Prognostic accuracy of syncope clinical prediction rules in older adults in the emergency department

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Abstract

Study objective: The objective of this study is to evaluate the prognostic accuracy of existing rules (San Francisco Syncope Rule [SFSR], Canadian Syncope Risk Score [CSRS], and FAINT score) in older adults.

Methods: This is a cohort study of adults aged ≥60 years presenting to an academic emergency department (ED) with syncope or near syncope. We used original criteria for all rules except for the FAINT score, in which N-terminal pro–brain natriuretic peptide was largely missing from the extracted data. Patients were deemed positive for each rule if classified as non-low risk. The primary outcome was the presence of 30-day serious outcome, as defined by syncope research guidelines. Sensitivity and negative likelihood ratio (NLR) were calculated with 95% confidence intervals (CIs).

Results: A total of 404 ED visits (mean age of patients, 75.5 years) were included. Of these, 44 (10.9%) had a 30-day serious outcome, and 24 (5.9%) had incomplete 30-day follow-up. SFSR was positive for 280 of 380 visits with complete follow-up. Its sensitivity and NLR for predicting 30-day serious outcomes were 86.4% (95% CI, 72.0%–94.3%) and 0.53 (95% CI, 0.25–1.15), respectively. The CSRS was positive for 299 of 380 visits (sensitivity was 88.6% [95% CI, 76.4%–95.7%], and NLR was 0.50 [95% CI, 0.22–1.17]). The modified FAINT score was positive for 318 of 380 visits (sensitivity was 90.9% [95% CI, 77.4%–97.0%), and NLR was 0.53 [95% CI, 0.20–1.38]).

Conclusion: Existing rules are suboptimal to predict 30-day serious outcomes in older adults presenting with syncope or near syncope to the ED.

Keywords
clinical prediction rules, geriatric emergency medicine, older adults, pre-syncope, prognosis, risk stratification, syncope
1 | INTRODUCTION

1.1 | Background

The presentation of syncope as a chief complaint or symptom to the emergency department (ED) occurs in about 2% of all ED visits.1,2 Syncope is traditionally defined as a transient loss of consciousness with a spontaneous return to baseline without the need for intervention. The chief complaint of syncope carries a broad differential diagnosis requiring a workup and evaluation of varying levels of intensity, resources, and cost. Approximately half of ED presentations for syncope have no associated etiology despite comprehensive ED workups.3 The morbidity and mortality associated with potential causes of syncope are variable, ranging from benign (vasovagal syncope) to precarious (cardiac causes).3 Given the heterogeneous prognosis, appropriate disposition of syncope patients is paramount.

1.2 | Importance

Many clinical prediction rules have been developed to assist clinicians in determining the potential risk of adverse events and appropriate disposition for patients with a syncopal or near-syncopal event. Notable examples include the San Francisco Syncope Rule (SFSR)4 and the Canadian Syncope Risk Score (CSRS).5 These rules have displayed mixed results in external validation studies.6–9 None of these rules have been widely adopted in clinical practice. Furthermore, guidelines for the management of syncope emphasize that existing risk scores should not be used alone for risk stratification because they have not performed better than unstructured clinical judgment.10–12 In general, these previous rules have been derived in a population of adults without evaluation of the subset of geriatric patients. Age is an important predictor of serious outcomes in patients with syncope.13 For this reason, the FAINT score was recently derived and internally validated using a study population of individuals aged 60 years or older presenting to EDs after an episode of syncope or near syncope.14 FAINT was designed to facilitate disposition decisions in an aging population. Although their derivation and internal validation showed promising results, external validation is yet warranted to evaluate its usefulness in other settings.

1.3 | Goals of this investigation

In this study, we aimed to evaluate 3 previously derived clinical prediction rules (SFSR, CSRS, and FAINT) in older adult ED patients who presented with syncope or near syncope. Specifically, we assessed their prognostic accuracy for serious outcomes within 30 days of the ED visit.

2 | MATERIALS AND METHODS

This article adhered to the Strengthening the Reporting of Observational Studies in Epidemiology15 guidelines for reporting observational studies and to the Standards for Reporting of Diagnostic Accuracy16 criteria. This study was deemed exempt by our institutional review board given its retrospective nature. In the state of Minnesota, only patients who provide “research authorization” for the use of their electronic health records (EHRs) are eligible for retrospective chart review studies.

