Death after Syncope: Can we predict it?

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December 2013
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“Those who suffer from frequent and severe fainting often die suddenly”

Hippocrates
Aphorism 2.41
1000 BC
Syncope – A Symptom, Not a Diagnosis

- Self-limited loss of consciousness and postural tone
- Relatively rapid onset
- Variable warning symptoms
- Spontaneous, complete, and usually prompt recovery without medical or surgical intervention

Underlying mechanism = transient global cerebral hypoperfusion
Incidence of Syncope According to Age and Sex

[Bar chart showing incidence rates per 1000 person-years for different age groups and genders.]

6.2/1,000 person year
Epidemiology

Referral from the general population to medical settings

ER 0.7
General practice 9.3
General population 18.1-39.7

J Cardiovasc Electrophysiol 2006
Age distribution and cumulative incidence of first episode of syncope in the general population from subjects up to 80 years

European Heart Journal 2009
The Significance of Syncope

- The only difference between syncope and sudden death is that in one you wake up.

Ann Intern Med 1978
What is amazing about syncope?

- That people come back (regain consciousness)
- Think about it!!!!!!
- Why should someone regain consciousness??
Overall Survival of Participants with Syncope According to Cause vs Participants without Syncope
In the United States

ABSTRACT

PURPOSE: Syncope is a common cause of hospitalization in the US. The main objective of this study is to determine the incidence and mortality rates when patients are admitted with a principle diagnosis of syncope.

METHODS: An observational cross-sectional study included patients with the principle diagnosis of syncope identified from the National Inpatient Sample database for the years 2000-2005. Incidence rate of syncope was adjusted according to the US Census data. In-hospital mortality and its predictors were identified by a logistic regression analysis, and Cochran-Armitage test was used for trend analysis.

RESULTS: After data cleansing, 305,932 patients were included in the analysis. Adjusted incidence rate of syncope varied between 0.80 and 0.93 per 1000 person-years and was unchanged over the years included in the analysis. Overall mortality rate is 0.28%, a trend that has not changed over the years \( (P = 0.07) \). The odds ratio (OR) of death increased with age, becoming more prominent after age 40 years. Hospital mortality is higher in men (OR 1.49; 95% confidence interval [CI], 1.30-1.71) and in patients with higher comorbidity index (OR 1.39; 95% CI, 1.20-1.62) for moderate, and (OR 4.14; 95% CI, 3.05-5.61) for severe comorbidity index. The median cost of hospitalization is $8579, which increased by 3- to 11-fold if patients had a cardiac pacemaker or implantable cardioverter-defibrillator.

CONCLUSIONS: Syncope remains a common cause of hospital admission. The hospital mortality rate for syncope is low. A better definition and a nationally implemented care path for syncope diagnosis could provide a substantial cost savings.

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• Patients without previous comorbidity admitted for syncope in Denmark from 2001 to 2009

• 37,017 patients with a first time diagnosis of syncope
  – Median age 47 years
  – Male 47%
  – All-cause mortality 8.2% (n=3,023)

• Control population 185,085
  – All-cause mortality 7.1% (n=14,251)
Prognosis among healthy individuals discharged with a primary diagnosis of Syncope

Figure 2: Cumulative Incidence Plot of Long-Term All-Cause Mortality in the Age Group 45 to 74 Years: Syncope Versus Control Group

A significant difference in the risk of all-cause mortality in the age group 45 to 74 years indicates that this age group may have syncope as a first symptom of future cardiovascular disease and adverse outcome.
In this study the authors found a significantly increased risk of death in the 25 to 44 year age group. This is important new information not previously shown in larger studies. They hypothesize that this group of patients may be underdiagnosed in terms of unrecognized cardiovascular disease revealing a worse prognosis.
Prognosis among healthy individuals discharged with a primary diagnosis of Syncope

**Figure 4** Competing Risk Model of Patients With Syncope Compared With Control Subjects and the Cumulative Incidence of Implantation of a Pacemaker or ICD

**Figure 5** Competing Risk Model of Patients With Syncope Compared With Control Subjects and the Cumulative Incidence of Stroke

JACC Jan 2013
Cardiac Rhythms During Unexplained Syncope

No Recurrence: 36% (31-48%)
Normal Sinus Rhythm: 31% (17-44%)
Other: 11%
Tachycardia: 6% (2-11%)
Bradycardia: 16% (11-21%)

Arrhythmia: 22% (13-32%)

Composite: n=133 to 7109

Europace. 2000
PACE 2002.
Risk Stratification

• All individuals with syncope should have a risk stratification
But what if the ECG findings suggest arrhythmic syncope

- Bundle Branch Block
- Bifascicular block (defined as RBBB combined with left anterior or left posterior fascicular block)
- Other intraventricular conduction abnormalities (QRS >0.12s)
- Mobitz I – second degree AV block
- Asymptomatic inappropriate sinus bradycardia, SA Block or sinus pause > 3 s
- Non sustained VT / Long or Short QT intervals
- Brugada syndrome / Epsilon waves
Bundle Branch Block and Syncope

• The most common etiology of syncope in patients with bundle branch block (BBB) is paroxysmal atrio-ventricular (A-V) block. However, other mechanisms such as ventricular tachycardia, supraventricular tachycardia, carotid sinus syndrome, neurally mediated, or orthostatic hypotension can also cause syncope in this population.

