What Is the Role of EPS and Catheter Ablation in Patients with Unexplained Syncope?

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Role of EP Studies in the Evaluation of Syncope

Mark W. Preminger, MD
### Diagnostic Tests in the Evaluation of TLOC

- **History & Physical Exam**
  - Most NMS can be dx by hx alone.

- **Head CT Scan**
  - No role in the absence of localizing features

- **EEG**
  - Hx of CVA; Head injury; Witnessed Sz activity; abnl neuro exam

- **Carotid Dopplers**
  - Unilateral Anterior circulation occlusion does not cause TLOC
  - Posterior circulation disease usually associated with vertigo.

- **2 D Echocardiogram**
  - Structural Heart Disease
    - Valvular Disease (AS)
    - HOCM
    - LV Dysfunction

- **EKG**
  - Useful in identifying underlying heart disease
  - Prior MI
  - Conduction disease (Sinus Bradycardia; BBB; heart blocks)

- **Holter Monitor (24 hrs)**
- **ZIO Patches (7-14 days)**
  - Limited value unless symptoms are very frequent

- **Event Monitors / MCOT**
  - Provide symptom /rhythm correlation

- **Implantable Loop Recorders**
- **SAECG / T wave alternans**
  - Lack sensitivity & specificity

- **Tilt Table Testing**
  - Confirms diagnosis.

- **Electrophysiology Studies**
Variations in diagnostic yield of head-up tilt test and electrophysiology in groups of patients with syncope of unknown origin

- 600 patients with syncope of unknown origin.
  - 600 underwent a tilt test.
  - 247 underwent electrophysiology study.

- Patients were divided into groups
  - age at the time of first syncope
  - ECG findings
  - Presence or absence of organic heart disease.

- Positive tilt tests were more common
  - Patients who had suffered their first syncope at an age \( \leq 65 \) (group I) than in older patients (group II) \((47\% \text{ vs } 33\%, P<0.05, \text{ OR } 1.8, \text{ CI } 1.2\text{–}2.78)\),
  - Patients with a normal ECG and without organic heart disease than in the other subgroups of patients \((47\% \text{ vs } 37\%, P<0.008, \text{ OR } 1.6)\).
  - The lowest rate of positive response was observed in older patients with an abnormal ECG and organic heart disease.

- Abnormal Findings at Electrophysiology Study
  - Patients who had suffered their first syncope at an age \( > 65 \) (group II) than in younger patients (group I) \((23\% \text{ vs } 7\%, P<0.001, \text{ OR } 3.7, \text{ CI } 1.7\text{–}9.2)\).
  - In patients with an abnormal ECG than in those with a normal ECG \((22\% \text{ vs } 3.7\%, P<0.0005, \text{ OR } 7.1)\).
  - Abnormal EP findings were especially low in patients with a normal ECG and without organic heart disease \(2.6\%).

Sagrista`-Sauleda J. et al.
Variations in diagnostic yield of head-up tilt test and electrophysiology in groups of patients with syncope of unknown origin

### Distribution of Patients

<table>
<thead>
<tr>
<th>Group</th>
<th>1st syncope at</th>
<th>Group II</th>
<th>1st syncope at</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>≤ 65 years</td>
<td></td>
<td>&gt; 65 years</td>
</tr>
<tr>
<td></td>
<td>(n=464 patients)</td>
<td></td>
<td>(n=136 patients)</td>
</tr>
<tr>
<td>A: no OHD, normal ECG</td>
<td>319 (68%)</td>
<td>40 (29%)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>B: no OHD, abnormal ECG</td>
<td>75 (16%)</td>
<td>47 (34%)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>C: OHD, normal ECG</td>
<td>33 (7%)</td>
<td>11 (8%)</td>
<td>ns</td>
</tr>
<tr>
<td>D: OHD, abnormal ECG</td>
<td>37 (8%)</td>
<td>38 (27%)</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

OHD = organic heart disease; subgroup A predominated in group I, while subgroups B and D predominated in group II.