2.1 | Study design and setting

This was a single-center retrospective cohort study of consecutive older adults presenting within 24 hours of syncope or near syncope to the ED. We reviewed the EHRs of all eligible patients who presented to the ED between January 1, 2019, and January 1, 2020. The study was conducted at an academic quaternary ED with approximately 80,000 ED visits, including 30,000 ED visits for older adults per year.

2.2 | Selection of participants

Patients aged ≥60 years who provided authorization for medical record review were eligible for inclusion. ED visits were identified for review if any of the following keywords were included in the chief complaint or first 5 ED diagnosis fields in the EHR: “syncope,” “near syncope,” “pre-syncope,” “unresponsive,” “loss of consciousness,” “faint,” and “spell.” Patients who presented with a chief complaint of “fall” were also considered if they had 1 of these keywords in the ED diagnosis field (eg, chief complaint of “fall” and ED diagnosis of “syncope”).

ED visits of patients who had either syncope or near syncope within 24 hours before presentation were included. Syncope was defined as a transient loss of consciousness resulting in a loss of postural tone with an immediate, spontaneous, and complete return to baseline without the need for intervention.17 Near syncope was defined by the sensation of impending loss of consciousness. Because of the challenge of establishing a near-syncopal episode retrospectively, we only included patients in which “near-syncpe” or “pre-syncpe” was specifically mentioned by the ED physician as the most likely presentation. Exclusion criteria included the following: patients who were transferred to our ED after initially presenting to an outside ED; patients who had loss of consciousness secondary to intoxication (alcohol or other drugs),
seizures, stroke/transient ischemic attack, head trauma before having syncope or loss of consciousness, or hypoglycemia; patients who were acutely altered or confused upon presentation to the ED; patients who had non-specific neurologic symptoms that did not meet the criteria for syncope or near syncope (eg, weakness, dizziness, fatigue); and patients who had a serious outcome (defined in section 2.5) during the index ED visit. These exclusion criteria were consistent with recommendations from syncope research guidelines.\(^\text{17}\)

## 2.3 Data extraction

We abstracted data from the EHR using a standardized chart review process.\(^\text{18}\) First, 2 investigators independently reviewed a sample of 70 visits to refine the data extraction rules. Interrater reliability was calculated for key variables deemed to be susceptible to abstraction error using Cohen's \(k\) statistic, including study inclusion, history of heart failure, ECG abnormality (defined in section 2.4), ED physician impression for the syncope diagnosis (cardiac, vasovagal, orthostatic, or unknown), and the primary outcome. Interobserver agreement was as follows: inclusion, \(k = 0.84\); history of heart failure, \(k = 0.86\); ECG abnormality, \(k = 0.94\); ED physician impression, \(k = 0.78\); and primary outcome, \(k = 1.00\). Disagreements were discussed and resolved by consensus. A third investigator was also trained in the same process by reviewing the same initial 70 visits. The remaining charts (n = 630) were then reviewed by 2 of the trained investigators. Clinical notes (eg, history of present illness, medical decision-making notes, consulting services notes) related to the ED visit of interest were reviewed. Variables that were available as structured data in our EHR (eg, patient demographics, laboratory values) were electronically retrieved to minimize abstraction error.

## 2.4 Measurement of predictor variables

Variables extracted from the EHR included all elements recommended by the syncope research reporting guidelines.\(^\text{17}\) The comprehensive data extraction form allowed us to obtain data for all predictors of the 3 syncope clinical prediction rules of interest.

For the SFSR, we measured the following variables: presence of abnormal ECG, shortness of breath, hematocrit <30%, triage systolic blood pressure <90 mmHg, and a history of heart failure.\(^\text{4}\) The presence of any of these 5 variables identified the patient as high risk (ie, SFSR positive). To determine ECG abnormality, we used the recorded final interpretation of the ECG. All ECGs performed in our ED are reviewed by a certified rhythm analysis technician (CRAT) and supervised by a cardiologist. An abnormal ECG was defined as the presence of any of the following: non-sinus rhythm (including paced rhythms), multiple premature ventricular complexes, sinus bradycardia (<40 beats/minute), ventricular hypertrophy, short PR-segment interval (<100 milliseconds), axis deviation, first-degree block (>200 milliseconds), complete bundle branch block, Brugada's pattern, Wolff-Parkinson-White’s pattern, abnormal QRS-interval duration (>120 milliseconds) or abnormal QTc-interval prolongations (>450 milliseconds), and Q/ST/T-segment abnormalities suggestive of acute or chronic ischemia. Shortness of breath was defined as the documented presence of such symptoms associated with the episode of syncope/near syncope. History of heart failure was defined as any prior documentation of heart failure in the EHR. For this variable, we reviewed the past medical history documented by the ED physician and prior encounter notes from a cardiologist or primary care physician (when available). Both hemocrit results and triage blood pressure were retrieved automatically from the EHR and categorized according to the SFSSR definition.

