Synkope
Patrick Badertscher, Jeanne du Fay de Lavallaz, Kardio Lunch, 03/2018
„What happens when your lights go out?“
Syncope: Definition

Guidelines for the diagnosis and management of syncope (version 2009)

The Task Force for the Diagnosis and Management of Syncope of the European Society of Cardiology (ESC)

Developed in collaboration with, European Heart Rhythm Association (EHRA)\(^1\), Heart Failure Association (HFA)\(^2\), and Heart Rhythm Society (HRS)\(^3\)
Impact of Syncope

- 40% will experience syncope at least once in a lifetime
- 1-6% of hospital admissions
- 1% of emergency room visits per year
- Major morbidity reported in 6% (e.g., fractures, ICB, motor vehicle accidents…)
- In the US in 2014: Hospital costs of $4.1 billion, with mean cost of $9,400 per admission

Reflex (neurally mediated) syncope

Vasovagal
Meditated by orthostatic or emotional stress

Situational
Cough, sneeze, gastrointestinal, micturition, post-exercise, post-prandial, others (laugh, brass instrument playing, weightlifting)

Carotis sinus syncope

Atypical forms
Without apparent triggers and/or atypical presentation

Syncope due to orthostatic hypotension

Primary autonomic failure
Pure autonomic failure, Multiple system atrophy, Parkinson's disease with autonomic failure, Lewy body dementia

Secondary autonomic failure
Diabetes, Amyloidosis, Uraemia, Spinal cord injuries

Drug induced
Alcohol, vasodilators, diuretics, phenothiazines, antidepressants

Volume depletion
Haemorrhage, diarrhoea, vomiting etc.

Cardiac syncope

Arrhythmias
Bradycardia
sinus node dysfunction, atrio-ventricular conduction system disease, implanted device malfunction

Tachycardia
supraventricular, ventricular (idiopathic, secondary to structural heart disease or to channelopathies)

Drug-induced

Structural heart disease

Cardiac
valvular disease (or prosthetic valve dysfunction), acute myocardial infarction/ ischemia, hypertrophic cardiomyopathy, cardiac masses, pericardial disease/ tamponade, congenital anomalies of coronary arteries

Other
pulmonary embolus, acute aortic dissection, pulmonary hypertension
Why is syncope a difficult problem?

- Physiologic response to a wide variety of medical conditions
- By definition it is a transient condition
- Occurs with unpredictable and random patterns
- Difficult to establish definitive diagnosis
- History from patient may not be reliable
Content

I. BASEL IX Syncope study

II. Syncope: What’s in the guidelines?

III. Syncope: Are we doing a good job?

IV. Prognosis of different Syncope etiologies

V. How can we improve risk stratification in the ED?

VI. Prevalence of PE in syncope patients
Content

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VI. Prevalence of PE in syncope patients
13 hospitals in 7 countries on 3 continents!!!
> 2300 patients enrolled worldwide
**Study Design**

**Aim:** to evaluate the diagnostic value of clinical judgement and novel biomarkers in the diagnosis and risk stratification of syncope patients

**Inclusion Criteria**
- Patients > 40 years
- Presenting to the ED with suspicion of syncope
- Within the last 12 hours

**Exclusion Criteria**
- No loss of consciousness
- Stroke
- Epileptic seizure
- Intoxication
Methods

History
ECG

Adjudication of Final Diagnosis

Blood (novel biomarkers)

Clinical Judgement

Follow up 6, 12, 24, 60 months

Orthostatic, Neurally mediated, C...
<table>
<thead>
<tr>
<th>Setting</th>
<th>Source</th>
<th>Reflex %</th>
<th>OH %</th>
<th>Cardiac %</th>
<th>Non-syncopal T-LOC, %</th>
<th>Unexplained</th>
</tr>
</thead>
<tbody>
<tr>
<td>General population</td>
<td>Framingham studies</td>
<td>21</td>
<td>9.4</td>
<td>9.5</td>
<td>9</td>
<td>37</td>
</tr>
<tr>
<td>ED</td>
<td>Ammirati</td>
<td>35</td>
<td>6</td>
<td>21</td>
<td>20</td>
<td>17</td>
</tr>
<tr>
<td></td>
<td>Sarasin</td>
<td>38</td>
<td>24</td>
<td>11</td>
<td>8</td>
<td>19</td>
</tr>
<tr>
<td></td>
<td>Blanc</td>
<td>48</td>
<td>4</td>
<td>10</td>
<td>13</td>
<td>24</td>
</tr>
<tr>
<td></td>
<td>Diserton</td>
<td>45</td>
<td>6</td>
<td>11</td>
<td>17</td>
<td>19</td>
</tr>
<tr>
<td></td>
<td>Olde Norkamp</td>
<td>39</td>
<td>5</td>
<td>5</td>
<td>17</td>
<td>33</td>
</tr>
<tr>
<td></td>
<td>Range</td>
<td>35-48</td>
<td>4-24</td>
<td>5-21</td>
<td>8-20</td>
<td>17-33</td>
</tr>
<tr>
<td>Basel IX</td>
<td>39</td>
<td>26</td>
<td>15</td>
<td>12</td>
<td>11</td>
<td></td>
</tr>
</tbody>
</table>
I. BASEL IX Syncope study
II. Syncope: What’s in the guidelines?
III. Syncope: Are we doing a good job?
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VI. Prevalence of PE in syncope patients
Content

