A Tale of Two Cities: Applying the Boston Syncope Criteria to Jerusalem

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ABSTRACT **Background:** Syncope is a common reason for emergency department (ED) visits; however, the decision to admit or discharge patients after a syncopal episode remains challenging for emergency physicians. Decision rules such as the Boston Syncope Criteria have been developed in an attempt to aid clinicians in identifying high-risk patients as well as those who can be safely discharged, but applying these rules to different populations remains unclear.

Objectives: To determine whether the Boston Syncope Criteria are valid for emergency department patients in Israel.

Methods: This retrospective cohort convenience sample included patients who visited a tertiary care hospital in Jerusalem from August 2018 to July 2019 with a primary diagnosis of syncope. Thirty-day follow-up was performed using a national health system database. The Boston Syncope Criteria were retrospectively applied to each patient to determine whether they were at high risk for an adverse outcome or critical intervention, versus low risk and could be discharged.

Results: A total of 198 patients fulfilled the inclusion criteria and completed follow-up. Of these, 21 patients had either an adverse outcome or critical intervention. The rule detected 20/21 with a sensitivity of 95%, a specificity of 66%, and a negative predictive value of 99%.

Conclusions: The Boston Syncope Criteria may be useful for physicians in other locations throughout the world to discharge low-risk syncope patients as well as identify those at risk of complications.

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KEY WORDS: Boston Syncope Criteria, cardiology, decision rule, emergency department, syncope

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The management of syncope continues to be a challenge for emergency physicians as there are a multitude of causes ranging from benign to life-threatening [1-3]. Syncope is defined as a transient loss of consciousness (LOC) due to cerebral hypoperfusion. It is characterized by a rapid onset, short duration, and spontaneous, complete recovery [4]. Syncope itself is a symptom and not inherently dangerous; however, the underlying cause may be life-threatening. Numerous studies have been conducted to help clinicians to try to effectively choose between patients at risk for adverse outcomes who require inpatient admission and workup and patients who can be discharged [5-8]. One of these decision rules is the Boston Syncope Criteria (BSC) [Table 1]. The BSC was created due to a need for a comprehensive rule designed to create consensus between emergency physicians concerning commonly accepted and utilized hospital admission criteria for patients presenting to the emergency department (ED) with syncope. Many patients who might otherwise be safely discharged home are admitted to the hospital for observation and further evaluation while others might be inadvertently discharged home. Yet, prior data suggest that approximately 4% of patients discharged from the ED with syncope who return within 72 hours are admitted or die [9].

The primary outcome of the original study [10] that derived the BSC was either a critical intervention or adverse outcome within 30 days of their emergency department visit. The researchers studied 362 patients with syncope and identified 66/68 who developed adverse outcomes or required critical interventions within 30 days of ED presentation, yielding a sensitivity of 97%, a specificity of 62%, a negative predictive value of 99%, and a positive predictive value of 44%. A high negative predictive value is critical for emergency physicians who must determine who should be appropriately discharged [10].

The primary objective of this study was to determine whether the BSC are also valid in patients seen in an urban tertiary care ED in Jerusalem.

PATIENT AND METHODS

STUDY DESIGN AND DATA COLLECTION

This retrospective study was comprised of a convenience sample that was collected from the medical records of 200 patients aged 18 years and older, from August 2018 to July 2019, who presented to an urban tertiary care hospital in Jerusalem with at least one episode of syncope. Data were collected from the hospital's electronic medical records and the OFEK national healthcare database. The OFEK health care database was initiated in 2004 as a computerized medical database for the Clalit Health Maintenance Organization (HMO) and then expanded on a national level in 2011 to allow information exchange between

Table 1. The Boston Syncope Criteria. Each of the criteria below is considered a risk factor for adverse outcome in syncope