### Distribution of Positive Results

<table>
<thead>
<tr>
<th>Group I (464 patients)</th>
<th>Group II (136 patients)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Head-up tilt test</td>
<td>Electrophysiology</td>
</tr>
<tr>
<td>----------------------</td>
<td>----------------------</td>
</tr>
<tr>
<td>A</td>
<td>160/319 (50%)</td>
</tr>
<tr>
<td>B</td>
<td>38/75 (50%)</td>
</tr>
<tr>
<td>C</td>
<td>9/33 (27%)</td>
</tr>
<tr>
<td>D</td>
<td>13/37 (35%)</td>
</tr>
<tr>
<td>Total</td>
<td>220/464 (47%)</td>
</tr>
</tbody>
</table>

A: no organic heart disease, normal ECG; B: no organic heart disease, abnormal ECG; C: organic heart disease, normal ECG; D: organic heart disease, abnormal ECG.

What Constitutes an Abnormal EP Study?

- **Sinus Node Function**
  - **Sinus Node Recovery Time:**
    - $\text{SNRT}_{\text{max}} > 1,500-1,720$
    - $\text{CSNRT}_{\text{max}} > 225$ msec
    - $\text{SNRT}_{\text{max}}$ occurring following a pacing drive > 600 msec.
  
  A CSNRT > 800 msec associated with an 8 fold increase in incidence of syncope compared with patients with CSNRT < 800.

- **Sino-Atrial Conduction Time:**
  - **Premature Atrial Stimulation Technique:**
    - Single atrial premature extra-stimuli are introduced during sinus rhythm. When introduced early enough, the return is less than fully compensatory. This interval less the sinus cycle length reflects the conduction time into and back out of the sinus node.
    - $\text{SACT} > 206$ msec
  
  **Constant Atrial Stimulation Technique:**
  - 8 paced beats are delivered 10 msec above the Sinus CL.
  - $\text{SACT} > 250$ msec
Role of EP Studies in SN Dysfunction

- Current SN Function tests are specific and therefore useful in confirming the presence of SN Dysfunction
- The Sensitivity of SN Function tests however is poor. A normal SN function test does not exclude SN dysfunction

<table>
<thead>
<tr>
<th>Study</th>
<th>CSRT/SNRT</th>
<th>SACT</th>
<th>Either&lt;sup&gt;B&lt;/sup&gt;</th>
<th>Sensitivity</th>
<th>Specificity</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>CSRT/SNRT</td>
<td>SACT</td>
<td>Either&lt;sup&gt;B&lt;/sup&gt;</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Reiffel et al.&lt;sup&gt;15&lt;/sup&gt;</td>
<td>13/23</td>
<td>7/23</td>
<td>16/23</td>
<td>22/23</td>
<td>21/23</td>
</tr>
<tr>
<td></td>
<td>(56%)</td>
<td>(30%)</td>
<td></td>
<td>(88%)</td>
<td>(88%)</td>
</tr>
<tr>
<td>Gupta et al.&lt;sup&gt;16&lt;/sup&gt;</td>
<td>3/17</td>
<td>N/A</td>
<td>N/A</td>
<td>15/15</td>
<td>N/A</td>
</tr>
<tr>
<td></td>
<td>(18%)</td>
<td></td>
<td></td>
<td>(100%)</td>
<td></td>
</tr>
<tr>
<td>Pop et al.&lt;sup&gt;19&lt;/sup&gt;</td>
<td>46/67</td>
<td>N/A</td>
<td>N/A</td>
<td>108/110</td>
<td>N/A</td>
</tr>
<tr>
<td></td>
<td>(69%)</td>
<td></td>
<td></td>
<td>(98%)</td>
<td></td>
</tr>
<tr>
<td>Seipel et al.&lt;sup&gt;24c&lt;/sup&gt;</td>
<td>N/A</td>
<td>36/57</td>
<td>N/A</td>
<td>N/A</td>
<td>78/136</td>
</tr>
<tr>
<td></td>
<td></td>
<td>(63%)</td>
<td></td>
<td></td>
<td>(57%)</td>
</tr>
<tr>
<td>Szatmary&lt;sup&gt;41&lt;/sup&gt;</td>
<td>9/35</td>
<td>N/A</td>
<td>N/A</td>
<td>14/16</td>
<td>N/A</td>
</tr>
<tr>
<td></td>
<td>(26%)</td>
<td></td>
<td></td>
<td>(88%)</td>
<td></td>
</tr>
<tr>
<td>Steinbeck and Luderitz&lt;sup&gt;51&lt;/sup&gt;</td>
<td>2/4</td>
<td>3/4</td>
<td>3/4</td>
<td>5/5</td>
<td>5/5</td>
</tr>
<tr>
<td></td>
<td>(50%)</td>
<td>(75%)</td>
<td></td>
<td>(100%)</td>
<td>(100%)</td>
</tr>
<tr>
<td>Benditt et al.&lt;sup&gt;52&lt;/sup&gt;</td>
<td>11/39</td>
<td>N/A</td>
<td>N/A</td>
<td>40/44</td>
<td>N/A</td>
</tr>
<tr>
<td></td>
<td>(28%)</td>
<td></td>
<td></td>
<td>(91%)</td>
<td></td>
</tr>
<tr>
<td>Steinbeck and Luderitz&lt;sup&gt;53&lt;/sup&gt;</td>
<td>8/18</td>
<td>4/14</td>
<td>9/14</td>
<td>6/6</td>
<td>7/8</td>
</tr>
<tr>
<td></td>
<td>(44%)</td>
<td>(29%)</td>
<td></td>
<td>(91%)</td>
<td></td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td>92/203</td>
<td>50/98</td>
<td>28/41</td>
<td>210/221</td>
<td>112/174</td>
</tr>
<tr>
<td></td>
<td>(45%)</td>
<td>(51%)</td>
<td></td>
<td>(95%)</td>
<td>(74%)</td>
</tr>
</tbody>
</table>