For the CSRS, we measured the following variables: predisposition to vasovagal symptoms (−1 point), history of heart disease (+1 point), triage systolic blood pressure <90 or >180 mmHg (+2 points), elevated troponin (+2 points), abnormal QRS axis (+1 point), prolonged QRS (>1 point), prolonged QTc-interval (+2 points), ED physician impression of vasovagal syncope (−2 points), and ED physician impression of cardiac syncope (+2 points).\(^\text{5}\) This score ranges from −3 to +11, and patients with a score >0 were identified as CSRS positive. To determine predisposition to vasovagal symptoms retrospectively, we defined this variable as the documented presence of an episode triggered by a painful or emotionally distressing stimulus. History of heart disease was defined as the documented presence of any of the following: history of heart failure, history of coronary artery disease (including past myocardial infarction [MI], percutaneous transluminal coronary angioplasty [PTCA], or coronary artery bypass graft [CABG]), history of congenital heart disease, history of structural heart disease (aortic stenosis or other valve diseases), history of arrhythmias (ventricular tachycardia, ventricular fibrillation, supraventricular tachycardias, atrial fibrillation, atrial flutter, sick sinus syndrome, Mobitz II or complete heart block, junctional rhythm), or history of implanted pacemaker or defibrillator. An abnormal axis was defined as axis deviations noted in the final interpretation. Prolonged QRS duration was defined as a QRS >120 milliseconds, and prolonged corrected QT-interval was defined as QTc >450 milliseconds. The diagnosis impression was ascertained based on the etiology that the ED physician noted as the most likely cause of the syncope episode. Whenever this was unclear, we classified it as “unknown.” Both troponin results and triage blood pressure were retrieved automatically from the EHR and categorized according to the CSRS definition.

For the FAINT score, we measured the following variables: history of heart failure (+1 point), history of arrhythmias (+1 point), presence of abnormal ECG (+1 point), elevated N-terminal pro-brain natriuretic peptide (NT-proBNP; +2 points), and elevated high-sensitivity troponin (+1 point).\(^\text{14}\) History of heart failure, history of arrhythmias, and abnormal ECG were defined as previously described (same definition was used across rules based on the FAINT derivation study).\(^\text{16}\) Both troponin and NT-proBNP results were retrieved electronically from the EHR and categorized according to the FAINT definition. Unfortunately, a very small proportion of patients had a NT-proBNP available, and, for this reason, we used a modified score without the NT-proBNP. The “new” score ranged from 0 to 4 points, and patients with a score >0 (presence of any of the variables) were identified as “non-low risk”
Primary outcome

Our primary outcome of interest was the presence of a serious outcome within 30 days of the index ED visit, including death, serious cardiac outcomes, pulmonary embolism, aortic dissection, clinically significant bleeding, or cardiopulmonary resuscitation. Serious cardiac outcomes included acute MI (Type I and Type II), significant cardiac arrhythmias (ventricular fibrillation, ventricular tachycardia, sick sinus disease, Mobitz II atrioventricular heart block, complete heart block, symptomatic bradycardia, or pacemaker malfunction), new diagnosis of structural heart disease (aortic stenosis with valve area \( \leq 1 \text{ cm}^2 \)), hypertrophic cardiomyopathy with outflow tract obstruction, severe pulmonary artery hypertension [mean arterial pressure > 30 mmHg], left atrial myxoma or thrombus with protrusion, or outflow tract obstruction, and cardiac intervention (placement of a pacemaker or automatic implantable cardioverter-defibrillator, PTCA, CABG, or other invasive cardiac procedures performed within 30 days of index ED visit). Clinically significant bleeding was defined as bleeding that required transfusion. The primary outcome definition was consistent with the syncope research reporting guidelines. Patients who had a serious outcome during the ED index visit (eg, MI) were excluded as we aimed to evaluate the accuracy of rules in the prognostication of outcomes that occur after the ED evaluation.