Signs and symptoms of acute coronary syndrome	
	Complaint of chest pain of possible cardiac origin
	Ischemic ECG changes (ST elevation or deep [> 0.1 mV] ST depression)
	Other ECG changes VT, VF, SVT, rapid atrial fibrillation or new (not known to be old) ST T wave change
	Complaint of shortness of breath
Worrisome cardiac history	
	History of CAD, including deep Q waves, hypertrophic or dilatated cardiomyopathy
	History of congestive heart failure or LV dysfunction
	History of ventricular tachycardia, ventricular fibrillation
	History of pacemaker
	History of ICD
	Pre-hospital use of anti-dysrhythmic medication excluding beta blockers or calcium channel blockers
Family history of sudden death	
	Family history (1st degree relative) with sudden death, HOCM, Brugada's syndrome, or long QT syndrome
Valvular heart disease	
	Heart murmur noted in history or on ED examination
Signs of conduction disease	
	Multiple syncopal episodes within the last 6 months
	Rapid heartbeat by patient history
	Syncope during exercise
	QT interval > 500 ms
	Second- or third-degree heart block or intraventricular block
Volume depletion	
	Gastrointestinal bleeding by hemoccult or history
	Hematocrit < 30
	Dehydration not corrected in the ED per treating physician discretion
Persistent (> 15 min) abnormal vital signs in the ED without the need of concurrent interventions such as oxygen, pressors, temporary pacemakers	
	Respiratory rate > 24 breaths/min
	O2 saturation < 90%
	Sinus rate < 50 beats/min or sinus rate > 100 beats/min, blood pressure < 90 mmHg
CNS (includes SAH, TIA, Stroke) or similar concerns	

CAD = coronary artery disease, CNS = central nervous system, ECG = electrocardiogram, ED = emergency department, HOCM = hypertrophic obstructive cardiomyopathy, ICD = implantable cardiac defibrillator, LV = left ventricular, SAH = subarachnoid hemorrhage, SVT = supraventricular tachycardia, TIA = transient ischemic attack, VT = ventricular tachycardia, VF = ventricular fibrillation

community physicians and every Israeli hospital [11]. Israel has universal healthcare and all citizens (except soldiers who receive primary health from military physicians) are enrolled in one of four-sharing HMOs. In this retrospective study the treating physicians were not directed to perform specific tests or to admit the patient. The study was approved by the hospital's institutional review board.

Syncope is defined as a sudden and transient (< 5 minutes) LOC producing a brief period of unresponsiveness and a loss of postural tone ultimately resulting in spontaneous recovery requiring no resuscitation measures. All adverse outcomes or clinical interventions, such as cardiopulmonary resuscitation, stroke, or cardiac arrest were noted after spontaneous recovery from the initial syncopal episode. Access to the OFEK system for each patient was allowed for 90 days from the patient's discharge. All study patients were followed for 30 days via review of medical records in the OFEK system. Exclusion criteria were persistent altered mental status, alcohol or illicit drug-related LOC, seizure, coma, hypoglycemia, transient ischemic attack, syncope caused by head trauma, pre-syncope, soldiers, or tourists. The last two groups were excluded as there was no mechanism for follow up.

The decision to admit or discharge a patient was based on the clinical decision of the treating physician and not the BSC. Therefore, the purpose of this study was to measure the ability of this rule to identify a patient who is either low risk or at risk for a critical intervention or adverse outcome in our patient population.

STATISTICAL ANALYSIS

Continuous variables are expressed as mean value ± standard deviation (SD) or medians with interquartile ranges. The Student's *t*-test was used for comparison of normally distributed data when appropriate. Categorical differences between groups were presented as numbers or percentages and evaluated through the chi-square test or Fisher's exact test. The results are reported as percentages along with the operating characteristics of the rules.

Sensitivities, specificities, and positive and negative predictive values are reported with 95% confidence intervals (CI) around the point estimates. For two-sided *P* values, a value of $P < 0.05$ was considered statistically significant.

