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COMMENTARY

Syncope Prediction Scores in the Emergency Department

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Abstract: Syncope is a common clinical presentation defined as a transient loss of consciousness (TLOC) due to cerebral hypoperfusion, characterized by a rapid onset, short duration, and spontaneous complete recovery. Different clinical decision rules (CDRs) and risk stratification scores have been developed to predict short- and long-term risks for adverse outcomes after syncope. The central theme of these prediction systems is consistent with the ESC syncope guidelines. Initial assessment according to the ESC guideline is essential until an optimal and well-validated risk score is available. The focus should be accurate risk stratification to allow prevention of adverse outcomes and optimize the use of limited healthcare resources. In this review article, we summarize and critically appraise the evidence regarding the CDRs for patients presenting with syncope.

Keywords: Syncope, clinical decision rules, healthcare, transient loss of consciousness, electrocardiogram, cardiac syncope.

1. INTRODUCTION

Syncope is a common clinical presentation defined as a transient loss of consciousness (TLOC) due to cerebral hypoperfusion, characterized by a rapid onset, short duration, and spontaneous complete recovery [1]. Syncope constitutes 1% to 3% of emergency department (ED) visits and up to 3% of hospitalizations from the ED [2]. The occurrence of syncope can be benign or the symptom of life-threatening diseases, even death [3, 4]. However, in clinical practice, it may be difficult for physicians to identify high-risk patients at the initial evaluation stages. Thus, many Clinical Decision Rules (CDRs) and risk stratification scores have been developed to predict short-term and long-term risks of adverse outcomes after syncope and improve the allocation of limited healthcare resources. Systematic reviews and meta-analyses comparing different prediction tools have rarely been performed [5-7]. The objective of this review is to systematically assess the prognostic accuracy of previously validated studies that predict adverse outcomes in patients presenting to the ED with syncope.

1.1. Search Strategy

We searched PubMed, the Cochrane Library, Web of Science, and EMBASE from their inception to March 25, 2021, without language restrictions. The terms syncope (unconsciousness, loss of consciousness, fainting, drop attack, near syncope) and prediction guides (risk, score, rules, algorithms, logistic models, decision support techniques) were used and combined together to search title and keywords. The conference abstracts, reference lists, and gray literature of all available records identified in the initial publications were also reviewed to avoid missing relevant articles.

1.2. Diagnostic Scores

Del Rosso *et al.* [8] developed a prospective cohort study including 516 patients with unexplained syncope in 2008. They reported a guideline-based score with high diagnostic sensitivity. An Evaluation of Guidelines in SYncope Study (EGSYS) score > 3 identified cardiac syncope and patients had higher all-cause mortality at two years in both the derivation and validation cohorts. This was the first score developed not only in the diagnosis of syncope but also for risk stratification. Kariman *et al.* [9] developed a cross-sectional study to validate the EGSYS score, reporting an acceptable accuracy for predicting cardiogenic causes of syncope using ≥3 as a cut-off. These findings indicate that this score can be used for initial triage and accurate risk stratification.

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2. PROGNOSTIC SCORES FOR SHORT-TERM OUTCOMES

In 1997, Martin *et al*. [10] identified historical and electrocardiogram (EGG) factors available at the time of presentation that can be used to stratify the risk of arrhythmias or mortality within 1 year in ED patients presenting with syncope. Later, risk scores such as the OESIL (Osservatorio Epidemiologico sulla Sincope nel Lazio), the San Francisco Syncope Rule (SFSR), and the Boston scores were reported to predict mortality and adverse outcomes after syncope.

2.1. San Francisco Syncope Rule (SFSR)

Quinn *et al.* [11] devised the SFSR by a single-center prospective cohort of 684 patients in 2004, which was validated and compared with physician judgment in the next 2 years [12,13]. These results suggested that this decision rule is highly sensitive but not specific. The strengths of the rule lie in its thorough derivation process and the number of validation studies [13-21] that have been performed. However, the validation studies have reported inconsistent results.

A systematic review and meta-analysis proceeded to evaluate the accuracy of the SFSR in 2011 [22], indicating that the SFSR was unsatisfactory. Serrano *et al.* [5] suggested differences in study design and ECG interpretation may account for the variable prognostic performance of the SFSR when validated in different practice settings. Saccilotto *et al.* [23] conducted a meta-analysis including prospective and retrospective studies for the SFSR. They reported similar pooled accuracy estimates, with a sensitivity of 0.87 (95% Confidence Intervals (CI) 0.79–0.93) and a specificity of 0.52 (95%CI 0.43-0.62). The most common cause of false-negative classification for serious outcomes was cardiac arrhythmias.

