocumented syncope (Class III)

Pacing not indicated
Aim

Although the efficacy of cardiac pacing in patients with neurally mediated syncope (NMS) and documented asystole is established, a more robust point estimate of the benefit, which is not possible with any individual study, is lacking.

Methods and results

We undertook a meta-analysis of individual participant data from four studies that reported follow-up data on syncope recurrence with cardiac pacing in patients with NMS who had had an electrocardiographic (ECG) documentation of an asystolic event by means of implantable loop recorder (ILR). Of a total of 1046 patients, who had ILR implanted, 383 (36.6%) patients had an ECG documentation of a diagnostic event during mean follow-up of 13 ± 10 months. Of these, 201 (52%) patients, corresponding to 19.2% of the total ILRs, had an asystolic event of 12.8 ± 11.0 s duration documented and met the criteria for pacemaker therapy. Follow-up was available in 121 (60%) of those patients with asystolic events. Syncope recurred after pacing in 18 (14.9%) patients with an actuarial rate of 13% [95% confidence interval (CI) ± 6] at 1 year, 21% (95% CI ± 10) at 2 years, and 24% (95% CI ± 11) at 3 years. On multivariable Cox regression analysis, positive tilt test response was the only significant predictor of syncope recurrence with a hazard ratio (95% CI) of 4.3 (1.4–13). On the contrary, type of asystolic event (sinus arrest or atrioventricular block), prodrome, cardiac abnormalities, number and duration of history of syncope, age, and gender were not predictors of recurrence of syncope.

Conclusion

A long asystolic pause, suitable for pacemaker therapy, was found in one of five patients with ILR. After pacemaker implantation, most of these patients remained free of syncope recurrence for up to 3 years. The benefit of pacemaker was greater in patients with negative tilt test.

Keywords

Syncope • Reflex • Neurally mediated • Implantable loop recorder • Sinus arrest • Atrioventricular block • Pacemaker • Cardiac pacing • Meta-analysis
Reflex syncope, also called neurally mediated syncope, accounts for most of the cases of syncope, with a balanced incidence over the various age categories.

<table>
<thead>
<tr>
<th>Age</th>
<th>Source</th>
<th>Reflex (%)</th>
<th>Orthostatic hypotension (%)</th>
<th>Cardiac (%)</th>
<th>Non-syncopal TLOC (%)</th>
<th>Unexplained (%)</th>
<th>Setting</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;40 years</td>
<td>Olde Nordkamp</td>
<td>51</td>
<td>2.5</td>
<td>1.1</td>
<td>18</td>
<td>27</td>
<td>ED and chest pain unit</td>
</tr>
<tr>
<td>40 – 60 years</td>
<td>Olde Nordkamp</td>
<td>37</td>
<td>6</td>
<td>3</td>
<td>19</td>
<td>34</td>
<td>ED and chest pain unit</td>
</tr>
<tr>
<td>&lt;65 years</td>
<td>Del Rosso</td>
<td>68.5</td>
<td>0.5</td>
<td>12</td>
<td>-</td>
<td>19</td>
<td>Cardiology department</td>
</tr>
<tr>
<td>&gt;60/65 years</td>
<td>Del Rosso</td>
<td>52</td>
<td>3</td>
<td>34</td>
<td>-</td>
<td>11</td>
<td>Cardiology department</td>
</tr>
<tr>
<td></td>
<td>Ungar</td>
<td>62</td>
<td>8</td>
<td>11</td>
<td>-</td>
<td>14</td>
<td>Geriatric department</td>
</tr>
<tr>
<td></td>
<td>Olde Nordkamp</td>
<td>25</td>
<td>8.5</td>
<td>13</td>
<td>12.5</td>
<td>41</td>
<td>ED and chest pain unit</td>
</tr>
<tr>
<td>&gt;75 years</td>
<td>Ungar</td>
<td>36</td>
<td>30</td>
<td>16</td>
<td>-</td>
<td>9</td>
<td>Geriatric department. Note: In a further 8% of patients, the diagnosis was multifactorial or drug-related</td>
</tr>
</tbody>
</table>

201/1046 ILRs ASYSTOLE

Positive Tilt Test was the only predictor for Recurrence
Table 1. A comparison of the clinical features of isolated vasovagal syncope and vasovagal disease.

<table>
<thead>
<tr>
<th>Isolated vasovagal syncope</th>
<th>Vasovagal disease</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Differences:</strong></td>
<td></td>
</tr>
<tr>
<td>• Onset at a young age</td>
<td>• Onset in old age</td>
</tr>
<tr>
<td>• Otherwise healthy people</td>
<td>• Patients with cardiovascular or neurological disease</td>
</tr>
<tr>
<td>• Typical vasovagal prodromes/triggers (“classical” form)</td>
<td>• Presentation without prodromes/atypical triggers (“non-classical” form)</td>
</tr>
<tr>
<td>• Affects about 50% of all individuals</td>
<td>• Often diagnosed only after a positive head-up tilt test</td>
</tr>
<tr>
<td>• 70% of population predisposed</td>
<td>• Overlap with carotid sinus syndrome</td>
</tr>
<tr>
<td>• Strong stressor</td>
<td>• Overlap with situational syncope</td>
</tr>
<tr>
<td>• No genetic basis</td>
<td>• Overlap with orthostatic hypotension or other dysautonomic symptoms</td>
</tr>
<tr>
<td>• No evidence of autonomic involvement or hormonal disorders</td>
<td>• High risk of trauma</td>
</tr>
<tr>
<td>• Low risk of trauma</td>
<td>• Sometimes progressively worsening over time</td>
</tr>
<tr>
<td>• Frequent spontaneous disappearance in advanced age</td>
<td></td>
</tr>
</tbody>
</table>

**Similarities:**

- Similar hypotension-bradycardia mechanism
- Similar rate of positive responses during tilt testing
- Similar rate of cardioinhibitory and vasodepressor forms during spontaneous syncope

• Exact mechanisms of VVS are unknown
• Mechanisms of recovery?
• It remains unclear if VVS can be aborted once the reflex is underway.
• Syncope can occur before asystole and even if asystole is prevented.
• There is no gold standard test (ILR/Tilt Test)
• Heart rate and blood pressure manifestations of VVS can vary
• Human violent conflicts theory
• Clot production theory
• Psychological defense theory
• Heart defense theory
• Brain self-preservation theory