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Case #1: 74-jährig, männlich, synkopiert

- **Jetziges Leiden**
  - Zuweisung mit der Sanität
  - Plötzlich schwarz vor Augen in der Dusche, vorher Tennis gespielt
  - keine weiteren Prodromi, Dauer unklar, keine Zeugen
  - Begleitender Sturz mit Fx Digitus I Fuss rechts
  - St. n. Synkope vor zwei Wochen auf dem Hometrainer

- **Status**
  - GCS 15, 153/87 mmHg, 93 bpm, 98% SO2, Auskultation bland, kompensiert
  - Sz Fuss re, sonst unauffällig

- **Persönliche Anamnese**
  - St. n. radikaler Prostatektomie bei Prostatakarzinom ca. 2007
  - Arterielle Hypertonie

- **Medikation**
  - Simcora, Exforge, Concor, Aldactone
Case #1: What would you do next?

Reassurance & Outpatient management
or
Admit & In-hospital work-up?
- **Short-term high-risk criteria requiring prompt hospitalization or intensive evaluation:**
  - Severe structural or coronary artery disease (HF, low EF or prior MI).
  - Clinical or ECG features suggesting arrhythmic syncope:
    - Syncope during exercise or supine.
    - Palpitations at the time of syncope.
    - Family history of Sudden cardiac death (SCD).
    - Non-sustained VT.
    - Bifascicular block (LBBB or RBBB combined with left anterior or left posterior fascicular block or other intraventricular conduction abnormalities with QRS duration ≥ 120 ms).
    - Inadequate sinus bradycardia (< 50 bpm) or sino-atrial block in absence of negative chronotropic medications or physical training.
    - Pre-excited QRS complex.
    - Prolonged or short QT interval.
    - RBBB pattern with ST-elevation in leads V1-V3 (Brugada pattern).
    - Negative T waves in right precordial leads, epsilon waves and ventricular late potentials suggestive of ARVC.
    - Family history of SCD.
  - Important co-morbidities (severe anemia, electrolyte disturbance).
T-LOC – suspected syncope

Initial evaluation

Syncope

Certain diagnosis
- Treatment

Uncertain diagnosis
- Risk stratification
  - High risk**: Early evaluation & treatment
  - Low risk recurrent syncopes: Cardiac or neurally-mediated tests as appropriate
  - Low risk: Single or rare
    - No further evaluation

T-LOC non syncopal
- Confirm with specific test or specific consultation
- Treatment

www.escardio.org/guidelines

European Heart Journal 2009;30:2631-2671
Case #1: What would you do next?

Transthoracic echocardiography: Yes or No?
Transthoracic echocardiography

### Recommendations:

<table>
<thead>
<tr>
<th>Indications</th>
<th>Class</th>
<th>Level</th>
</tr>
</thead>
<tbody>
<tr>
<td>Echocardiography is indicated for diagnosis and risk stratification in patients who are suspected of having structural heart disease.</td>
<td>I</td>
<td>B</td>
</tr>
</tbody>
</table>

### Diagnostic criteria

- Echocardiography alone is diagnostic of the cause of syncope in severe aortic stenosis, obstructive cardiac tumors or thrombi, pericardial tamponade, aortic dissection, and congenital anomalies of coronary arteries.

<table>
<thead>
<tr>
<th>COR</th>
<th>LOE</th>
<th>Recommendations</th>
</tr>
</thead>
<tbody>
<tr>
<td>IIa</td>
<td>B-NR</td>
<td>Transthoracic echocardiography can be useful in selected patients presenting with syncope if structural heart disease is suspected.</td>
</tr>
<tr>
<td>IIb</td>
<td>B-NR</td>
<td>CT or MRI may be useful in selected patients presenting with syncope of suspected cardiac etiology.</td>
</tr>
<tr>
<td>III: No Benefit</td>
<td>B-R</td>
<td>Routine cardiac imaging is not useful in the evaluation of patients with syncope unless cardiac etiology is suspected on the basis of an initial evaluation, including history, physical examination, or ECG.</td>
</tr>
</tbody>
</table>
Role of echocardiography in the evaluation of syncope: a prospective study

F P Sarasin, A-F Junod, D Carballo, S Slama, P-F Unger, M Louis-Simonet

Patients with non-diagnostic initial evaluation and undergoing routine echocardiography (n = 155)

Positive cardiac history and/or abnormal ECG (n = 88)

- Left ventricular ejection fraction ≤ 40% (n = 24)
  - Final diagnosis of arrhythmia: 12/24 (50%)*

- Normal (n = 34) or non relevant (n = 30) echocardiography
  - Final diagnosis of arrhythmia: 12/64 (19%)

Negative cardiac history and normal ECG (n = 67)

- Normal (n = 50) or non relevant (n = 17) echocardiography
  - Final diagnosis of arrhythmia: 0%
Case #1: What would you do next?

In-hospital continuous ECG monitoring
Yes or No?
In-hospital continuous ECG monitoring

**Indications**

- ECG monitoring is indicated in patients who have clinical or ECG features suggesting arrhythmic syncope (listed in Table 10). The duration (and technology) of monitoring should be selected according the risk and the predicted recurrence rate of syncope:
  - Immediate in-hospital monitoring (in bed or telemetric) is indicated in high-risk patients defined in Table 11.