RESULTS

During the research period, more than 800 files of patients with a suspected syncopal episode were reviewed. Of this group, 200 met inclusion criteria and were enrolled. One patient was excluded due to an incomplete history and physical examination. Thirty-day follow-up was completed for 198/199 (99.5%) patients. A total of 48/199 (24%) patients were admitted, with 20/21 outcomes occurring during hospitalization. Figure 1 shows a flow diagram of the performance of the BSC in predict-

Table 2. Co-morbidity and adverse outcomes/critical intervention and adverse outcomes or critical intervention within 30 days

Co-morbidity	Outcome absent (n=178)	Outcome present (n=21)	Total (n=199)
Admitted to hospital	28, 15.7%	20, 95%	48, 24.1%
Age (mean ± standard deviation)	52.3 ± 25.4	71.5 ± 18.5	54.4 ± 25.4
Gender, % female	55%	52%	55%
Signs and symptoms of acute coronary syndrome	**2, 1%**	**3,14%**	**5, 2.5%**
Chest pain	1, 0%	1,10%	2, 1%
Ischemic ECG	0, 0%	0, 0%	0, 0%
Abnormal heart rhythm or new ECG changes	1, 1%	1, 5%	2, 1%
SOB	0, 0%	1, 5%	1, 0.5%
Worrisome cardiac history	**21, 12%**	**6, 29%**	**27,13.6%**
History of CAD	12, 7%	3, 14.3%	15, 7.5%
History of CHF/LV dysfunction	4, 2%	1, 5%	5, 2.5%
Ventricular tachycardia	1,1%	0, 0%	1, 0.5%
History of pacemaker	3, 2%	1, 5%	4, 2%
ICD	0, 0%	0, 0%	0, 0%
Antidysrhythmic medication	1, 1%	1, 5%	2, 1%
Family history of sudden death	**0, 0%**	**0, 0%**	**0, 0%**
Valvular heart disease	**7, 4%**	**2, 9.5%**	**9, 5%**
Significant heart murmur	7, 4%	2, 9.5%	9, 5%
Signs of conduction disease	**14, 8%**	**5, 23%**	**19, 9.5%**
Recurrent syncope	10, 6%	2, 10%	12, 6%
Palpitations	1, 1%	0, 0%	1, 0.5%
Syncope during exercise	3, 2%	1, 5%	4, 2%
QT interval > 500 ms	0, 0%	0, 0%	0, 0%
Heart block	0, 0%	2, 10%	2, 1%
Volume depletion	**14, 8%**	**5, 23%**	**19, 9.5%**
GI bleed	0, 0%	2, 9.5%	2, 1%
Hematocrit < 30	2, 1%	3, 14%	5, 2.5%
Profound dehydration	12, 7%	0, 0%	12, 6%
Persistent abnormal vital signs	**2,1%**	**1, 5%**	**3, 1.5%**
Respiratory rate > 24 breaths/minute	0, 0%	0, 0%	0, 0%
O2 saturation < 90%	1, 1%	0, 0%	1, 0.5%
Sinus rate < 50 or > 100 beats/min	0, 0%	1, 5%	1, 0.5%
Blood pressure < 90 mmHg	1, 1%	0, 0%	1, 1%
Primary CNS event	**1, 1%**	**1, 5%**	**2, 1%**

Outcome	Total outcome
Pacemaker/ICD placement	7
Myocardial infarction	0
PCI or surgery	3
Alteration in antidysrhythmic therapy	1
Stroke	1
Cardiac arrest/CPR	0
Death	2
Cerebral bleed	2
Other hemorrhage	0
GIB*	3
Ventricular dysrhythmia	0
Atrial dysrhythmia**	0
Sepsis	2
PE	2
Carotid stenosis	0
Life-threatening sequelae of syncope***	1
Total	**24**