2.2. The Boston Rule and the Anatolian Syncope Rule (ASR)

Grossman *et al.* [24] found that the sensitivity of the Boston rule to assess the prognosis of patients with syncope was 97%, and the specificity was 62%. The verification results of other studies showed that this rule is beneficial to reduce the unnecessary hospitalization rate for syncope [25-27]. Subsequently, Kayayurt *et al.* [18] proposed a new risk score in 2012, namely the Anatolian Syncope Rule (ASR). Similar to the Boston rule, the ASR appeared to be highly sensitive for identifying patients at risk for serious short-term outcomes. However, the sample sizes of the above two studies were small, and the ASR was validated only in the Turkish population. Decision rules need to be validated prospectively in different ethnicities before physicians can consider them in clinical decision-making.

2.3. Risk Stratification of Syncope in the Emergency department (ROSE)

Reed *et al.* [15] suggested that the ROSE rule has high sensitivity and a high negative predictive value for the identification of patients with high-risk syncope. They arrived at the conclusion that BNP was one of the main predictors of vascular outcome and all-cause death. However, the ROSE includes multiple laboratory indicators such as hemoglobin, fecal occult blood, and BNP, which are not conducive to the rapid evaluation of syncope patients in practice, limiting its clinical application.

2.4. The Canadian Syncope Risk Score (CSRS)

In 2016, Thiruganasambandamoorthy *et al.* [28] conducted a multicenter large sample study including 5010 patients and developed the CSRS score. Items included Troponin level and arrhythmia details. The CSRS was successfully validated later, and its use is recommended in guiding ED management of patients when serious causes are not identified during index ED evaluation [29]. This study on the prognosis of syncope and the results were relatively reliable. However, one-fifth of the syncope patients who met the criteria were not included in the study due to various reasons, which may have led to bias in selection.

2.5. The FAINT Score

Probst *et al*. performed a multicenter observational study [30] of 3173 patients aged＞65 years with syncope or presyncope in the ED in 2019. They combined five clinical variables and found that the incidence of adverse outcomes at 30 days was 5.45% (95% CI: 4.69-6.30%). The set of clinical variables comprises the FAINT Score. This is the newest risk score and the first tool to combine N-terminal pro-B-type natriuretic peptide (NT-proBNP) and high-sensitive cardiac troponin T (hs-cTnT) to predict adverse outcomes at 30-day follow-up, with a sensitivity and specificity of 0.97 and 0.22, respectively. However, the FAINT Score requires additional validation studies to guide clinical management.

3. PROGNOSTIC SCORES FOR LONG-TERM OUTCOMES

3.1. Osservatorio Epidemiologico sulla Sincope nel Lazio (OESIL)

Colivicchi *et al*. [31] developed and subsequently validated the OESIL for patients presenting with syncope to the emergency department. A multivariate analysis allowed the recognition of the following predictors: (1) age > 65 years; (2) cardiovascular disease in clinical history; (3) syncope without prodromes; and (4) abnormal electrocardiogram. The OESIL was significantly different in inclusion criteria and endpoint compared to the SFSR. The study calculated a sensitivity of 96.8% and a specificity of 72.8%, which may allow more accurate stratification and targeting of diagnostic procedures and therapeutic interventions. Similarly, other studies [15, 18, 20, 32-34] have validated the OESIL risk score using different study designs, different endpoints, and different individuals who interpreted the ECG. The results suggested that the prediction accuracy of OESIL in other syncope populations is significantly reduced, so it has not been promoted in clinical applications.

3.2. The Short-Term Prognosis of Syncope (STePS) Study

The data from the STePS study [35] identified the following risk factors: age＞65 years, history of neoplasms, cerebrovascular diseases, structural heart diseases, and ventricular arrhythmias for predicting serious outcomes from the 11^{th} day up to 1 year after the ED visit. The STePS study first included early readmission as a serious adverse event and suggested that early readmission was one of the factors affecting the prognosis of syncope patients.

3.3. Evaluation of Guidelines in SYncope Study (EGSYS)

In addition to the diagnostic role of cardiac syncope as mentioned above, the EGSYS score is useful for identifying patients with a high risk of mortality. Del Rosso *et al.* [8] showed that when compared with patients with a score < 3, the patients with an EGSYS score >3 had a mortality of 17% and 21% in the derivation and validation cohorts, respectively. Furthermore, an analysis of the EGSYS 2 study [36] confirmed the predictive value of the EGSYS score.