Data analysis

We calculated the sensitivity, specificity, positive likelihood ratio (PLR), and negative likelihood ratio (NLR) with corresponding 95% confidence intervals (CIs) for the 3 clinical prediction rules of interest. CIs for sensitivity and specificity were calculated using a binomial approximation, and CIs for PLR and NLR were calculated using a logarithmic transformation on binomial proportions. As a sensitivity analysis, we explored best- and worst-case scenarios for patients who were lost to follow-up to evaluate its impact on the results. Also, we analyzed data after excluding repeat visits from the same patient and after including only those who presented for syncope (ie, excluding the subset with near syncope). The sensitivity analysis excluding patients with near syncope was added because the CSRS was originally derived with syncope patients only. All statistical analyses were performed with R software version 3.6.2 (R Foundation for Statistical Computing) by a biostatistician. We focused the results on the sensitivity and NLR because a very sensitive test will have fewer false negatives. In this investigation, we were interested in determining which rule had fewer missed patients cataloged as low risk by the rule. The likelihood ratio (LR) incorporates the sensitivity and specificity to provide a single estimate, and an NLR (or LR of a negative test) refers to the odds of having a bad outcome when the syncope decision rule is negative. LR is the ratio between the likelihood that a given decision rule result would be expected in a patient who experienced a bad outcome after syncope, compared with the likelihood of that same result in a patient who did not have a bad outcome. The sensitivity, specificity, and LR are properties of the test. LRs are less affected by the change in disease prevalence and can be used to calculate posttest probabilities.

RESULTS

There was a total of 700 ED visits by patients aged \( \geq 60 \) years that were initially eligible for inclusion. After exclusion criteria were applied, a total of 455 visits with syncope or near syncope were included. Of those, 51 were excluded for having a serious outcome during the ED visit (Appendix S1), yielding 404 visits eligible for analysis. A total of 380 (94.1%) visits with 365 unique patients had complete 30-day follow-up. A detailed flowchart of enrollment is shown in Figure 1. Of visits with complete follow-up, 44 had at least 1 serious outcome within 30 days (Table 1). Our cohort had a mean age of 75.5 years (standard deviation, 9.4) with 49% women and mostly White patients (96%). Baseline characteristics stratified by the presence of a 30-day serious outcome are detailed in Table 2.

TABLE 1 Serious outcomes identified within 30 days of index ED visit (N = 44a)

| Serious outcome                                      | n |
|------------------------------------------------------|---|
| Death                                                | 7 |
| Cardiopulmonary resuscitation                        | 0 |
| Any serious arrhythmia                               | 13|
| Ventricular fibrillation                             | 1 |
| Symptomatic ventricular tachycardia                  | 1 |
| Sinus pause > 3 seconds                              | 6 |
| Mobitz II AV block                                   | 2 |
| Complete heart block                                 | 2 |
| Symptomatic bradycardia                              | 3 |
| Any cardiac intervention                             | 22|
| Pacemaker placement                                  | 16|
| AICD placement                                       | 2 |
| CABG placement                                       | 2 |
| PTCA                                                 | 2 |
| Myocardial infarction                                | 2 |
| Any newly diagnosed structural heart disease         | 1 |
| Aortic stenosis (valve area \( \leq 1 \text{ cm}^2 \)) | 1 |
| Pulmonary embolism                                   | 0 |
| Aortic dissection                                    | 0 |
| Internal hemorrhage or anemia requiring transfusion  | 8 |

Abbreviations: AV, atrioventricular; AICD, automatic implantable cardioverter-defibrillator; CABG, coronary artery bypass graft; PTCA, percutaneous transluminal coronary angioplasty.

aThese 44 patients may have had >1 outcome considered as serious within 30 days.
TABLE 2  Baseline characteristics of the study cohort