*GIB was defined as haematocrit < 30, or need for blood transfusion or endoscopy

**Includes SVT, tachy/brady syndrome, and atrial fibrillation with rapid ventricular response

***Includes rhabdomyolysis, long bone or cervical fractures

CAD = coronary artery disease, CHF = congestive heart failure, CNS = central nervous system, CPR = cardiopulmonary resuscitation, ECG = electrocardiogram, GI = gastrointestinal, GIB = gastrointestinal bleeding, ICD = implantable cardiac defibrillator, LV = left ventricular, PCI = percutaneous coronary intervention, PE = pulmonary embolus, SD = standard deviation, SOB = shortness of breath, SVT = supraventricular tachycardia

ing a critical intervention or adverse outcome. The presence of adverse outcomes by co-morbidity is depicted in Table 2. The average age was 49.5 ± 25 years; 55% were female. All enrolled patients had a complete history, physical examination, and electrocardiogram (ECG).

Less than 5% of the 800 files were excluded because of logistical reasons whereby the patient was not able to be followed through the OFEK system. However, none of these files exhibited any significant findings during their hospital course.

One patient did have a significant hospital course but then was lost to 30-day follow up. He presented with syncope after an upper gastrointestinal bleed and was admitted to the hospital. He received a blood transfusion and underwent an upper endoscopy, which revealed a bleeding gastric ulcer. Several days later he left the hospital prior to official discharge. There was no follow-up either in another hospital or in the HMO.

One patient, a 60-year-old female patient who presented with

Table 3. Performance of the decision rule

	Outcome+	Outcome-	Total
Identified by the rule	20	61	81
Not identified	1	117	118

Sensitivity	95%
Specificity	66%
Positive predictive value	24%
Negative predictive value	99%
Prevalence	11%
Accuracy	69%

syncope without any other symptoms, was missed by the rule. A troponin, drawn based on the decision of the triage nurse, was positive. A second troponin was further elevated. Serial ECGs were all normal. She was admitted to the cardiology department and an echocardiogram revealed hypokinesia of the apex and basal septum. Cardiac catheterization found two-vessel disease leading to a primary coronary intervention.

A total of 21 patients (10.5%) met the primary outcome of critical intervention or adverse outcome within 30 days [Table 3]. The BSC identified 20 patients with a subsequent critical intervention or adverse outcome for a sensitivity of 95% and a specificity of 66%, with a negative predictive value of 99% [Table 3].

DISCUSSION

Numerous guidelines and decision rules exist for the workup of syncope in the emergency department. Both the American College of Cardiology and the American Heart Association, in collaboration with the Heart Rhythm Society and the European Society of Cardiology recently released syncope guidelines [4,12]. Both societies agree on the main points, however, the European Society of Cardiology puts a stronger emphasis on the use of syncope units. Many of the other differences, such as the subgroup of patients who require a loop recorder, electrophysiologic studies, or advanced pharmacologic treatments, are not immediately relevant to ED physicians. These decisions can be made after admission to the cardiology service or outpatient referral to an electrophysiologist [13].

While these guidelines cover all aspects of syncope, several decision rules have been developed internationally to attempt to help ED physicians decide who can be safely discharged home. The OESIL risk score was developed and prospectively validated in the Lazio region of Italy [5]. Using multivariate analysis, they found four predictors of mortality: age > 65 years, clinical history of cardiovascular disease, absence of prodromes, and an abnormal electrocardiogram. Each of these factors was given a score of "one" and the risk of mortality by 12 months increased with a higher score. There were no deaths by 6 months in those with a score of either 0 or 1 [5].

Another score derived and validated in Italy was the Evaluation of Guidelines in SYncope Study (EGSYS) rule. Predictors of cardiac syncope included the absence of autonomic prodromes, absence of predisposing and/or precipitating factors, syncope while supine, effort syncope, heart disease or abnormal ECG, and palpitations preceding syncope. Each predictor received a score between -1 and 4. Those with a score ≥ 3 identified cardiac syncope with a sensitivity of 92% and a specificity of 69% in the validation cohort [6].

The San Francisco Syncope Rule had been widely popular particularly due to its ease of use with the mnemonic **CHESS**: **C**ongestive heart failure history, **H**ematocrit less than 30%, **E**lectrocardiogram abnormalities, **S**hortness of breath, and **S**ystolic blood pressure less than 90 mmHg [7]. However, there have been questions about external validity [14].

