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Prospective validation of prognostic and diagnostic syncope scores in the emergency department

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ABSTRACT

Background: Various scores have been derived for the assessment of syncope patients in the emergency department (ED) but stay inconsistently validated. We aim to compare their performance to the one of a common, easy-to-use $CHADS_2$ score.

Methods: We prospectively enrolled patients ≥ 40 years old presenting with syncope to the ED in a multicenter study. Early clinical judgment (ECJ) of the treating ED-physician regarding the probability of cardiac syncope was quantified. Two independent physicians adjudicated the final diagnosis after 1-year follow-up. Major cardiovascular events (MACE) and death were recorded during 2 years of follow-up. Nine scores were compared by their area under the receiver-operator characteristics curve (AUC) for death, MACE or the diagnosis of cardiac syncope.

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Results: 1490 patients were available for score validation. The $CHADS_2$-score presented a higher or equally high accuracy for death in the long- and short-term follow-up than other syncope-specific risk scores. This score also performed well for the prediction of MACE in the long- and short-term evaluation and stratified patients with accuracy comparative to OESIL, one of the best performing syncope-specific risk score. All scores performed poorly for diagnosing cardiac syncope when compared to the ECJ.
Conclusions: The $CHADS_2$-score performed comparably to more complicated syncope-specific risk scores in the prediction of death and MACE in ED syncope patients. While better tools incorporating biochemical and electrocardiographic markers are needed, this study suggests that the $CHADS_2$-score is currently a good option to stratify risk in syncope patients in the ED.
Trial registration: NCT01548352

Key questions

- What is already known about this subject: The diagnosis and risk-stratification of syncope patients in the ED is difficult. Several scores have been derived to fill this gap.
- What does this study add? In a large cohort of syncope patients presenting to the ED, several syncope-specific scores performed poorly in the diagnosis of cardiac syncope. A simple $CHADS_2$ score showed similar accuracy to predict death or major cardiovascular events than more complicated syncope-specific risk-stratification scores.
- How might this impact on clinical practice? Complicated and time-consuming syncope-specific risk scores could be replace with a simple $CHADS_2$-score. There is a need for better diagnostic and risk-stratification tools incorporating novel biochemical and electrocardiographic markers for syncope patients in the ED.

1. Introduction

Syncope is a transient loss of consciousness (T-LOC) associated with an inability to maintain postural tone due global cerebral hypoperfusion [1]. It is frequent and represents 1–2% of all Emergency Department (ED) visits [2]. The underlying etiologies range from benign conditions, such as vasovagal reactions, to life-threatening cardiac diseases [1, 3, 4]. Early risk stratification during initial evaluation is important to guide decisions regarding treatment and disposition and prevent long-term morbidity and mortality [1]. Syncope outcomes are mainly linked to the underlying etiology and the associated comorbidities. In the ED, the rapid identification of the underlying cause and associated risks are challenging, thus leading to a high hospitalization rate. However, only 25% of these hospitalizations have been considered appropriate [5] and, despite extensive cardiovascular investigations, 75% of patients in whom the cause of the syncope remains unexplained after initial clinical assessment will not receive a final diagnosis of causality [6].

In an attempt to improve the identification of patients at risk of adverse outcomes, numerous syncope-specific risk scores [7–9] have been derived. However, as highlighted in the recent ACC/AHA/HRS "Guideline for the Evaluation and Management of Patients With Syncope" [10], these scores were derived in only a few centers, are based on inconsistent definitions of outcomes, time frames and predictors, and have been subject to limited external validation [10]. Furthermore, these tools have not been implemented in most institutions, partly due to their perceived complexity. The $CHADS_2$ score is widely known and used for prediction of thromboembolic episodes and initiation of treatment with anticoagulants in patients with atrial fibrillation [11]. In addition, it has recently been applied as a risk stratification tool for predicting mortality after an episode of syncope and was recommended in current guidelines [10, 12]. However, a prospective validation in a multicenter study is lacking. Our study aims to validate syncope-specific risk scores [7–9] and compare their performance to the one of a common, easy-to-use $CHADS_2$ score in a large, multicenter cohort of prospectively enrolled patients presenting following a syncopal episode to the ED and provide a valid overview of the diagnostic and prognostic accuracy of these tools.

2. Methods

2.1. Study design, setting and selection of participants

BAsel Syncope EvaLuation Study (BASEL IX) is an ongoing prospective international diagnostic multicenter study enrolling patients in thirteen hospitals in eight countries (Switzerland, Spain, Germany, Italy, Poland, New Zealand, Australia and the United States of America). The study is designed to contribute to and improve the management of patients presenting with syncope (ClinicalTrials.gov registry, number NCT01548352). Patients aged >40 years presenting to the ED with syncope within the last 12 h were recruited, after written informed consent was obtained.

Patients with the final diagnosis of a non-syncopal loss of consciousness (e.g. epilepsy, fall, alcohol intoxication) were excluded of the analysis. As the majority of scores requested ECG data for their correct computation, patients who did not undergo electrocardiographic testing upon arrival to the ED were excluded as well. Patients in whom the final diagnosis remained unclear even after central adjudication were excluded for the validation of diagnostic scores (Supp. Fig. 1).

The study was carried out according to the principles of the Declaration of Helsinki and approved by the local ethics committees. The authors designed the study, gathered, and analyzed the data according to the STARD guidelines for studies of diagnostic accuracy, vouched for the data and analysis, wrote the paper, and decided to publish.

2.2. Clinical assessment

All patients underwent a clinical assessment that included standardized and detailed assessment of predefined details of medical history, including previous syncope events and circumstances of current syncope, vital signs, physical examination, routine laboratory tests, radiologic testing, and a 12-lead ECG. Additionally, patients may have also undergone 24-hour ECG, external or implantable loop device, cardiac exercise test, Shellong test, tilt table testing, coronary angiography, continuous rhythm monitoring, pulse oximetry, echocardiography, results from device controls (e.g. pacemaker) or electrophysiological examinations, and recording of findings of further investigations during recurrent hospitalization or ambulant treatment. Additional tests and treatment of patients were left to discretion of the attending physician.

Clinical judgment by the ED physician regarding the presence of cardiac syncope was quantified using a visual analogue scale within 90 min after presentation and following initial patients' assessment encompassing patient history and status as conducted by the ED physician, first standard laboratory values and the ECG.

2.3. Follow-up and adjudicated final diagnosis

Patients were contacted 6, 12 and 24 months after discharge by telephone or in written form. Information regarding recurrent syncope, hospitalization and cardiac events during follow up was furthermore obtained from the patient's hospital notes, the family physician's records and national mortality registries, where available. To determine the final diagnosis for the index syncope in each patient, two independent physicians reviewed all available medical records from the clinical data set and the study-specific data set. The clinical data set included data from the clinical assessment, while study-specific data included standardized forms uniformly collecting predefined details of patient history, the circumstances of syncope, and physical examination, as well as at least 12 months follow-up. In situations of disagreement between adjudicators, cases were reviewed and adjudicated in conjunction with a third physician. Further details regarding the adjudicated diagnosis are available in the supplemental material.

2.4. Score selection and computation

The scores listed in the recent AHA/ACC/HRS Guidelines [10], for which our study contained appropriate data to allow their validation, were computed according to the original score definition (Supplemental Table 1). In total, seven syncope-specific scores mentioned in these guidelines were computed in all patients for this analysis: The score

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