**Severe structural or coronary artery disease** (heart failure, low LVEF, or previous myocardial infarction)

**Clinical or ECG features suggesting arrhythmic syncope**

- Syncope during exertion or supine
- Palpitations at the time of syncope
- Family history of SCD
- Non-sustained VT
- Bifascicular-block (LBBB or RBBB combined with left anterior or left posterior fascicular block) or other intraventricular conduction abnormalities with QRS duration ≥120 ms
- Inadequate sinus bradycardia (<50 bpm) or sinoatrial block in absence of negative chronotropic medications or physical training
- Pre-excited QRS complex
- Prolonged or short QT interval
- RBBB pattern with ST-elevation in leads V1–V3 (Brugada pattern)
- Negative T waves in right precordial leads, epsilon waves, and ventricular late potentials suggestive of ARVC

**Important co-morbidities**

- Severe anaemia
- Electrolyte disturbance

Continuous ECG monitoring is useful for hospitalized patients admitted for syncope evaluation with suspected cardiac etiology.\(^{77,182,183}\)
In-hospital continuous ECG monitoring

- **the diagnostic yield of inpatient telemetry is low**
  - 172 patients with syncope presenting to the ED and admitted to a telemetry unit revealed a diagnostic yield in 18% of patients, with **15% demonstrating bradyarrhythmias**
  - A large, prospective evaluation of 2,106 patients admitted with syncope demonstrated high telemetry use (95%) **but a diagnostic yield of only 5%**
  - **Basel IX: 18% in-hospital continuous ECG monitoring with 12.6% demonstrating arrhythmias**
- Continuous telemetry in the hospital for patients presenting with syncope not suspected of a cardiac etiology is **not cost-effective**

---


Case #1: What would you do next?

Which ECG monitoring strategy?

1) Loop Recorder?  
2) Holter-ECG  
3) Event Recorder
ECG monitoring is indicated in patients who have clinical or ECG features suggesting arrhythmic syncope (listed in Table 10). The duration (and technology) of monitoring should be selected according to the risk and the predicted recurrence rate of syncope:

- Immediate in-hospital monitoring (in bed or telemetric) is indicated in high risk patients defined in Table 11
- Holter monitoring is indicated in patients who have very frequent syncope or pre-syncope (≥1 per week)
- 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 11 and a high likelihood of recurrence within battery longevity of the device
  - High risk patients in whom a comprehensive evaluation did not demonstrate a cause of syncope or lead to a specific treatment
- External loop recorders should be considered in patients who have an inter-symptom interval ≤4 weeks
1/5 patients who experienced a recurrence of their symptoms failed to activate the device properly.

ILR in unexplained syncope with normal work-up

- Asystole / bradycardia: 56%
- Tachycardia: 11%
- No arrhythmia: 33%

Diagnostic yield: 35%
(175/506 patients)

Birgnole et al. Europace 2009; 11, 671-687
Case #1: Performed diagnostic tests

- **Blutbild und Chemogram inkl. hs-cTnT**
- **Rx Th**: Unscharf begrenzte fokale Transparenzminderung UL li, DD atypisches pneumonisches Infiltrat, DD Überlagerung.
- **TTE**: Normale LVEF, keine WBST, keine Vitien, LA dilatiert, V. cava leer
- **CT Schädel**: bland
- **Holter-EKG**: durchgehend VHF
- **HNO-Konsil**: kein Anhalt auf BPLS

- **Austrittsdiagnose**
  - Synkope, am ehesten vasovagal auf dem Boden einer Dehydratation
  - nc VHF
- **Therapie**
  - 4d Hospitalisation, Beginn OAK, Pradaxa
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Content

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Syncope: Are we doing a good job?

Perfomed diagnostic tests at presentation

- ECG
- X-Ray Chest
- Schellong
- Cranial CT
- TTE
- Telemetry Monitoring
- 24h-Holter-Monitoring
- Carotis Duplex
- EEG
- Coronary Angiography
- Ergometry
- MPS
- Loop Recorder
Syncope: Are we doing a good job?

- 50.3% admitted patients for a median of 4 days
- 51% Discharge diagnosis
- 31% Mismatches: failure to distinguish causes of syncope
How important is it to detect the cause of syncope?
“Vasovagal and other causes” includes vasovagal, orthostatic, medication-induced, and other, infrequent causes of syncope.
Patients with cardiac syncope, syncope of unknown origin and syncope due to OH are at increased risk for death
# Clinical Events at 720 days