|                      | With 30-day serious outcome (n = 44) | Without 30-day serious outcome (n = 336) | Incomplete follow-up (n = 24) | Total (N = 404) |
|----------------------|--------------------------------------|------------------------------------------|-----------------------------|-----------------|
| **Patient demographics** |                                       |                                          |                             |                 |
| Age, years, mean (SD) | 74.1 (9.0)                            | 75.9 (9.5)                               | 72.9 (8.9)                  | 75.5 (9.4)      |
| Female, n (%)        | 8 (18.2)                              | 175 (52.1)                               | 15 (62.5)                   | 198 (49.0)      |
| White, n (%)          | 42 (95.5)                             | 324 (96.4)                               | 22 (91.7)                   | 388 (96.0)      |
| African American, n (%) | 1 (2.3)                              | 2 (0.6)                                | 0 (0)                       | 3 (0.7)         |
| Asian, n (%)          | 0 (0)                                 | 5 (1.5)                                 | 0 (0)                       | 5 (1.2)         |
| Other, n (%)          | 0 (0)                                 | 5 (1.5)                                 | 0 (0)                       | 5 (1.2)         |
| Unknown race, n (%)   | 1 (2.3)                               | 0 (0)                                   | 2 (8.3)                     | 3 (0.7)         |
| Hispanic or Latino, n (%) | 0 (0)                      | 3 (0.9)                                | 0 (0)                       | 3 (0.7)         |
| Not Hispanic or Latino, n (%) | 41 (93.2)               | 325 (96.7)                              | 22 (91.7)                   | 388 (96.0)      |
| Other, n (%)          | 1 (2.3)                               | 1 (0.3)                                 | (0)                         | 2 (0.5)         |
| Unknown ethnicity, n (%) | 2 (4.5)                          | 7 (2.1)                                 | 2 (8.3)                     | 11 (2.7)        |
| **SFSR, n (%)**       |                                       |                                          |                             |                 |
| Abnormal ECG          | 37 (84.1)                             | 232 (69.0)                               | 19 (79.2)                   | 288 (71.3)      |
| Shortness of breath   | 9 (20.5)                              | 21 (6.2)                                 | 1 (4.2)                     | 31 (7.7)        |
| Hematocrit <30%       | 6 (13.6)                              | 21 (6.2)                                 | 1 (4.2)                     | 28 (6.9)        |
| SBP <90 mmHg          | 1 (2.3)                               | 10 (3.0)                                 | 1 (4.2)                     | 12 (3.0)        |
| History of heart failure | 14 (31.8)                           | 59 (17.6)                               | 2 (8.3)                     | 75 (18.6)       |
| SFSR score >0 (positive) | 38 (86.4)                        | 250 (74.4)                               | 20 (83.3)                   | 308 (76.2)      |
| **CSRS, n (%)**       |                                       |                                          |                             |                 |
| Predisposition to vasovagal symptoms | 1 (2.3)                          | 6 (1.8)                                 | 0 (0)                       | 7 (1.7)         |
| History of heart disease | 31 (70.5)                          | 183 (54.5)                               | 10 (41.7)                   | 224 (55.4)      |
| SBP <90 or >180 mmHg | 1 (2.3)                               | 21 (6.2)                                 | 3 (12.5)                    | 25 (6.2)        |
| Elevated troponin     | 28 (63.6)                             | 140 (41.7)                               | 7 (29.2)                    | 175 (43.4)      |
| Abnormal QRS axis     | 8 (18.2)                              | 37 (11.0)                                | 2 (8.3)                     | 47 (11.6)       |
| Prolonged QRS         | 9 (20.5)                              | 32 (9.5)                                 | 5 (20.8)                    | 46 (11.4)       |
| Prolonged QTc-interval | 23 (52.3)                            | 150 (44.6)                               | 15 (62.5)                   | 188 (46.5)      |
| ED impression of vasovagal syncope | 5 (11.4)                          | 52 (15.5)                               | 4 (16.7)                    | 61 (15.1)       |
| ED impression of cardiac syncope | 16 (36.4)                         | 58 (17.3)                               | 2 (8.3)                     | 76 (18.8)       |
| CSRS score >0 (positive) | 39 (88.6)                        | 260 (77.4)                               | 16 (66.7)                   | 315 (78.0)      |
| **FAINT score, n (%)** |                                       |                                          |                             |                 |
| History of heart failure | 14 (31.8)                          | 59 (17.6)                               | 2 (8.3)                     | 75 (18.6)       |
| History of cardiac arrhythmia | 16 (36.4)                          | 92 (27.4)                               | 6 (25.0)                    | 114 (28.2)      |
| Abnormal ECG          | 37 (84.1)                             | 232 (69.0)                               | 19 (79.2)                   | 288 (71.3)      |
| Elevated NT-proBNP<sup>a</sup> | 10 (22.7)                          | 30 (8.9)                                 | 1 (4.2)                     | 41 (10.1)       |
| Elevated troponin     | 28 (63.6)                             | 140 (41.7)                               | 7 (29.2)                    | 175 (43.3)      |
| FAINT score >0 (positive) | 40 (90.9)                           | 279 (83.0)                               | 19 (79.2)                   | 338 (83.7)      |
| Modified FA(N)NT score >0 (ignoring BNP criteria) | 40 (90.9)                          | 278 (82.7)                               | 19 (79.2)                   | 337 (83.4)      |

Abbreviations: BNP, brain natriuretic peptide; CSRS, Canadian Syncope Risk Score; ED, emergency department; NT-proBNP, N-terminal pro–brain natriuretic peptide; SBP, systolic blood pressure; SD, standard deviation; SFSR, San Francisco Syncope Rule.