N/A = not available; sensitivity = test positives/true positives; specificity = test negatives/true negatives.

<sup>A</sup>Criteria for abnormal test: CSRT 525 msec, SNRT 1600 msec, SACT 206 msec.

<sup>B</sup>Interpret with caution because of small number of patients reported.

<sup>C</sup>Data estimated from figures 4 to 6, ref. 24.
What Constitutes an Abnormal EP Study?

- **AV Nodal Function:**
  - AH > 130 msec
  - AV Wenkebach at pacing rates < 110 bpm

- In General AH prolongation does not progress to high grade AV block and account for syncope.

- The site of AV block in patients with persistent Complete Heart Block occurs in the AV node (Above the His Bundle) in 15-35%.
  - Lyme Disease
  - Congenital Complete Heart Block
  - Infiltrative Diseases
What Constitutes an Abnormal EP Study?

- **His-Purkinje Function:**
  - **HV interval (normal: 35-55 msec)**
    - HV < 60 msec associated with a 2-4% progression to AV Block.
  - **HV > 100 msec**
    - HV > 100 msec associated with a 24% progression to AV Block
    - Class I indication for pacing
  - **HV = 70-100 msec**
    - 12%-21% risk of progression to AV block.
    - Incremental Atrial Pacing or IV Procainamide
      - Intra or Infra His Block
      - Prolongation of HV
      - Pacing Induced increase in HV by 10 msec or infra-His block associated with a 30-40% progression to AV block over 22-48 mo.
      - Class IA Induced HV > 120 ms or infra-His block associated with 40-68% progression to AV block over 24-48 mo.
Pacing Induced Infra-His Block
### Location of Block in 2’ AV Block

**Relationship between type and site of second-degree atrioventricular (AV) block**

<table>
<thead>
<tr>
<th>Type of block</th>
<th>No. of patients</th>
<th>Above the His bundle</th>
<th>Intra-His</th>
<th>Infra-His</th>
</tr>
</thead>
<tbody>
<tr>
<td>Type I</td>
<td>72</td>
<td>52 (72%)</td>
<td>6 (8%)</td>
<td>14 (20%)</td>
</tr>
<tr>
<td>Type II</td>
<td>38</td>
<td>—</td>
<td>11 (29%)</td>
<td>27 (71%)</td>
</tr>
<tr>
<td>2:1 or 3:1</td>
<td>93</td>
<td>27 (29%)</td>
<td>19 (20%)</td>
<td>47 (51%)</td>
</tr>
</tbody>
</table>