<table>
<thead>
<tr>
<th>Clinical Endpoints</th>
<th>Overall</th>
<th>Non-Cardiac Syncope</th>
<th>Cardiac Syncope</th>
<th>(p) value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>n (%)</strong></td>
<td>1231</td>
<td>1051</td>
<td>180</td>
<td></td>
</tr>
<tr>
<td><strong>All CE and Death</strong></td>
<td>322 (26.2)</td>
<td>187 (17.8)</td>
<td>135 (75.0)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Death of any cause</td>
<td>134 (10.9)</td>
<td>101 (9.6)</td>
<td>33 (18.3)</td>
<td>0.001</td>
</tr>
<tr>
<td>Acute Coronary Syndrome</td>
<td>37 (3.0)</td>
<td>21 (2.0)</td>
<td>16 (8.9)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>PTCA/CABG</td>
<td>41 (3.3)</td>
<td>19 (1.8)</td>
<td>22 (12.2)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Cardiopulmonary resuscitation</td>
<td>13 (1.1)</td>
<td>4 (0.4)</td>
<td>9 (5.0)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Arrhythmia</td>
<td>28 (2.3)</td>
<td>8 (0.8)</td>
<td>20 (11.1)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Pacemaker-Implantation</td>
<td>81 (6.6)</td>
<td>9 (0.9)</td>
<td>72 (40.0)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>ICD-Implantation</td>
<td>11 (0.9)</td>
<td>5 (0.5)</td>
<td>6 (3.3)</td>
<td>0.001</td>
</tr>
<tr>
<td>Acute Heart Failure</td>
<td>29 (2.4)</td>
<td>17 (1.6)</td>
<td>12 (6.7)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Valve Replacement</td>
<td>14 (1.1)</td>
<td>3 (0.3)</td>
<td>11 (6.1)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Pulmonary Embolus</td>
<td>13 (1.1)</td>
<td>8 (0.8)</td>
<td>5 (2.8)</td>
<td>0.04</td>
</tr>
<tr>
<td>Blood transfusion</td>
<td>10 (0.8)</td>
<td>8 (0.8)</td>
<td>2 (1.1)</td>
<td>0.647</td>
</tr>
<tr>
<td>GI-Bleeding</td>
<td>21 (1.7)</td>
<td>17 (1.6)</td>
<td>4 (2.2)</td>
<td>0.533</td>
</tr>
<tr>
<td>Intracerebral Bleeding</td>
<td>8 (0.6)</td>
<td>6 (0.6)</td>
<td>2 (1.1)</td>
<td>0.331</td>
</tr>
<tr>
<td>Sepsis</td>
<td>5 (0.4)</td>
<td>4 (0.4)</td>
<td>1 (0.6)</td>
<td>0.547</td>
</tr>
<tr>
<td>Stroke</td>
<td>19 (1.5)</td>
<td>14 (1.3)</td>
<td>5 (2.8)</td>
<td>0.26</td>
</tr>
</tbody>
</table>
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Content

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Are there circadian, weekly, seasonal and temperature-dependent patterns of syncope etiologies?
Day-time dependant cardiac vulnerability?
Circadian Rhythm

Etiology
- Reflex
- Orthostatic
- Other, Noncardiac
- Cardiac
- Etiology unknown

J. Du Fay de Lavallaz, P. Badertscher, Submitted
Circadian Rhythm

Etiology
- Reflex
- Orthostatic
- Other, Noncardiac
- Cardiac
- Etiology unknown

4a.m.-4p.m. : 80%

J. Du Fay de Lavallaz, P. Badertscher, Submitted
Circadian Rhythm

Etiology
- Reflex
- Orthostatic
- Other, Noncardiac
- Cardiac
- Etiology unknown

8 a.m.-2 p.m. : 70%

J. Du Fay de Lavallaz, P. Badertscher, Submitted
Seasonal rhythm

J. Du Fay de Lavallaz, P. Badertscher, Submitted
Seasonal rhythm

Relative reduction in Summer

Relative increase in Summer

J. Du Fay de Lavallaz, P. Badertscher, Submitted
Conclusion

- All etiologies are more common during the day, but no possible diagnostic discrimination using the time syncope happened.
- Less reflex/orthostatic syncope in Summer, constant number of cardiac syncope, small relative increase in cardiac etiologies.
Is there a role for risk scores in syncope patients?
Risk scores: Useful?

- History
- Comorbidities
- ECG
- Lab values

Scores

- Cardiac syncope
- 1-2y mortality
- 7-days adverse events

- Complex/time consuming to calculate
- Predict different outcomes

- Derived only in few centers, never largely validated.
Table 8  Risk stratification at initial evaluation in prospective population studies including a validation cohort

<table>
<thead>
<tr>
<th>Study</th>
<th>Risk factors</th>
<th>Score</th>
<th>Endpoints</th>
<th>Results (validation cohort)</th>
</tr>
</thead>
<tbody>
<tr>
<td>S. Francisco Syncope Rule&lt;sup&gt;44&lt;/sup&gt;</td>
<td>Abnormal ECG, Congestive heart failure, Shortness of breath, Haematocrit &lt;30%, Systolic blood pressure &lt;90 mmHg</td>
<td>No risk = 0 item Risk ≥ 1 item</td>
<td>Serious events at 7 days</td>
<td>98% sensitive and 56% specific</td>
</tr>
<tr>
<td>Martin et al. &lt;sup&gt;40&lt;/sup&gt;</td>
<td>Abnormal ECG, History of ventricular arrhythmia, History of congestive heart failure, Age &gt; 45 years</td>
<td>0 to 4 (1 point each item)</td>
<td>1-year severe arrhythmias or arrhythmic death</td>
<td>0% score 0 5% score 1 16% score 2 27% score 3 or 4</td>
</tr>
<tr>
<td>OESIL score&lt;sup&gt;61&lt;/sup&gt;</td>
<td>Abnormal ECG, History of cardiovascular disease, Lack of prodrome, Age &gt; 65 years</td>
<td>0 to 4 (1 point each item)</td>
<td>1-year total mortality</td>
<td>0% score 0 0.6% score 1 14% score 2 29% score 3 53% score 4</td>
</tr>
<tr>
<td>EGSYS score&lt;sup&gt;42&lt;/sup&gt;</td>
<td>Palpitations before syncope (+4), Abnormal ECG and/or heart disease (+3), Syncope during effort (+3), Syncope while supine (+2), Autonomic prodrome&lt;sup&gt;2&lt;/sup&gt; (-1), Predisposing and/or precipitating factors&lt;sup&gt;2&lt;/sup&gt; (-1)</td>
<td>Sum of + and − points</td>
<td>2-year total mortality</td>
<td>Cardiac syncope probability 2% score &lt;3 21% score ≥3 13% score 3 33% score 4 77% score &gt;4</td>
</tr>
</tbody>
</table>

