Corso Avanzato GIMSI sulla Sincope

Il nuovo ruolo del tilt test

Michele Brignole
Centro Aritmologico & Syncope Unit - Lavagna
Tilt table testing: limitations

- Too often negative in pts with likely VVS ("low sensitivity")
- Too often positive in pts without VVS syncope ("low specificity")
- No value in assessing efficacy of treatment with drugs or pacemaker

Someone stopped to perform it ("clinical history better than tilt table testing")
Tilt testing: positivity rate

- 92% Typical VVS, emotional trigger (Clom)
- 78% Typical VVS, situational trigger (TNT)
- 73%-65% Typical VVS, miscellaneous (Clom) (TNT)
- 56%-51% Likely reflex, atypical (TNT)
- 47% Cardiac syncope (TNT)
- 45% Likely tachyarrhythmic syncope (Passive)
- 36%-30% Unexplained syncope (TNT) (Clom)
- 13%-8% Subjects without syncope (Passive) (Clom) (TNT)

Sutton & Brignole. Eur Heart J 2014; 35: 2211-12
Twenty-eight years of research permit reinterpretation of tilt-testing: hypotensive susceptibility rather than diagnosis

Richard Sutton\textsuperscript{1}\textsuperscript{*} and Michele Brignole\textsuperscript{2}

A positive tilt test suggests the presence of a \textbf{hypotensive susceptibility}, which plays a role in causing syncope irrespective of the etiology and mechanism of syncope.
## Changed indications for Tilt Table Testing

<table>
<thead>
<tr>
<th>Old (initial) indications</th>
<th>New indications</th>
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<tr>
<td>Diagnosis of VVS</td>
<td>Susceptibility to orthostatic stress, irrespective of the etiology of syncope</td>
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*Sutton & Brignole. Eur Heart J 2014; 35: 2211-12*
ISSUE 3

SYNCOPE

Study design

ILR screening phase

Pts affected by severe, recurrent reflex syncopes, aged >40 yrs

↓

Tilt Table Testing (Passive + TNT)

↓

ILR implantation (Reveal DX/XT)

↓

ILR follow-up (max 2 yrs)

↓

ILR eligibility criteria:
- Asystolic syncope ≥3 s, or
- Non-syncopal asystole ≥6 s

R

Pm ON

Pm OFF

ISSUE 3 therapy phase
First syncope recurrence
(intention-to-treat)

Kaplan-Meier survival estimates
log rank: p=0.039
RRR at 2 yrs: 57%

Number at risk
Pm OFF: 39, 31, 25, 21, 21, 18, 15, 12, 8
Pm ON: 38, 32, 27, 22, 16, 14, 13, 13, 11

Brignole et al. Circulation 2012;125:2566-2571
### Factors predicting recurrence of syncope after pacemaker therapy (II)

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Recurrence n=9</th>
<th>No recurrence n=43</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Tilt testing: positive</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>- Asystolic (Vasis 2B)</td>
<td>44%</td>
<td>23%</td>
<td>ns</td>
</tr>
<tr>
<td>- Non-asystolic</td>
<td>44%</td>
<td>19%</td>
<td>ns</td>
</tr>
<tr>
<td><strong>ILR findings (asystole)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>- Asystole duration, sec</td>
<td>9</td>
<td>8</td>
<td>ns</td>
</tr>
<tr>
<td>- Type 1A (sinus arrest)</td>
<td>44%</td>
<td>63%</td>
<td>ns</td>
</tr>
<tr>
<td>- Type 1B (sinus brady + AV block)</td>
<td>33%</td>
<td>14%</td>
<td>ns</td>
</tr>
<tr>
<td>- Type 1C (AV blocK)</td>
<td>22%</td>
<td>24%</td>
<td>ns</td>
</tr>
<tr>
<td><strong>Systolic blood pressure</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>- Supine, mmHg</td>
<td>135</td>
<td>130</td>
<td>ns</td>
</tr>
<tr>
<td>- Standing, mmHg</td>
<td>127</td>
<td>118</td>
<td>ns</td>
</tr>
</tbody>
</table>
Syncope recurrence after PM therapy according to tilt test results

5% vs 55% at 21 months
log rank: p=0.004

Brignole M et al. Circ Arrhythm Electrophysiol 2014;7:10-16
A Positive Response to Head-Up Tilt Testing Predicts Syncopal Recurrence in Carotid Sinus Syndrome Patients With Permanent Pacemakers

Germano Gaggioli, MD, Michele Brignole, MD, Carlo Menozzi, MD, Gianluigi Devoto, MD, Daniele Oddone, MD, Lorella Gianfranchi, MD, Enrico Gostioli, MD, Nicola Bottoni, MD, and Gino Lalli, MD