<sup>a</sup>Only 49 patients had a pro-BNP available in the ED or within 30 days of the index visit.
3.1 San Francisco Syncope Rule

Of the 380 patient visits with complete 30-day follow-up, 288 (75.8%) were classified as positive for the San Francisco rule (ie, had at least 1 of its criteria present). Among the 44 with 30-day serious outcomes, the SFSR identified 6 as being low risk. The sensitivity of a positive SFSR for predicting 30-day serious outcome was 86.4% (95% CI, 72.0%–94.3%), whereas its NLR was 0.53 (95% CI, 0.25–1.15). The specificity was 25.6% (95% CI, 21.1%–30.7%), and its PLR was 1.16 (95% CI, 1.02–1.33) (Tables 3 and 4).

3.2 Canadian Syncope Risk Score

Of the 380 patient visits with complete 30-day follow-up, 299 (78.7%) were classified as positive for the Canadian rule (ie, had a score that classified them as being medium, high, or very high risk according to their criteria). Among the 44 with 30-day serious outcomes, the CSRS identified 5 of these as being low risk. The sensitivity of a positive CSRS

**TABLE 3** Two-by-two contingency tables of syncope risk score classifications and 30-day serious outcomes.

|                  | With 30-day serious outcomes (n = 44) | Without 30-day serious outcomes (n = 336) |
|------------------|--------------------------------------|------------------------------------------|
| **SFSR**         |                                      |                                          |
| SFSR positive    | 38                                   | 250                                      |
| SFSR negative    | 6                                    | 86                                       |
| **CSRS**         |                                      |                                          |
| CSRS positive    | 39                                   | 260                                      |
| CSRS negative    | 5                                    | 76                                       |
| Modified FAI(N)T risk score |                                      |                                          |
| Modified FAI(N)T positive | 40                                 | 278                                      |
| Modified FAI(N)T negative | 4                                   | 58                                       |

Abbreviations: CSRS, Canadian Syncope Risk Score; SFSR, San Francisco Syncope Rule.
### Table 4 Prognostic accuracy of syncope prediction rules in ED older adults for serious outcomes within 30 days

|                                | Main analysis (N = 380) | Incomplete follow-up as non-events (n = 404) | Incomplete follow-up as events (n = 404) |
|--------------------------------|-------------------------|---------------------------------------------|------------------------------------------|
| San Francisco Syncope Rule (positive defined as >1 criteria) |                         |                                             |                                          |
| Accuracy                       | 32.6% (28.0–37.6)       | 31.7% (27.2–36.5)                           | 35.6% (31.0–40.6)                       |
| Sensitivity                    | 86.4% (72.0–94.3)       | 86.4% (72.0–94.3)                           | 85.3% (74.2–92.3)                       |
| Specificity                    | 25.6% (21.1–30.7)       | 25.0% (20.7–29.9)                           | 25.6% (21.1–30.7)                       |
| Positive likelihood ratio      | 1.16 (1.02–1.33)        | 1.15 (1.01–1.31)                            | 1.15 (1.02–1.29)                        |
| Negative likelihood ratio      | 0.53 (0.25–1.15)        | 0.55 (0.25–1.17)                            | 0.57 (0.32–1.05)                        |
| Canadian Syncope Risk Score (positive defined as score >0) |                         |                                             |                                          |
| Accuracy                       | 32.9% (28.2–37.9)       | 30.4% (26.0–35.2)                           | 32.4% (27.9–37.3)                       |
| Sensitivity                    | 88.6% (74.6–95.7)       | 88.6% (74.6–95.7)                           | 80.9% (69.2–89.0)                       |
| Specificity                    | 22.6% (18.3–27.5)       | 23.3% (19.1–28.1)                           | 22.6% (18.3–27.5)                       |
| Positive likelihood ratio      | 1.15 (1.02–1.29)        | 1.16 (1.03–1.30)                            | 1.05 (0.92–1.19)                        |
| Negative likelihood ratio      | 0.50 (0.22–1.17)        | 0.49 (0.21–1.14)                            | 0.85 (0.50–1.43)                        |
| Modified FAI(N)T risk score (positive defined as score >0) |                         |                                             |                                          |
| Accuracy                       | 25.8% (21.5–30.6)       | 25.5% (21.4–30.1)                           | 29.0% (24.6–33.7)                       |
| Sensitivity                    | 90.9% (77.4–97.0)       | 90.9% (77.4–97.0)                           | 86.8% (75.9–93.4)                       |
| Specificity                    | 17.3% (13.5–21.8)       | 17.5% (13.8–21.9)                           | 17.3% (13.5–21.8)                       |
| Positive likelihood ratio      | 1.10 (0.99–1.22)        | 1.10 (0.99–1.22)                            | 1.05 (0.94–1.16)                        |
| Negative likelihood ratio      | 0.53 (0.20–1.38)        | 0.52 (0.20–1.36)                            | 0.77 (0.40–1.47)                        |

