CLINICAL RESEARCH STUDY

THE AMERICAN JOURNAL of MEDICINE®

Diagnostic and Prognostic Value of High-sensitivity Cardiac Troponin T in Patients with Syncope

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ABSTRACT

OBJECTIVE: We examined the diagnostic and predictive value of high-sensitivity cardiac troponin T (cTnThs) in patients with syncope.

METHODS: We performed an analysis of consecutive patients with syncope presenting to the emergency department. The primary end point was the accuracy to diagnose a cardiac syncope. In addition, the study explored the prognostic relevance of cTnThs in patients with cardiac and noncardiac syncope.

RESULTS: A total of 360 patients were enrolled (median age, 70.5 years; male, 55.8%; 23.9% aged >80 years). Cardiac syncope was present in 22% of patients, reflex syncope was present in 40% of patients, syncope due to orthostatic hypotension was present in 20% of patients, and unexplained syncope was present in 17.5% of patients. A total of 148 patients (41%) had cTnThs levels above the 99% confidence interval (CI) (cutoff point). The diagnostic accuracy for cTnThs levels to determine the diagnosis of cardiac syncope was quantified by the area under the curve (0.77; CI, 0.72-0.83; $P < .001$). A comparable area under the curve (0.78; CI, 0.73-0.83; $P < .001$) was obtained for the predictive value of cTnThs levels within 30 days: Patients with increased cTnThs levels had a 52% likelihood for adverse events, patients with cTnThs levels below the cutoff point had a low risk (negative predictive value, 83.5%). Increased cTnThs levels indicate adverse prognosis in patients with noncardiac causes of syncope, but not in patients with cardiac syncope being a risk factor for adverse outcome by itself.

CONCLUSIONS: Patients with syncope presenting to the emergency department have a high proportion of life-threatening conditions. cTnThs levels show a limited diagnostic and predictive accuracy for the identification of patients with syncope at high risk.

 • *The American Journal of Medicine (2015) 128, 161-170*

KEYWORDS: Cardiac troponin; Emergency service; Healthcare; Hospital; Quality of Healthcare; Quality Indicators; Syncope

Syncope is a sudden, transient loss of consciousness due to temporary global cerebral hypoperfusion with spontaneous recovery and usually is accompanied by a loss of postural tone.[1] Affected patients frequently present to the emergency department (1%-3% of emergency department visits[2-8]) for further evaluation and account for up to 6% of hospital

Funding: None.

Conflict of Interest: MC and TB have received financial support for clinical studies by Roche Diagnostics GmbH (Mannheim, Germany). CM has received research support from the European Union, the Swiss National Science Foundation, the Swiss Heart Foundation, the Cardiovascular Research Foundation Basel, Abbott, Alere, Brahms, Nanosphere, Roche, Siemens, and the Department of Internal Medicine, University Hospital Basel (Basel, Switzerland); and is a speaker for and receives consulting honoraria from Abbott, Alere, AstraZeneca, BG Medicine, bioMérieux Clinical Diagnostics, Brahms, Cardiorentis, Lilly, Novartis, Radiometer, Roche, and Siemens.

Authorship: All authors had access to the data and played a role in writing this manuscript.

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0002-9343/$ -see front matter
http://dx.doi.org/10.1016/j.amjmed.2014.09.021

admissions.[2,9-11] Evaluation of patients with syncope is challenging because patients present with complex symptoms and a variety of differential diagnoses, ranging from benign to life-threatening conditions.[1,12] Because of cognitive impairment, physiologic changes of older patients, and comorbid diseases including concurrent medication, older adults experience a higher incidence of syncope and are at increased risk of adverse outcome.[12-14]

Biomarkers such as natriuretic peptide and cardiac troponin (cTn) have been proposed to identify patients with syncope at risk for adverse events.[4,5,15-21] Reed et al report that only 1.4% of patients with syncope were diagnosed with acute myocardial infarction. While natriuretic peptide levels provide independent prognostic information in syncope, these and other studies suggest that cTnI measurement provides only marginal diagnostic and prognostic information in syncope evaluation.[4,5,15-21] Nevertheless, cardiac biomarkers including cTn levels are often measured in clinical practice to screen for a cardiac cause of syncope.[22] cTn levels may be helpful for the identification of patients at greatest risk,[23] and a possible value may be hypothesized especially in the subgroup of patients at intermediate risk.[24]

We performed a prospective observational study to examine the diagnostic accuracy of high-sensitivity cardiac troponin T (cTnThs) to identify patients with cardiac syncope. In addition, the predictive value of circulating cTnThs for adverse outcome was evaluated.