Second Degree AV Block – type I + Narrow QRS is always due to AV Node Block
Second Degree AV Block – type I + Wide Complex may occur in Above, intra- or infra His locations
Value of EP study in Syncope Patients with BBB

- A Negative EP Study is not predictive of No Risk
- ISSUE Study
  - ILR’s placed in 52 patients with bundle branch block, syncope & negative EP Study.
  - Follow-up 3-15 months
  - 19 (37%) developed recurrent syncope.
  - 17 prolonged asystole due to AV block or Sinus arrest
  - 2 (4%) presyncope associated with AV block
  - 3 (6%) asymptomatic stable AV block
  - 1 (2%) Death

Mechanism of syncope in patients with bundle branch block and negative electrophysiological test.
What Constitutes an Abnormal EP Study?

- **Inducible Arrhythmias:**
  - Reproducibly Induced Supraventricular Tachycardia
    - AV Nodal Reentrant Tachycardia
    - AV Reentrant Tachycardia
    - Atrial Tachycardia
  - Associated with Hemodynamic Compromise:
    - Hypotension
    - SVT rates \( \geq 180 \text{ bpm} \)

- Reproducibly induced Monomorphic VT
  - Absence of Structural Heart Disease
    - RBBB LAD (Belhassen’s VT); LBBB inf Axis (RVOT; LVOT) RBBB Inf axis (Aorto-mitral continuity)
  - Structural Heart Disease
    - Coronary Artery Disease (Usually post MI)
    - Cardiomyopathies
      - Idiopathic Cardiomyopathy
      - ARVD
      - HOCM
    - The Negative predictive Value in the absence of CAD is less certain.
• 36 year old male with a history of symptomatic palpitations.

• Sustained loss of consciousness resulting in a motor vehicle accident.
Elimination of Left Lateral Accessory pathway conduction and termination of Orthodromic AV RT with RF energy application.
72 year old male with hx of IWMI 10 yrs ago.

Presents following an episode of syncope.
- EKG: SR, IWMI age indet.
- Echo: Inf Akinesis; EF=40%

EP Study:
- Monomorph VT cycle length 272 msec induced with triple extra-stimuli at RV Apex
- Terminated with RV Burst pacing

ICD implanted

Recurrent Syncope
EP Guided Management of Syncope

- 67 Consecutive patients with Coronary Artery Disease and Unexplained syncope

**Evaluation:**
- H & P
- ECG
- Assessment of LVEF
- 24 Holter or Telemetry
- Cath or perfusion imaging

**All Patients underwent EP testing**
- Inducible Pts
  - ICD Rx or EP guided AA drug therapy (1)
- Non-Inducible patients
  - Tilt Table Testing.

Mittal S. et al. JACC 1999; 34:1082
EP Guided Management of Syncope

- Results:
  - Sinus Node Dysfunction: 7
  - HV > 100 msec: 1
  - Dual AV node physiology: 15
    - AVNRT: 0
  - Inducible Monomorphic VT 29 (43%)
    - Includes 4/7 Pts with SND
    - Includes 1 Pt with severe HP disease
  - Treatment
    - ICD therapy 26/29
      - 11 (43%) > appropriate Rx for VT/VF
    - Amiodarone 1
    - Refused 1

Mittal S. et al. JACC 1999; 34:1082
Prognostic Value of PES in Syncope & CAD

Despite frequent appropriate ICD therapies, Inducible Patients had higher total and cardiac mortality.