Garcia Gomes *et al.* [25] reported the IC-FUS, a simple and easily obtained score that detected patients with an increased risk of death after discharge from a syncopal event. The CHADS2 was known to be used to assess the stroke risk in patients with atrial fibrillation. Analysis of 37705 patients by Ruwald *et al.* [37] found that a high CHADS2 score was associated with the risk of cardiovascular death in syncope patients. However, these risk scores still require external validation before they can be recommended for routine clinical use. Table **1** shows the basic characteristics of the main syncope risk scores.

Table 1. The basic characteristics of main syncope risk scores.

Study/Reference	Year	Variables	Endpoints	Results
Martin *et al.*	1997	Abnormal ECG; History of ventricular arrhythmia; History of CHF; Age >45 years	1-year arrhythmias or deaths	4.4% score 0; 57.6% score 3 or 4
OESIL	2002	Abnormal ECG; History of cardiovascular disease; Lack of prodrome; Age >65 years	1-year mortality	0% score 0; 53% score 4
Sarasin *et al.*	2003	Abnormal ECG; History of CHF; Age >65 years	Arrhythmias in unexplained ED syncope	2% score 0; 27% score 3
SFSR	2004	Abnormal ECG; History of CHF; Shortness of breath; Hematocrit < 30%; Triage systolic BP <90 mmHg;	7-day serious events	Sensitivity 98%; Specificity 56%
Boston Syncope Rule	2007	Compilation of 25 plausible variables	30-day serious events	Sensitivity 97%; Specificity 62%
STePS	2008	Abnormal ECG; Trauma; No prodrome; Male sex	10-day and 1-year events	Not Reported
EGSYS	2008	Palpitations before syncope (+4); Abnormal ECG and/or heart disease (+3); Syncope during effort (+3); Syncope while supine (+2); Autonomic prodrome (−1)	Cardiac syncope Probability; 2-year total mortality	Score ≥3， sensitivity 92%, specificity 69%
Sun *et al.*	2009	Age >90 years (+1); Male sex (+1); History of arrhythmia (+1); Triage systolic BP >160 (+1); Abnormal ECG (+1); Abnormal troponin I (+1); Near-syncope (−1)	30-day events among older (≥ 60 years)	2.5% score≤0 ； 20% score≥3
ROSE	2010	BNP level ≥300 pg/ml; Bradycardia ≤50 in ED/pre-hospital; Positive fecal occult blood on rectal; Anemia – Hemoglobin ≤ 90 g/L; Chest pain with syncope; Q wave on ECG (except in lead III); O2 saturation ≤ 94% on room air	1-month serious events	Score ≥1， sensitivity 87.2%, specificity 67.5%
ASR	2012	Dyspnoea ； Ortostatism ； Precipitating cause for syncope ； Age > 58 ； Congestive heart failure history ； Abnormal ECG	7-day serious events and death	ASR＞2， sensitivity 97%, specificity 72% for serious events and sensitivity 100%, specificity 78% for death
CHADS2	2013	congestive heart failure, hypertension, age ≥75 years, diabetes, and previous stroke or TIA	1-week, 1-year, and long-term mortality	15.1/1000人/year for score=0 ; 310.9/1000人/year for score 5-6
IC-FUS	2016	previous syncope (+2); abnormal ECG (+3); history of heart disease (+4)	Death and unplanned hospital admission at 30 days and 12 months	12-month event rate for 18.6% when score=0 and 80.0% when score=9
CSRS	2016	Predisposition to vasovagal symptoms –1 History of heart disease 1 Any systolic pressure reading < 90 or > 180 mmHg 2 Elevated troponin level 2; Abnormal QRS axis 1; QRS duration > 130 ms 1; Corrected QT interval > 480 ms 2; Diagnosis in emergency department : Vasovagal syncope –2; Cardiac syncope 2	30-day adverse events	Sensitivity 99.2% and specificity 97.7% for score≥ −2

Study/Reference	Year	Variables	Endpoints	Results
THC3S	2018	Dyspnea ; Palpitation ; Dizziness ; Chest pain	3-month adverse events.	Sensitivity 70% and specificity 91%
FAINT score	2019	history of heart Failure; history of cardiac Arrhythmia; Initial abnormal electrocardiogram; elevated pro B-type Natriuretic peptide; elevated high-sensitivity Troponin T.	30-day mortality or serious cardiac outcome	Score≥1 had sensitivity 96.7% and specificity 22.2%