Risk scores: What’s in the guidelines?
### Table 6. Examples of Syncope Risk Scores

<table>
<thead>
<tr>
<th>Study/Reference</th>
<th>Year</th>
<th>Sample N</th>
<th>Events N</th>
<th>Outcome Definition</th>
<th>ED Events*</th>
<th>Predictors</th>
<th>NPV (%)†</th>
</tr>
</thead>
<tbody>
<tr>
<td>Martin (90)</td>
<td>1997</td>
<td>252</td>
<td>104</td>
<td>1-y death/arrhythmia</td>
<td>Yes</td>
<td>Abnormal ECG#: &gt;45 y of age; VA; HF</td>
<td>93</td>
</tr>
<tr>
<td>Sarasin (74)</td>
<td>2003</td>
<td>175</td>
<td>30</td>
<td>Inpatient arrhythmia</td>
<td>Yes</td>
<td>Abnormal ECG#: &gt;65 y of age; HF</td>
<td>98</td>
</tr>
<tr>
<td>OESIL (67)</td>
<td>2003</td>
<td>270</td>
<td>31</td>
<td>1-y death</td>
<td>N/A</td>
<td>Abnormal ECG#: &gt;65 y of age; 100 Cardiac etiology</td>
<td>N/A</td>
</tr>
<tr>
<td>SFSR (72)</td>
<td>2004</td>
<td>684</td>
<td>79</td>
<td></td>
<td>N/A</td>
<td>Abnormal ECG#: trauma; no prodrome; male sex</td>
<td>---</td>
</tr>
<tr>
<td>Boston Syncope Rule (70)</td>
<td>2007</td>
<td>293</td>
<td>68</td>
<td></td>
<td>N/A</td>
<td>Abnormal ECG#: &gt;90 y of age; male sex; positive troponin; history of arrhythmia; systolic BP &gt;160 mm Hg; near-syncope (a low-risk factor)</td>
<td>97</td>
</tr>
<tr>
<td>Del Rosso (69)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>N/A</td>
<td>Abnormal ECG#; B-natriuretic peptide; hemoglobin; O₂Sat; fecal occult blood</td>
<td>98</td>
</tr>
<tr>
<td>STePS (68)</td>
<td>2008</td>
<td>676</td>
<td>41</td>
<td></td>
<td>Yes</td>
<td>Abnormal ECG#; trauma; no prodrome; male sex</td>
<td>---</td>
</tr>
<tr>
<td>Syncope Risk Score (75)</td>
<td>2009</td>
<td>2,584</td>
<td>173</td>
<td></td>
<td>No</td>
<td>Abnormal ECG#: &gt;90 y of age; male sex; positive troponin; history of arrhythmia; systolic BP &gt;160 mm Hg; near-syncope (a low-risk factor)</td>
<td>97</td>
</tr>
<tr>
<td>ROSE (73)</td>
<td>2010</td>
<td>550</td>
<td>40</td>
<td></td>
<td>Yes</td>
<td>Abnormal ECG#; B-natriuretic peptide; hemoglobin; O₂Sat; fecal occult blood</td>
<td>98</td>
</tr>
</tbody>
</table>
## Risk scores: Can we simplify?

### Table 5. Short- and Long-Term Risk Factors

<table>
<thead>
<tr>
<th>History: Outpatient Clinic or ED Evaluation</th>
<th>Long-Term Risk Factors (&gt;30 d)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male sex (74,85,101,102)</td>
<td>Male sex (68,90)</td>
</tr>
<tr>
<td>Older age (&gt;60 y) (88)</td>
<td>Older age (90)</td>
</tr>
<tr>
<td>No prodrome (68)</td>
<td>Absence of nausea/vomiting preceding syncopal event (93)</td>
</tr>
<tr>
<td>Palpitations preceding loss of consciousness (83)</td>
<td>VA (68,90)</td>
</tr>
<tr>
<td>Exertional syncope (83)</td>
<td>Cancer (68)</td>
</tr>
<tr>
<td>Structural heart disease (70,83,88,101,103)</td>
<td>Structural heart disease (68,103)</td>
</tr>
<tr>
<td>HF (74,83,85,88)</td>
<td>HF (90)</td>
</tr>
<tr>
<td>Cerebrovascular disease (70)</td>
<td>Cerebrovascular disease (68)</td>
</tr>
<tr>
<td>Family history of SCD (70)</td>
<td>Diabetes mellitus (104)</td>
</tr>
<tr>
<td>Trauma (68,101)</td>
<td>High CHADS-2 score (95)</td>
</tr>
</tbody>
</table>

### Physical Examination or Laboratory Investigation

<table>
<thead>
<tr>
<th>Evidence of bleeding (83)</th>
<th>Abnormal ECG (84,90,93)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Persistent abnormal vital signs (70)</td>
<td>Lower GFR</td>
</tr>
<tr>
<td>Abnormal ECG (68,72,74,75,105)</td>
<td></td>
</tr>
<tr>
<td>Positive troponin (75)</td>
<td></td>
</tr>
</tbody>
</table>
What about a simple CHADS$_2$ Score for the risk prediction?