Mittal S. et al.  JACC 1999; 34:1082
Role of PES in non-ischemic Cardiomyopathy

- Syncope in NIDCM associated with high mortality
  - Knight et al. JACC 1999 (33):1964
  - Compared 14 consecutive pts with syncope & - EPS treated w/ ICD
  - vs 19 consecutive pts with cardiac arrest treated with ICD
  - Brilakis et al. PACE 2001;24:1623
  - 54 pts w/ NIDCM & Syncope
    - 37/54 underwent EPS
      - 10 Inducible VT
      - 12 Cond +/- NMS
      - 15 – EPS
  - Therapy
    - 17 ICD (10 EP+)
    - 15 PPM
    - 22 No CIED
  - ICD Rx for VT
    - 47% (1yr); 74% (3yr) EP +
    - 40% (1yr); 40% (3yr) EP –
  - Overall survival was worst in EP negative pts without ICD
Patients with Implantable Defibrillators may present with Syncope.

- In patients with structural Heart disease and syncope who present without receiving ICD therapy.
- VT may be occurring below the rate cut-off of the device.
  - Due to a high Lower Rate cut-off for VT detection (typical of primary prevention devices)
  - Due to the addition of anti-arrhythmic agents that may prolong the VT cycle length.
- Due to delayed detection of VT due to under-sensing of the ventricular arrhythmia or a long detection time in the setting of a rapid ventricular arrhythmia.
Role of EP Studies in the Evaluation of Syncope

- **Sinus Node Dysfunction.**
  - Best Assessed by ILR or MCOT Monitoring
  - SNRT & SACT are specific for Sinus node dysfunction but not sensitive.
  - EP findings do not provide symptom–arrhythmia correlation

- **Infra-Infra His Conduction Disease.**
  - An HV > 100 is strongly suggestive as a cause of the syncope
  - The risk of progression to complete heart block in this setting is high
  - Moderate His-Purkinje disease is less clearly associated as the cause of syncope
    - Stressing the His Purkinje system with IA AA agents or pacing
  - Intra-His Conduction disease
    - Usually manifested by split His potential or block between H1 and H2

- **Induction of Sustained hemodynamically compromising or very rapid arrhythmias with programmed stimulation may provide a clue as to the cause of syncope.**
  - High Risk Patients
  - Patients with structural Heart Disease
  - Patients with palpitations preceding their syncope.
ACC/AHA Guidelines

- **Class I**
  - EP testing is recommended in patients with syncope of unknown cause with impaired LV function or structural heart disease.
  - Level of Evidence B.

- **Class IIa**
  - EP testing can be useful in patients with syncope when bradyarrhythmias or tachyarrhythmias are suspected and in whom non-invasive diagnostic studies are not conclusive.
  - Level of evidence B
ESC Guidelines

- **Class I**
  - EPS is indicated when the initial evaluation suggests an arrhythmic cause of syncope.
    - Abnormal EKG
    - Structural Heart Disease
    - Syncope associated with Palpitations or chest pain
    - Syncope during exertion or in the supine position
    - Family history of sudden death

- **Class II**
  - To evaluate the nature of an arrhythmia that has already been identified as the cause of the syncope
    - For the purpose of ablation
  - In patients with high risk occupations, in whom every effort to exclude a cardiac cause is warranted.

- **Class III**
  - In patients with normal EKG, no structural heart disease or palpitations.
Summary

- Diagnostic EP Studies are of Limited Value in the evaluation of Syncope.
  - In Patients without structural Heart disease
    - Low yield
    - Limited to patients with palpitations preceding the event
    - Patients with specific EKG abnormalities:
      - WPW, infarction Q waves; possible Brugada syndrome, borderline QT prolongation.
  - In certain patients with structural heart disease.
    - Evidence of cardiac conduction abnormalities (bundle branch block)
    - Coronary artery disease or history of MI
      - Specific and provide prognostic information
      - Not sensitive
    - No role in the evaluation of the syncope patient with:
      - Non-ischemic Cardiomyopathy
      - Hypertrophic Cardiomyopathy
      - Infiltrative cardiomyopathies
  - Implantable Loop recorders should be considered in all patients with structural heart disease and negative EP studies who do not otherwise meet criteria for ICD implantation