OESIL = Osservatorio Epidemiologico sulla Sincope nel Lazio; SFSR = San Francisco Syncope Rule; STePS = Short-Term Prognosis of Syncope; EGSYS = Evaluation of Guidelines in Syncope Study; ROSE = risk stratification of syncope in the emergency department; ASR = Anatolian Syncope Rule; CSRS=The Canadian Syncope Risk Score, THC3S = Tehran Heart Center Syncope Stratifying Score; ECG = Electrocardiogram, CHF = Congestive Heart Failure, BNP = Brain type or B-type Natriuretic Peptide; TIA= transient ischemic attack.

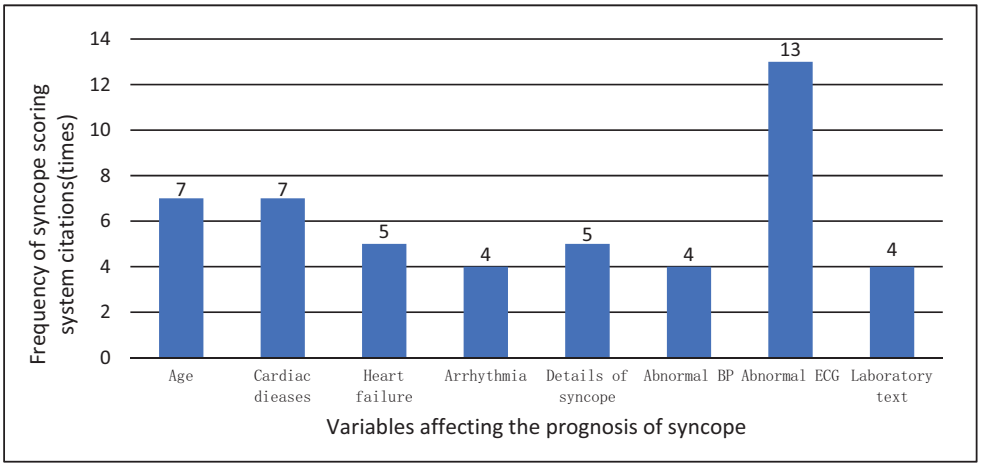

Fig. (1). The different variables used in the syncope scores. (BP = Blood Pressure; ECG = Electrocardiogram).

There are several standards for CDRs summarized as follows: 1) Blinding. To reduce the risk of bias, outcome ascertainment should be made without knowledge of the predictor variables, and clinically assessment must be done without the knowledge of the outcome; 2) Validation. The reliability or accuracy of the predictor variables must be clearly demonstrated; Prospective validation on a new set of patients is an essential step in the evolution of this form of decision support. 3) Bias minimization. The subjects in the study should be selected without bias and should represent a wide spectrum of patients with and without the outcome; Universality. 4) Clinically utility: CDRs should have a clear purpose, demonstrate content validity, and must be relevant, concise, and easy to use in the intended clinical context.

However, no syncope rule system has met all the above requirements so far. At present, only OESIL, SFSR, and ROSE have been validated in three or more clinical practice settings. Other risk scores [8, 16, 25, 36, 37], such as the Canadian Syncope Arrhythmia Risk Score (CSARS), the ASR, and the FAINT Score need to be validated in large prospective studies several times, although they have higher diagnostic, predictive value. Serrano *et al.* [5] compared the prognostic value of CDRs in a meta-analysis conducted in 2010. They concluded that the methodological quality and prognostic accuracy of CDRs for syncope are limited. A meta-analysis [6] compared OESIL, EGSYS, and SFSR with clinical judgment. The results indicate that syncope prediction tools do not have better sensitivity, specificity, or prognostic yield than clinical judgment in predicting serious short-term outcomes in syncope.

4. PREDICTIVE VALUE OF INDIVIDUAL COMPONENTS OF PROGNOSTIC SCORES

The 2018 European Society of Cardiology (ESC) syncope guideline [1] recommended the diagnostic evaluation of TLOC of suspected syncopal nature as the initial syncope evaluation, which consists of history, physical examination, and electrocardiograph. Nearly all risk scores took the items mentioned above into consideration. The different variables used in the syncope scores are shown in Fig. (**1**).