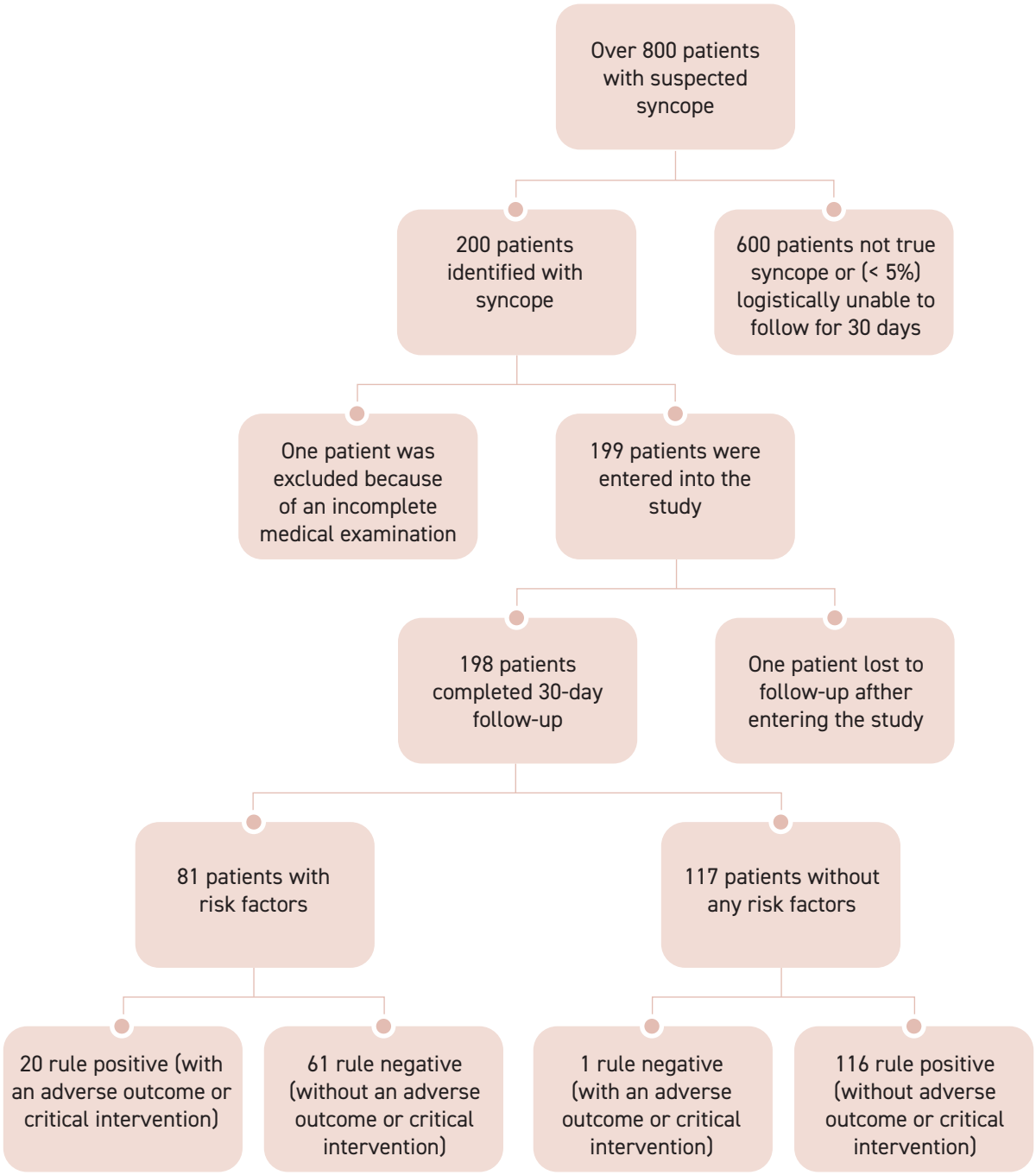
The Risk Stratification of Syncope in the Emergency Department (ROSE) rule also uses a mnemonic **BRACES** (**B**NP level/ **B**radycardia, **R**ectal examination, **A**nemia, **C**hest pain, **E**CG, **S**aturation) to determine which patients should be admitted to the hospital. Independent predictors of morbidity and mortality include BNP level ≥ 300 pg/ml, bradycardia ≤ 50 in the ED, rectal examination showing fecal occult blood (if suspicion of gastrointestinal bleed), anemia with hemoglobin ≤ 9 g/dl, chest pain associated with syncope, ECG showing Q waves (not in lead III), and a saturation ≤ 94% on room air. The rule, which was derived and then validated, showed a sensitivity of 87.2%, a specificity of 65.5%, and a negative predictive value of 98.5% [8].