Note: All measures are provided along with their 95% confidence intervals in parentheses. Abbreviation: ED, emergency department.

was 88.6% (95% CI, 74.6%–95.7%), whereas its NLR was 0.50 (95% CI, 0.22–1.17). The specificity was 22.6% (95% CI, 18.3%–27.5%), and its PLR was 1.15 (95% CI, 1.02–1.29) (Tables 3 and 4).

### 3.3 Modified FAI(N)T score

Among the 404 patient visits eligible for analysis, only 49 had a NT-proBNP available in the ED or within 30 days of the index visit, which led us to evaluate a modified score without the use of such variable. Of the 380 patient visits with complete 30-day follow-up, 318 were classified as positive (ie, had a score >0 that classified them at higher risk). Among the 44 with 30-day serious outcomes, the modified FAI(N)T identified 4 of these as being low risk. The sensitivity of a positive modified FAI(N)T for predicting 30-day serious outcomes was 90.9% (95% CI, 77.4%–97.0%), whereas its NLR was 0.53 (95% CI, 0.20–1.38). Its specificity was 17.3% (95% CI, 13.5%–21.8%) (Tables 3 and 4).

### 3.4 Sensitivity analysis

For those 24 patient visits who did not have complete 30-day follow-up, best- and worst-case scenarios were evaluated to assess whether this would influence the main results of our analysis. Sensitivity along with other measures of prognostic accuracy remained relatively similar, with the modified FAI(N)T score retaining the highest point estimate of sensitivity (Table 4).

There were 15 visits included in the main analysis from patients who had already been included for a previous visit. After excluding these repeat visits, there were 365 unique patients with complete 30-day follow-up. A total of 43 (11.8%) resulted in at least 1 serious outcome within 30 days. Sensitivity and specificity estimates remained similar after considering only the first visit from each patient (Appendix S2).

After excluding those who presented for near syncope, 252 unique patients were included for the sensitivity analysis of syncope only and had complete 30-day follow-up. There were 38 (15.1%) patients who experienced at least 1 serious outcome within 30 days. Sensitivity and specificity estimates in this subset of patients were also similar to the main analysis (Appendix S3).

### 4 LIMITATIONS

This study has several limitations. First, the use of medical records for research and its retrospective nature result in some necessary information being unavailable for extraction. This limitation was encountered in our study where clinician ordering practices, judgment for a
cause of syncope, and outcomes data were potentially incomplete or absent. Second, data abstractors were not blinded to patient outcomes and study objectives. To minimize errors in data abstraction, agreement analysis was performed for the initial 10% of charts reviewed to assess the reliability of variables with the highest potential for interrater variability among chart reviewers. Furthermore, charts with conflicting data were flagged for review by all investigators involved. Third, this study was performed at a single academic medical center with a population that represents Minnesota’s older population; however, it lacks racial diversity, and it is predominantly White. Subsequent multicenter studies including academic and non-academic medical centers will be important to continue to externally validate and refine the rules. Fourth, the interpretation of ECGs used in our study was the interpretation provided by a CRAT and supervised by a cardiologist. Fifth, we used a modified FAI(N)T score as an NT-proBNP was not consistently obtained in our sample. As such, we were unable to perform a validation of the original FAINT score (with NT-proBNP) in older patients and had to use a modified score. Lastly, the relatively small number of outcomes with only 44 events precluded us from having more precise CIs for the effect estimates of prognostic accuracy of the rules.