4.1. Medical History

Gender – The STePS study and Sun *et al.* [38] took gender as one of the variables in the risk stratification tool. They suggested that males have a higher risk of death and adverse outcomes. Otherwise, five prediction rules [8, 16, 25, 36, 37] considered age as the prediction factor. It was generally believed that older patients were associated with improved mortality or major adverse cardiac and cerebrovascular events, but the cut-off value for age was not consistent among various rules.

Cardiovascular complications - History of cardiovascular diseases such as congestive heart failure, ventricular arrhythmia, neoplasms, cerebrovascular diseases, and others was included in the clinical syncope rules. Cardiovascular disease, especially congestive heart failure, is the most frequent item used in the prognostic studies of patients with syncope.

Details of syncope - The occurrence and duration of prodromal symptoms, palpitations prior to syncope, position

during the episode, any predisposing factors, and injuries suffered or not are essential to exclude the vasovagal syncope, which is benign, and the prognoses are usually good. Fabrizio D'Ascenzo *et al.* [7] conducted a meta-analysis and identified that the most powerful predictors of adverse outcomes were palpitations before syncope and syncope during exertion.

4.2. Physical Examination

There were three risk rules that took blood pressure into account [11, 18, 35]. Systolic blood pressure < 90mmHg was a factor in the SFSR and the Boston rule, but in the ASR, orthostatic hypotension was considered to predict adverse outcomes. Also, the analysis by Grossman *et al.* [24] found that vital signs such as oxygen saturation and respiratory rate abnormal for more than 15 minutes were also significant in risk assessment in patients presenting with syncope.

4.3. Electrocardiogram

Almost all the scores considered abnormal ECG as one of the indicators of poor prognosis, even if the definition of which was variable in different scores. For example, an abnormal ECG was defined as an ECG with new changes or a non-sinus rhythm in the SFSR [11]. However, Del Rosso [8] considered an ECG abnormal in the following cases: sinus bradycardia, atrioventricular block greater than first degree, bundle branch block, acute or old myocardial infarction, supraventricular or ventricular tachycardia, left or right ventricular hypertrophy, ventricular preexcitation, long QT and Brugada pattern. There are some authors who have advocated the inclusion of ECG variables, such as the QTc duration or the presence of ventricular arrhythmia, as part of the risk prediction system.

4.4. Laboratory Examination

The laboratory examination items are hematocrit value [9,36], hemoglobin [15], BNP [15, 30], and troponin [28, 30, 35]. Troponin and BNP are performed for the presence and severity of cardiac disease and for risk stratification after syncope in recent years. Reed *et al*. [15] and Sun *et al.* [16] were the first to include BNP and troponin, respectively. Probst *et al.* [30] reported high-sensitivity cardiac troponin T and NT-proBNP showed a high sensitivity for excluding death and serious cardiac outcomes in older adults with syncope of cardiac cause. The ESC syncope guidelines suggest that cardiovascular markers for the diagnosis of syncope still need further evidence. Therefore, there are no recommendations for markers such as troponin and BNP.

CONCLUSION

Different syncope scores have been developed, but their clinical utility remains to be elucidated, given the paucity of external validation studies. Therefore, clinicians are recommended to follow established guidelines for the management of syncope before the validation of such scores. Further studies are needed to evaluate the clinical utility of these scores for screening and risk stratification at the individual patient level and estimating or even guiding healthcare resource utilization at the systems level.

LIST OF ABBREVIATIONS

TLOC	=	transient Loss of Consciousness
ED	=	Emergency Department
CDRs	=	Clinical Decision Rules
EGSYS	=	Evaluation of Guidelines in SYncope Study
SFSR	=	San Francisco Syncope Rule
ECG	=	Electrocardiogram
CI	=	Confidence Interval
ASR	=	Anatolian Syncope Rule
ROSE	=	Risk stratification Of Syncope in the Emergency department
CSRS	=	The Canadian Syncope Risk Score
NT-proBNP	=	N-terminal pro-B-type natriuretic peptide
hs-cTnT	=	High-sensitive cardiac Troponin T
OESIL	=	Osservatorio Epidemiologico sulla Sincope nel Lazio
STePS	=	Short-Term Prognosis of Syncope
CSARS	=	Canadian Syncope Arrhythmia Risk Score
ESC	=	European Society of Cardiology

CONSENT FOR PUBLICATION

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CONFLICT OF INTEREST

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