• In addition, some of these patients are at high risk of sudden death, primarily related to the presence and severity of structural heart disease.
Bundle Branch Block and Syncope

Diagnosis, management, and outcomes of patients with syncope and bundle branch block

Angel Moya1*, Roberto García-Civera2, Francesco Croci3, Carlo Menozzi4, Josep Brugada5, Fabrizio Ammirati6, Atilio Del Rosso7, Alejandro Bellver-Navarro8, Jesús García-Sacristán9, Miriam Bortnik10, Lluís Mont11, Ricardo Ruiz-Granell12, and Xavier Navarro13 on behalf of the Bradycardia detection in Bundle Branch Block (B4) study

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Methods and results

Patients with $\geq 1$ syncope in the last 6 months, with QRS duration $\geq 120$ ms, were prospectively studied following a three-phase diagnostic strategy: Phase I, initial evaluation; Phase II, electrophysiological study (EPS); and Phase III, insertion of an implantable loop recorder (ILR). Overall, 323 patients (left ventricular ejection fraction $56 \pm 12\%$) were studied. The aetiological diagnosis was established in 267 ($82.7\%$) patients (102 at initial evaluation, 113 upon EPS, and 52 upon ILR) with the following aetiologies: bradyarrhythmia (202), carotid sinus syndrome (20), ventricular tachycardia (18), neurally mediated (9), orthostatic hypotension (4), drug-induced (3), secondary to cardiopulmonary disease (2), supraventricular tachycardia (1), bradycardia–tachycardia (1), and non-arrhythmic (7). A pacemaker was implanted in 220 (68.1\%), an implantable cardioverter defibrillator in 19 (5.8\%), and radiofrequency catheter ablation was performed in 3 patients. Twenty patients (6\%) had died at an average follow-up of $19.2 \pm 8.2$ months.
Bifascicular block and Syncope

• Pacing is not indicated for asymptomatic bifascicular block because the rate of progression to more advanced degrees of block is very slow

• Similarly, if the cause of syncope in the presence of bifascicular block cannot be determined with certainty, prophylactic pacing is indicated
Bifascicular block and Syncope

• A mortality rate of 2–14% per year has been reported in an unselected Bifascicular block, which is higher than in an age and sex matched population without block.

• Syncope is a predictor of subsequent development of high degree AV block.

• Pacing therapy in such patients often relieves the transient neurologic symptoms (syncope) but does not prevent sudden death.
Some studies have shown that BFB per se is an independent risk factor of mortality, whereas others have reported that BFB merely reflects underlying heart disease, explaining the higher mortality rate in this population.

Similar to all-cause mortality, a higher incidence of SCD has also been reported in patients with BFB occurring in 3–7% of patients per year.
Prevention of Syncope Through Permanent Cardiac Pacing in Patients With Bifascicular Block and Syncope of Unexplained Origin

The PRESS Study

• In patients with bifascicular block and syncope of undetermined origin, the use of a dual chamber pacemaker led to a significant reduction of syncope or symptomatic events associated with a cardioinhibitory origin. Symptoms associated with a new onset of rhythm disease were found in 15% of the population at 2 years.

Circulation: Arrhythmia and Electrophysiology. 2013
## Risk stratification in prospective population studies

<table>
<thead>
<tr>
<th>Study</th>
<th>Risk factors</th>
<th>Score</th>
<th>Endpoints</th>
<th>Results</th>
</tr>
</thead>
</table>
| S. Francisco Syncope   | - Abnormal ECG  
- CHF  
- Shortness of breath  
- Hematocrit < 30%  
- Systolic BP < 90 mmHg | No risk = 0 item  
Risk = ≥ 1 item | Serious events at 7 days | 98% sensitive and 56% specific |
| Rule                   |                                                                              |                                             |                                                   |                                              |
| Martin et al           | - Abnormal ECG  
- Hx of ventricular arrhythmia  
- Hx of CHF  
- Age > 45 years | 0 to 4 (1 point each item) | 1-year severe arrhythmia or arrhythmic death | 0% score 0  
5% score 1  
16% score 2  
27% score 3 or 4 |
| OESIL score            | - Abnormal ECG  
- Hx of cardiovascular disease  
- Lack of prodrome  
- Age > 65 years | 0 to 4 (1 point each item) | 1-year mortality | 0% score 0  
0.6% score 1  
14% score 2  
29% score 3  
53% score 4 |
| EGSYS score            | - Palpitations before syncope (+4)  
- Abnormal ECG and/or heart disease (+3)  
- Syncope during effort (+3)  
- Syncope while supine (+2)  
- Autonomic prodrome (-1)  
- Predisposing and/or precipitating factors (-1) | Sum of + and – points | 2-year mortality | 2% score < 3  
21% score ≥ 3 |
|                        |                                                                              |                                             | Cardiac syncope probability                       |                                              |
|                        |                                                                              |                                             |                                                   |                                              |

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**Syncope in the Elderly**

- Incidence >6 % per year
- Prevalence 10%
- Two-year recurrence 30%

Most common causes of syncope:
- Orthostatic hypotension (20-30% of patients)
- Carotid sinus hypersensitivity (up to 20% of patients)
- Neurally-mediated syncope (up to 15%)
- Cardiac arrhythmias (up to 20%)
In this study of elderly patients with syncope, the 2-year total mortality was 18%. Syncope recurrence occurred in 33% of elderly patients.
In the EGSYS 2 follow-up study with 380 patients, death of any cause occurred in 35 (9.2%). The mean follow-up was 614+73 days. Six deaths (17% of total) occurred during the first month of follow-up. Patients who died were older, had a higher incidence of structural heart disease and/or abnormal ECG, had injuries related to syncope and higher EGSYS score. Syncope recurred in 63 (16.5%) patients.
The outcome in patients with syncope is often related to the severity of the underlying disease rather than the syncopal event itself.

Discovering a chronic bifascicular block or BBB commonly raises questions in the medical underwriting process, this holds especially true when this diagnosis is associated with symptoms such as syncope or pre-syncope.

Structural heart disease and orthostatic hypotension in the elderly patient are associated with an increased risk of death due to comorbidities.