One of the newest rules to be published is the **FAINT** score, which is designed for use in adults ≥ 60 years of age. This score looks at history of heart **F**ailure, history of cardiac **A**rrhythmia, **I**nitial abnormal ECG result, elevated pro-B-type **N**atriuretic peptide, and elevated high-sensitivity **T**roponin. A FAINT score of 0 versus ≥ 1 had a sensitivity of 96.7% and specificity 22.2% [15].

Since the initial publication of the BSC in 2007, other studies have validated the rule in different populations. Subsequent real-time application of the rule proved to reduce hospital admissions [16]. Most recently, a focused syncope management pathway based on the criteria was shown to reduce hospital admissions and adverse events following discharge [17]. The BSC have also been shown to reduce admissions in patients with near syncope [18]. Although a systematic review suggests that current prediction tools do not show better prognostic yield compared with clinical judgment in predicting short-term serious outcome after syncope, the BSC remain unique in their comprehensive 25 point set of diagnostic criteria designed to mimic the critical thinking necessary for normative decision making involved in the risk stratification and disposition of patients with syncope [19].

Our study demonstrates that the BSC can be useful and applicable in EDs outside of the United States. Its high negative predictive value is vitally important to help emergency physicians make decisions whether to safely discharge the patient

Figure 1. Flow diagram of the performance of the Boston Syncope Criteria in predicting a critical intervention or adverse outcome



home. The number of admissions in our study was lower compared to the original one conducted in the United States. We believe this result is multifactorial. Admissions may be higher in the United States due to a greater fear of litigation relative to Israel if there is a poor outcome in a discharged patient. Furthermore, in Israel every patient is a member of an HMO and thus has access to a family physician with the ability to obtain quick follow-up and testing.

LIMITATIONS

As the study was retrospective, there was no automatic decision to admit or discharge patients based on the BSC. Disposition was based on the clinical decision of the admitting physician and outcomes were based on whether there was a critical intervention or adverse event. Another limitation was the use of 30-day follow-up through the OFEK system as the availability of patient's files and information was limited to 3 months from patient discharge and resulted in the inability to retrieve older records or enroll more patients in the study.

The study was specifically designed to evaluate the application of the BSC in Israel. Its ease of use compared to other scores should be evaluated.

CONCLUSIONS

Syncope remains a challenge for emergency physicians. This study validates the high negative predictive value of the Boston Syncope Criteria which may aid emergency physicians in safely discharging low-risk syncope patients.

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Capsule

Viral vulnerability in hepatocytes

Chronic viral infections of the liver can lead to organ dysfunction and hepatocellular carcinoma. **Hsin** et al. found these infections may arise due to the activity of the protease hepsin, which is abundant in the liver. Hepsin cleaved and inactivated STING, thereby preventing the STING-mediated induction of type I interferons (IFNs) in response to viral infection in human hepatocytes. This mechanism also appeared to account for the failure of prostate cancer cells, which also produce hepsin, to mount a STING-dependent type I IFN response to viral infection.

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