A CHADS$_2$ or CHA$_2$DS$_2$VASc score perform equally to more syncope-specific risk-scores for the prediction of death or MACE.

MACE: all-cause death, life-threatening arrhythmia, pacemaker/implantable Cardioverter Defibrillator implantation, stroke, acute myocardial infarction (AMI) and pulmonary embolism.

J. Du Fay de Lavallaz, P. Badertscher, Submitted
Lower score-performance for the diagnosis of cardiac syncope

All scores show a much lower performance than the clinical judgment of the ED physician

J. Du Fay de Lavallaz, P. Badertscher, Submitted
Conclusion

- Scores for syncope: « Reasonable » but not really useful?
- The CHADS$_2$ or CHA$_2$DS$_2$VASc-scores are **satisfactory risk-stratifiers** in patients presenting with syncope to the ED
  - But CHADS/CHADVASc also useful in the death/MACE prediction of many other diseases (patients with CAD, risk of arrhythmia post-AMI etc..)
- Aren’t there any syncope-specific risk-markers?
- The accuracy of all scores for the diagnosis of cardiac syncope is poor
  - Need to look for/integrate biochemical/electrocardiographic markers

_Ruwald et al., Int J Cardiol 2014_  
_Huang et al., Intern Emerg Med 2017_
Is there a role for biomarkers in syncope patients?
What about high-sensitive cardiac troponin?

- prospective, single-center study enrolling 360 patients presenting with syncope

\[ \text{cTnThs levels show a limited diagnostic and predictive accuracy for the identification of patients with syncope at high risk} \]
What about high-sensitive cardiac troponin?

• prospective, multi-center study **enrolling 5’010** patients presenting with syncope
• developed a risk-tool for **predicting 30-day arrhythmia or death**

<table>
<thead>
<tr>
<th>Items</th>
<th>Points</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Clinical Evaluation</td>
<td></td>
</tr>
<tr>
<td>a) Vasovagal predisposition*</td>
<td>-1</td>
</tr>
<tr>
<td>b) History of heart disease†</td>
<td>+1</td>
</tr>
<tr>
<td>c) Any ED systolic blood pressure &lt; 90 or &gt; 180 mmHg‡</td>
<td>+1</td>
</tr>
<tr>
<td>2. Investigations</td>
<td></td>
</tr>
<tr>
<td>a) Troponin elevated (&gt; 99%ile normal population)</td>
<td>+1</td>
</tr>
<tr>
<td>b) QRS duration &gt;130 milliseconds</td>
<td>+2</td>
</tr>
<tr>
<td>c) Corrected QT interval &gt;480 milliseconds</td>
<td>+1</td>
</tr>
<tr>
<td>3. Final ED Diagnosis</td>
<td></td>
</tr>
<tr>
<td>a) ED diagnosis of vasovagal syncope</td>
<td>-1</td>
</tr>
<tr>
<td>b) ED diagnosis of cardiac syncope</td>
<td>+2</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Total Score</th>
<th>Risk $^\S$</th>
<th>Category</th>
</tr>
</thead>
<tbody>
<tr>
<td>-2</td>
<td>0.2%</td>
<td>Very Low</td>
</tr>
<tr>
<td>-1</td>
<td>0.5%</td>
<td>Very Low</td>
</tr>
<tr>
<td>0</td>
<td>0.9%</td>
<td>Very Low</td>
</tr>
<tr>
<td>1</td>
<td>1.9%</td>
<td>Low</td>
</tr>
<tr>
<td>2</td>
<td>3.8%</td>
<td>Medium</td>
</tr>
<tr>
<td>3</td>
<td>7.5%</td>
<td>Medium</td>
</tr>
<tr>
<td>4</td>
<td>14.3%</td>
<td>High</td>
</tr>
<tr>
<td>5</td>
<td>25.4%</td>
<td>High</td>
</tr>
<tr>
<td>6</td>
<td>41.1%</td>
<td>Very High</td>
</tr>
<tr>
<td>7</td>
<td>58.8%</td>
<td>Very High</td>
</tr>
<tr>
<td>8</td>
<td>74.5%</td>
<td>Very High</td>
</tr>
</tbody>
</table>

What about BNP/NTproBNP?