CLINICAL SIGNIFICANCE

- The diagnostic and prognostic value of high-sensitivity cardiac troponin T (cTnThs) measurement in patients with syncope presenting to the emergency department is not well characterized.
- Increased cTnThs levels do not independently identify cardiac causes of syncope.
- Circulating cTnThs levels do not independently predict adverse outcome within 180 days of follow-up.
- The discriminative value of cTnThs measurement in patients with syncope is limited and should not be used in their routine evaluation.

MATERIALS AND METHODS

Study Design and Setting

This is a prospective, single-center observational study of consecutive patients presenting with syncope or near syncope to the emergency department from July 17 to October 31, 2011. The study site is a large community hospital and level III trauma center, with an annual census of approximately 80,000 patients. The study was approved by the institutional review board (Ethik-Kommission der Friedrich-Alexander-Universität Erlangen-Nürnberg, from June 21, 2011; registered at clinicaltrials.gov: ID NCT01916070). Because of the observational nature of this study, verbal consent of patients to participate in this registry was obtained during follow-up contact. Patients lost to follow-up with no consent were not included in the data analysis (**Figure 1**). We performed and reported the study according to the Standards for Reporting of Diagnostic Accuracy criteria for diagnostic studies.[25]

Selection of Study Patients

All consecutive patients aged 18 years or more who fulfilled the definition of syncope (transient loss of consciousness) or near syncope (near transient loss of consciousness[1,11,26,27]) were enrolled. Exclusion criteria were persistent altered mental status or illicit drug-related loss of consciousness, seizure, coma, hypoglycemia, and transient loss of consciousness caused by head injury (**Figure 1**).

Troponin Measurement

Routine blood samples were drawn into a serum tube (Sarstedt, Nümbrecht, Germany) at presentation. cTnThs was measured by a Roche assay performed on a cobas e411 (Roche Diagnostics, Mannheim, Germany). The cTnThs assay has a limit of detection of 3 ng/L, a 99th percentile cutoff point of 13.5 ng/L, and a coefficient of variation of $<10\%$ at 13 ng/L.

Outcome Measures

The primary end point was the presence of a cardiac cause of syncope including dysrhythmias or structural disease of the heart. The secondary end point was a composite end point including a critical intervention or a serious adverse outcome during the emergency department stay or hospitalization, or during follow-up within 30 days and 180 days after the initial presentation.[2,5,8,11] Critical intervention was defined as pacemaker/implantable cardiac defibrillator placement, percutaneous coronary intervention or surgery, blood transfusion, cardiopulmonary resuscitation, or endoscopy with intervention. Serious adverse outcome was defined as sudden death, pulmonary embolus, stroke, severe infection/sepsis, severe water and electrolyte imbalance, acute heart failure, severe valvular disease of the heart, acute renal injury, ventricular dysrhythmia, atrial dysrhythmia (including supraventricular tachycardia and atrial fibrillation with rapid ventricular response), intracranial bleeding, hemorrhage, acute myocardial infarction, or life-threatening sequelae of syncope (eg, rhabdomyolysis, long bone or cervical spine fractures, major head injury) and readmission to the emergency department due to syncope within 30 or 180 days. All enrolled patients had at least 1 episode of syncope or near syncope meeting the earlier definition to be eligible for enrollment. All adverse outcomes or clinical interventions, such as cardiopulmonary resuscitation, stroke, or cardiac arrest, were noted after spontaneous recovery from the initial syncopal episode.[11]