Which Elements of the History and Examination Suggest a Cardiac Cause of Syncope?

TAKE-HOME MESSAGE

Age older than 35 years, dyspnea, angina, witnessed cyanosis during the event, and a medical history of atrial fibrillation or flutter or structural heart disease are associated with an increased likelihood of a cardiac cause of syncope.

METHODS

DATA SOURCES

Authors searched the MEDLINE, EMBASE, Cumulative Index of Nursing and Allied Health, and Cochrane databases for articles in English until April 9, 2019, using Medical Subject Headings terms and a search strategy evaluating physical examination and historical elements associated with "syncope or consciousness or unconsciousness or seizures," with appropriate Emtree terms when searching EMBASE.

STUDY SELECTION

Investigators included prospective or retrospective studies of patients with syncope who were aged 12 years or older and included at least 10 patients. Studies had to include a validated reference standard (ie, noninvasive cardiac evaluation, invasive cardiac evaluation, or cardiology consultation). Studies restricted to patients with unexplained recurrent syncope, a single defined cause of syncope, or completed invasive cardiac interrogation were excluded.

EBEM Commentators
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Editor's Note: This is a clinical synopsis, a regular feature of the *Annals'* Systematic Review Snapshot (SRS) series. The source for this systematic review snapshot is: **Albassam OT, Redelmeier RJ, Shadowitz S, et al. Did this patient have cardiac syncope? *JAMA*. 2019;321:2448.**

Jestin N. Carlson, MD, MS, and Alan Jones, MD, serve as editors of the SRS series.

Results

Clinical predictors of cardiac syncope versus noncardiac syncope.

Characteristic	Patients (Percentage With Cardiac Syncope), No. (%)	Sensitivity (95% CI), %	Specificity (95% CI), %	LR+ (95% CI)	LR– (95% CI)
Historical features					
≥35 y	323 (88)	0.91 (0.85–0.97)	0.72 (0.66–0.78)	3.3 (2.6–4.1)	0.13 (0.06–0.25)
Atrial fibrillation/flutter	323 (88)	0.13 (0.06–0.20)	0.98 (0.96–1.0)	7.3 (2.4–22)	0.89 (0.82–0.97)
Structural heart disease	222 (98)	0.35–0.51	0.84–0.93	3.3–4.8	0.58–0.70
History of CHF	1,633 (299)	0.16–0.41	0.88–0.94	2.7–3.4	0.39–0.78

DATA EXTRACTION AND SYNTHESIS

Pairs of investigators independently extracted data from the included studies. Primary outcomes included sensitivity, specificity, and likelihood ratios with confidence intervals. Authors used univariate or bivariate random-effect models and determined heterogeneity. Pairs of investigators independently completed qualitative methodological review using the Quality Assessment of Diagnostic Accuracy Studies tool.[1] A third investigator resolved any irreconcilable differences. Authors evaluated level of evidence with the grading system developed for the Rational Clinical Examination series.[2]

Authors included 11 studies, 9 of which were prospective and 2 retrospective, comprising 4,317 patients, with 6 studies including patients from the emergency department (ED). Among the included studies, 9% to 58% of patients received a final diagnosis of cardiac syncope, whereas 3% to 37% remained without a diagnosis. Age older than 35 years, dyspnea or chest pain before the episode, witnessed cyanosis during the event, and medical history of atrial fibrillation or flutter or structural heart disease were associated with a higher likelihood of a cardiac cause of syncope (Table). Mood change and inability to remember mood change were associated with a lower likelihood of cardiac syncope, with likelihood ratios of 0.21 and 0.25, respectively. Biomarkers including high-sensitivity cardiac troponin T greater than 42 ng/mL and N-terminal pro-brain natriuretic peptide were associated with a positive likelihood ratio of 5.1 and 5.8, respectively, for cardiac syncope, whereas levels less than 5 ng/mL and 69 pg/mL were associated with likelihood ratios of 0.15 and 0.16, respectively.

Continued.

Characteristic	Patients (Percentage With Cardiac Syncope), No. (%)	Sensitivity (95% CI), %	Specificity (95% CI), %	LR+ (95% CI)	LR– (95% CI)
Signs or symptoms					
Previous dyspnea	699 (176)	0.18 (0.08–0.36)	0.95 (0.80–0.99)	3.5 (1.5–9.1)	0.87 (0.74–0.94)
Previous angina	1,680 (255)	0.06–0.19	0.95–0.98	3.4–3.8	0.71–0.79
Cyanosis during event	323 (88)	0.08 (0.02–0.14)	0.99 (0.98–1.0)	6.2 (1.6–24)	0.93 (0.88–0.99)

CI, Confidence interval; *LR+*, positive likelihood ratio; *LR–*, negative likelihood ratio; *CHF*, congestive heart failure.

Commentary

Syncope is a transient loss of consciousness with spontaneous recovery and may be due to a wide variety of causes. It is a frequent presenting complaint, responsible for 2% of all ED visits and 6% of admissions, and is associated with significant morbidity and missclassification.[3] A cardiac cause (eg, dysrhythmia, structural heart condition) can carry a poor prognosis, highlighting the importance of differentiating cardiac from other potentially benign causes, and many risk scores seek to stratify patients according to this risk of cardiac cause, such as the San Francisco Syncope Rule and the Canadian Syncope Risk Score.[4,5]

This systematic review and meta-analysis sought to clarify the accuracy of history and examination in identifying patients with a cardiac cause of syncope.[6] A previous Systematic Review Snapshot suggested that brain natriuretic peptides and troponin have insufficient sensitivity in determining risk of major cardiac adverse events in patients with syncope, but this current review examined specific brain natriuretic peptides and high-sensitivity cardiac troponin T thresholds and their association with risk of cardiac cause for syncope.[6,7] Although these biomarkers show promise for identifying cardiac syncope, the European Society of Cardiology and American College of Cardiology/American Heart Association guidelines state that providers should not routinely use these biomarkers in the evaluation of syncope.[8,9] Rather, the sole recommended test is an ECG.[8,9]

This meta-analysis has several limitations. This review is limited by misclassification bias in assessment of cardiac versus noncardiac syncope; a patient with a history consistent with vasovagal syncope and a normal echocardiogram result is not likely to undergo further evaluation, which overestimates the sensitivity and specificity. Patients with unexplained syncope were excluded from several of the included studies, which can elevate the specificity and sensitivity estimates. Approximately 13% of patients had a final diagnosis of unexplained syncope; the diagnostic utility of biomarkers is

often limited for this population and so their inclusion may decrease the pooled sensitivity and specificity estimates. Five of the 11 included studies were retrospective ones susceptible to myriad sources of bias and data inaccuracies.[10] Next, there were multiple studies for which the meta-analysis authors could not confirm independence between the test and reference standard, which is imperative to generate accurate diagnostic test characteristics.[11] Finally, this meta-analysis focused on individual findings, but did not assess existing risk-stratification tools such as the San Francisco Syncope Rule and Canadian Syncope Risk Score.[4,5]

Clinicians should incorporate age and other factors from the history and examination to risk stratify patients with syncope. Although troponin and brain natriuretic peptides may be able to risk stratify patients at low risk for a cardiac cause of syncope, further high-quality randomized controlled data are required on use of other risk-prediction tools and biomarkers.

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