<table>
<thead>
<tr>
<th>Study</th>
<th>Design</th>
<th>Population</th>
<th>N</th>
<th>N</th>
<th>Marker</th>
<th>Cut-off</th>
<th>Findings</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tanimoto</td>
<td>Retrospective</td>
<td>Consecutive syncope patients who were hospitalized</td>
<td>118</td>
<td>118</td>
<td>BNP</td>
<td>&gt;40 pg/mL</td>
<td>Cardiac cause of syncope, diagnosed during admission following ED visit: aortic stenosis, hypertrophic cardiomyopathy, pulmonary embolism, cardiac tamponade, tachycardia &gt;220 bpm, bradycardia &lt;40 bpm</td>
</tr>
<tr>
<td>Reed (2007)</td>
<td>Prospective</td>
<td>Adult (≥16 years) ED syncope patients</td>
<td>99</td>
<td>72</td>
<td>BNP</td>
<td>≥100 pg/mL</td>
<td>3-month serious outcome: all-cause death, MI, life-threatening arrhythmia, pulmonary embolism, stroke, subarachnoid hemorrhage, hemorrhage requiring ≥2 units red blood cells, acute surgical or endoscopic intervention</td>
</tr>
<tr>
<td>Pfister (2012)</td>
<td>Prospective</td>
<td>Syncope patients admitted to cardiology</td>
<td>161</td>
<td>161</td>
<td>NT-ProBNP</td>
<td>&gt;156 pg/mL</td>
<td>6-month adverse events: all-cause death, coronary revascularization, intervention for left ventricular outflow obstruction, urgent anti-arrhythmic drug treatment, cardioversion, pacemaker/ICD insertion, cardiovascular hospitalization following index visit discharge</td>
</tr>
</tbody>
</table>
Prohormones in the Early Diagnosis of Cardiac Syncope

Patrick Badertscher, MD;* Thomas Nestelberger, MD;* Jeanne du Fay de Lavallaz, MD; Martin Than, MD; Beata Morawiec, MD; Damian Kawecki, MD; Óscar Miró, MD; Beatriz López, MD; F. Javier Martin-Sanchez, MD; José Bustamante, MD; Nicolas Geigy, MD; Michael Christ, MD; Salvatore Di Somma, MD, PhD; W. Frank Peacock, MD; Louise Cullen, MD, PhD; François Sarasin, MD; Dayana Flores, MD; Michael Tschuck, MD; Jasper Boeddinghaus, MD; Raphael Twerenbold, MD; Karin Wildi, MD; Zaid Sabti, MD; Christian Puelacher, MD; Maria Rubini Giménez, MD; Nikola Kozhuharov, MD; Samyut Shrestha, MD; Ivo Strebel, PhDc; Katharina Rentsch, PhD; Dagmar I. Keller, MD; Imke Poepping, MD; Andreas Buser, MD; Wanda Kloos, MD; Jens Lohrmann, MD; Michael Kuehne, MD; Stefan Osswald, MD; Tobias Reichlin, MD; Christian Mueller, MD

---

**Diagram:**
- **Cardiac**
- **Reflex**
- **Orthostatic**
- **Other**

<table>
<thead>
<tr>
<th>MRproANP (pmol/L)</th>
<th>CTproET1 (pmol/L)</th>
</tr>
</thead>
<tbody>
<tr>
<td>100</td>
<td>30</td>
</tr>
<tr>
<td>300</td>
<td>60</td>
</tr>
<tr>
<td>500</td>
<td>90</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Copeptin (pmol/L)</th>
<th>MRproADM (nmol/L)</th>
</tr>
</thead>
<tbody>
<tr>
<td>50</td>
<td>0.5</td>
</tr>
<tr>
<td>100</td>
<td>1.0</td>
</tr>
<tr>
<td>150</td>
<td>1.5</td>
</tr>
</tbody>
</table>
Diagnostic Accuracy for Cardiac Syncope

Cardiac Syncope Diagnosis Nomogram

Is there a role for biomarkers in syncope patients?

- none of the cardiac biomarkers are robust enough to be used in isolation for identification of cardiac syncope or patients at risk for death or adverse outcomes

- Using biomarkers in conjunction with clinical judgement/risk scores and/or the 12-lead ECG, may improve the early rule-out and/or rule-in of cardiac syncope

<table>
<thead>
<tr>
<th>IIb</th>
<th>C-LD</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Usefulness of brain natriuretic peptide and high-sensitivity troponin measurement is uncertain in patients for whom a cardiac cause of syncope is suspected (125,127,129,130).</td>
</tr>
</tbody>
</table>
Content

I. BASEL IX Syncope study

II. Syncope: What’s in the guidelines?

III. Syncope: Are we doing a good job?

IV. Prognosis of different Syncope etiologies

V. How can we improve risk stratification in the ED?

VI. Prevalence of PE in syncope patients
Content

I. BASEL IX Syncope study

II. Syncope: What’s in the guidelines?

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IV. Prognosis of different Syncope etiologies

V. How can we improve risk stratification in the ED?

VI. Prevalence of PE in syncope patients
Prevalence of Pulmonary Embolism among Patients Hospitalized for Syncope

Paolo Prandoni, M.D., Ph.D., Anthonie W.A. Lensing, M.D., Ph.D.,

560 Patients were included in the study

- 330 Had low pretest probability for pulmonary embolism and negative D-dimer assay (59%)
- 230 Had high pretest probability for pulmonary embolism, positive D-dimer assay, or both (41%)

- 180 Underwent computed tomographic scanning
  - 49 Underwent ventilation–perfusion scanning
  - 1 Died and an autopsy was performed

- 463 Had pulmonary embolism ruled out (83%)
- 97 Had pulmonary embolism confirmed (17%)
Conclusion

Pulmonary embolism was identified in nearly one of every six patients admitted for first-time syncope.