Am J Cardiol 1995; 76: 720

**TABLE I** Comparison Between Patients With and Without Syncopal Recurrence at Follow-Up

<table>
<thead>
<tr>
<th>Factors</th>
<th>Syncope (n = 24)</th>
<th>No Syncope (n = 145)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Head-up tilt test</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Positive</td>
<td>15 (63)*</td>
<td>55 (38)*</td>
</tr>
<tr>
<td>Negative</td>
<td>9 (38)*</td>
<td>90 (62)*</td>
</tr>
<tr>
<td>Underlying heart disease</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>12 (50)</td>
<td>88 (61)</td>
</tr>
<tr>
<td>No</td>
<td>12 (50)</td>
<td>57 (39)</td>
</tr>
<tr>
<td>Age</td>
<td></td>
<td></td>
</tr>
<tr>
<td>&gt;70 yr</td>
<td>15 (63)</td>
<td>92 (63)</td>
</tr>
<tr>
<td>≤70 yr</td>
<td>9 (38)</td>
<td>53 (37)</td>
</tr>
<tr>
<td>Pacemaker mode</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dual-chamber</td>
<td>14 (58)</td>
<td>96 (66)</td>
</tr>
<tr>
<td>VVI</td>
<td>10 (42)</td>
<td>49 (34)</td>
</tr>
<tr>
<td>Type of carotid sinus syndrome</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cardioinhibitory</td>
<td>13 (54)</td>
<td>83 (57)</td>
</tr>
<tr>
<td>Mixed</td>
<td>11 (46)</td>
<td>62 (43)</td>
</tr>
<tr>
<td>Gender</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>19 (79)</td>
<td>107 (74)</td>
</tr>
<tr>
<td>Female</td>
<td>5 (21)</td>
<td>38 (26)</td>
</tr>
<tr>
<td>Number of syncopal episodes</td>
<td></td>
<td></td>
</tr>
<tr>
<td>&gt;3</td>
<td>14 (58)</td>
<td>61 (42)</td>
</tr>
<tr>
<td>≤3</td>
<td>10 (42)</td>
<td>84 (58)</td>
</tr>
</tbody>
</table>

% ABSENCE OF SYNCOPE

log-rank: p <0.004

YEARS
Recurrence of syncope according to tilt test results

Log rank: p=0.008

Number at risk
Group: 1
44 37 31 28 22 13 6 2 2
Group: 2
15 14 13 12 8 8 6 2 1
Group: 3
82 63 51 35 27 17 13 8 5

Clinical context and outcome of carotid sinus syndrome diagnosed by means of the ‘method of symptoms’

Solari D et al. Europace 2013
SUP 2 study: 3-years extended follow-up

Recurrence of syncope

Log rank for trend:
- Pm, TT Negative: p = 0.03
- Pm, TT Positive: p = n.s.
- No Pm, ILR: p = 0.01

Number at risk
- Group 1: 20 18 17 12 11 6 4
- Group 2: 61 57 50 41 30 21 8
- Group ILR: 142 115 90 58 37 22 10

Europace 2016
### Changed indications for Tilt Table Testing

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<tr>
<td>Identification of candidates for permanent pacing (CI form)</td>
<td>Identification of non-responder to cardiac pacing (any positive response)</td>
</tr>
</tbody>
</table>

*Sutton & Brignole. Eur Heart J 2014*
Reflex syncope: Dual-action model

Hypotensive susceptibility

YES (Tilt +)
Low reflex threshold

+ 
(neuro and/or humoral)

Vasovagal syncope (hypotension-bradycardia)

Hypotension phenotype domain (pacing low responder)

Trigger

+++ 
Cardio-inhibitory reflex syncope

Bradycardia phenotype domain (pacing high-responder)

NO (Tilt -)
High reflex threshold
Tilt table testing: asystolic form (VASIS 2B)

- 44%  Typical emotional VVS (Clom)
- 24%  Typical emotional VVS (TNT)
- 21%  Likely reflex, no trigger (TNT)
- 17%  Typical peripheral trigger VVS (Clom)
- 10%  Typical peripheral trigger VVS (TNT)
-  8%  Unexplained syncope (Clom)
-  7%  Unexplained syncope (TNT)
-  6%  Subjects w/t syncope (Passive)
-  0%  Cardiac syncope (TNT)
-  0%  Subjects w/t syncope (TNT)
Correlation between tilt test responses and ILR-documented mechanism

- Tilt test +: Total 76 pts
- ILR +

Asystole (Vasis 2B):
- 28
- 24 (86%)
- 4 (14%)

M or VD (Vasis 1,2A,3):
- 48
- 23 (48%)
- 25 (52%)

Asystole:
- 47

Slight rhythm variations:
- 29

Positive predictive value of asystolic tilt: 0.86 (95% CI 0.70-0.95)

Brignole M et al. Circ Arrhythm Electrophysiol 2014;7:10-16
**SUP 2 study: 3-years extended follow-up**

Recurrence of syncope

![Graph showing recurrence of syncope over months with log rank for trend: \( p = 0.01 \)](image)

<table>
<thead>
<tr>
<th>Months</th>
<th>ILR</th>
<th>PM-CSS</th>
<th>PM-VASIS 2B</th>
<th>PM-ILR</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>142</td>
<td>78</td>
<td>21</td>
<td>38</td>
</tr>
<tr>
<td>6</td>
<td>115</td>
<td>69</td>
<td>18</td>
<td>37</td>
</tr>
<tr>
<td>12</td>
<td>90</td>
<td>61</td>
<td>17</td>
<td>32</td>
</tr>
<tr>
<td>18</td>
<td>58</td>
<td>51</td>
<td>11</td>
<td>26</td>
</tr>
<tr>
<td>24</td>
<td>37</td>
<td>40</td>
<td>8</td>
<td>21</td>
</tr>
<tr>
<td>30</td>
<td>22</td>
<td>26</td>
<td>6</td>
<td>13</td>
</tr>
<tr>
<td>36</td>
<td>10</td>
<td>17</td>
<td>1</td>
<td>6</td>
</tr>
</tbody>
</table>

**Number at risk**
- Group: ILR  
  - 142
- Group: PM-CSS  
  - 78
- Group: PM-ILR  
  - 21
- Group: PM-VASIS 2B  
  - 38
Benefit of dual-chamber pacing with Closed Loop Stimulation (CLS) in tilt-induced cardio-inhibitory reflex syncope.

A randomized double-blind parallel trial

M. Brignole (PI) - M. Tomaino (Co-PI)
Italian Multidisciplinary Group for the Study of Syncope:

Established in 2003 by 5 national societies:
- arrhythmology,
- internal medicine,
- emergency medicine,
- geriatrics
- neurology