Should all patients with syncope undergo systematic work-up for PE?
Patients with syncope 
\( n = 1069 \ (100\%) \)

Ruled-in
High pre-test probability or positive D-dimer assay or both
\( n = 591 \ (55.3\%) \)

CT or V/P scanning
\( n = 66 \ (7.2\%) \)
- PE Confirmed
  \( n = 9 \ (0.8\%) \)
- PE Ruled-out
  \( n = 57 \ (0.1\%) \)

Ruled-out
Low pre-test probability and negative D-dimer assay
\( n = 478 \ (44.7\%) \)

Long-term follow-up*
\( n = 525 \ (49.1\%) \)
- PE Confirmed
  \( n = 6 \ (0.6\%) \)
- PE Ruled-out
  \( n = 519 \ (48.6\%) \)

PE confirmed
\( n = 15 \ (1.4\%) \)

PE ruled-out
\( n = 1054 \ (98.6\%) \)

*Median follow-up 741 days (IQR 720-786)
Patients hospitalized with syncope  
\[ n = 497 \text{ (100\%)} \]

**Ruled-in**
- High pre-test probability or positive D-dimer assay or both  
\[ n = 311 \text{ (62.6\%)} \]

- **CT or V/P scanning**  
\[ n = 48 \text{ (9.7\%)} \]
  - PE Confirmed  
  \[ n = 7 \text{ (1.4\%)} \]
  - PE Ruled-out  
  \[ n = 41 \text{ (8.2\%)} \]

- PE Confirmed  
\[ n = 10 \text{ (2.0\%)} \]

**Ruled-out**
- Low pre-test probability and negative D-dimer assay  
\[ n = 186 \text{ (37.4\%)} \]

- **Long-term follow-up**  
\[ n = 263 \text{ (52.9\%)} \]
  - PE Confirmed  
  \[ n = 3 \text{ (0.6\%)} \]
  - PE Ruled-out  
  \[ n = 260 \text{ (52.3\%)} \]

- PE Confirmed  
\[ n = 487 \text{ (98.0\%)} \]

*Median follow-up 741 days (IQR 720-786)
Thank you very much for your attention!

patrick.badertscher@usb.ch
jeanne.dufaydelavallaz@usb.ch
Backup Slides
<table>
<thead>
<tr>
<th>Class</th>
<th>Benefit vs. Risk</th>
<th>Level</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>I (Strong)</td>
<td>Benefit &gt;&gt;&gt; Risk</td>
<td>Level A</td>
<td>High-quality evidence; from more than 1 RCT; Meta-analyses of high-quality RCTs; One or more RCTs corroborated by high-quality registry studies</td>
</tr>
<tr>
<td>IIa (Moderate)</td>
<td>Benefit &gt;&gt; Risk</td>
<td>Level B-R</td>
<td>Moderate-quality evidence; from 1 or more RCTs; Meta-analyses of moderate-quality RCTs</td>
</tr>
<tr>
<td>IIb (Weak)</td>
<td>Benefit &gt; Risk</td>
<td>Level B-NR</td>
<td>Moderate-quality evidence; from 1 or more well-designed, well-executed nonrandomized studies, observational studies, or registry studies; Meta-analyses of such studies</td>
</tr>
<tr>
<td>III: No Benefit (Moderate)</td>
<td>Benefit = Risk</td>
<td>Level C-LD</td>
<td>Limited Data; Randomized or nonrandomized observational or registry studies with limitations of design or execution; Meta-analyses of such studies; Physiological or mechanistic studies in human subjects</td>
</tr>
<tr>
<td>III: Harm (Strong)</td>
<td>Risk &gt; Benefit</td>
<td>Level C-EO</td>
<td>Consensus of expert opinion based on clinical experience</td>
</tr>
</tbody>
</table>

COR and LOE are determined independently (any COR may be paired with any LOE). A recommendation with LOE C does not imply that the recommendation is weak. Many important clinical questions addressed in guidelines do not lend themselves to clinical trials. Although RCTs are unavailable, there may be a very clear clinical consensus that a particular test or therapy is useful or effective.

* The outcome or result of the intervention should be specified (an improved clinical outcome or increased diagnostic accuracy or incremental diagnostic information).

† For comparative-effectiveness recommendations (COR I and IIa; LOE A and B only), studies that support the use of comparator verbs should include direct comparisons of the interventions or strategies being evaluated.

The method of assessing quality is evolving, including the application of standardized, widely used, and preexisting validated evidence grading tools; and for systematic reviews, the incorporation of an Evidence Review Committee.

COR indicates Class of Recommendation; EO, expert opinion; LD, limited data; LOE, Level of Evidence; NR, nonrandomized; R, randomized; and RCT, randomized controlled trial.
**Recommendations**

**Tilt testing**

- Diagnostic criteria:
  - In patients without structural heart disease, the induction of reflex hypotension/bradycardia *with* reproduction of syncope or progressive OH (with or without symptoms) are diagnostic of reflex syncope and OH respectively.
  - In patients without structural heart disease, the induction of reflex hypotension/bradycardia *without* reproduction of syncope may be diagnostic of reflex syncope.
  - In patients without structural heart disease, arrhythmia or other cardiovascular cause of syncope should be excluded prior to considering positive tilt test results as diagnostic.
  - Induction of LOC in absence of hypotension and/or bradycardia should be considered diagnostic of psychogenic pseudo syncope.