5 | DISCUSSION

In this study of 404 ED visits with patients aged >60 years presenting with syncope or near syncope at a single academic center, we assessed the test characteristics of 3 syncope rules for the prediction of 30-day outcomes (as recommended and defined by the syncope research reporting guidelines).17 Among the rules studied, we found that the modified FAI(N)T score had the highest point estimate of sensitivity (90.9%) for predicting 30-day serious outcomes, followed by the CSRS (88.6%) and the SFSR (86.4%). These findings suggest that the modified FAI(N)T rule may provide the most utility among the scores when risk stratifying syncope patients aged >60 years. Nevertheless, the imperfect sensitivity of all these rules highlights the importance of not exclusively relying on them during discharge decisions of older adults in the ED.

In our cohort, the modified FAI(N)T score had the highest sensitivity for predicting serious 30-day outcomes. The original FAINT score was derived and internally validated as a geriatric-specific (age ≥60 years) syncope risk stratification tool in 11 different EDs in the United States.14 For patients having a score >0 (ie, non-low risk), Probst and colleagues reported a sensitivity of 97% and a specificity of 22%. In their derivation study, NT-proBNP was the strongest predictor of serious outcomes.14 In our data set, the absence of NT-proBNP for most patients led us to use a modified FAI(N)T score without using NT-proBNP, which undermined our attempt to validate this score in our study population. Moreover, we used outcomes recommended by the syncope research reporting guidelines,17 which varied from the original FAINT derivation study. The syncope research reporting guidelines not only included all the outcomes of the derivation study but also included hemorrhage requiring transfusion, aortic dissection, and pulmonary embolism, which were not included in the FAINT derivation study. None of our patients had a 30-day outcome of aortic dissection or pulmonary embolism, but 8 patients did have an internal hemorrhage requiring transfusion. If these 8 patients were excluded from the analysis, the sensitivity would slightly decrease to 88% (data not shown). Also, it is important to note that our 30-day event rate was 11.6% (9.5% if we exclude internal hemorrhage requiring transfusion) compared with 5.7% in the original FAINT study, likely attributed to the inclusion of more comprehensive 30-day outcomes by following the syncope research reporting guidelines17 recommendations. Future studies with complete NT-proBNP data are needed to validate the FAINT score as we were unable to do so retrospectively in this study.

Among our cohort of patients aged >60 years, the CSRS >0 had a sensitivity of 88.6% and a specificity of 22.6% for serious outcomes. Results were similar when we excluded patients who presented with near syncope to comply with the original derivation in which only syncope patients were included. The CSRS used 30-day outcomes recommended by the syncope research reporting guidelines and was originally derived in a prospective cohort including 4030 adults aged >16 years presenting to 6 Canadian EDs.5 In the derivation study, the sensitivity and specificity were 87.9% and 76.5%, respectively, for a threshold score of >0 (ie, non-low risk). The CSRS was subsequently externally validated in a prospective multicenter cohort study conducted at 9 EDs across Canada7 including 3819 patients and was shown to have a sensitivity of 91.4% and specificity of 78.1% for a score of >0. The lower specificity observed in our cohort is likely because our cohort was older (mean age, 75.5 years) than the cohorts in which the Canadian rule was derived (mean age, 53.6 years)5 and validated (mean age, 53.9 years).7 In our study, most patients (78.7%) were classified as positive (ie, had a score that classified them as being medium, high, or very high risk according to their criteria). It is important for clinicians to acknowledge that most geriatric patients will be considered non-low risk if this rule is applied.

The SFSR was originally derived using a study population of 684 patients aged >18 years and assessed for 7-day serious outcomes.4 The SFSR was derived before the introduction of the syncope research reporting guidelines, but the outcomes studied were similar except that aortic dissection was not originally included. Saccilotto and colleagues performed a systematic review of the SFSR in adult patients presenting to the ED with syncope in which there was no identified cause during their visit and found a pooled sensitivity and specificity for the SFSR of 88% and 54%, respectively.37 As opposed to the original derivation and other validation studies, our study applied the SFSR to a population that only included patients aged >60 years and examined outcomes within 30 days. In our cohort, the sensitivity of the SFSR for predicting 30-day serious outcomes was 86.4%, whereas its specificity was 25.6%. The lower specificity observed in our cohort, again, can be partly explained by the difference in age between the cohorts (mean age, 75.5 years in the current cohort vs 62.1 years in the original derivation cohort).
Finally, it should be stated that although the pursuit of a strong syncope clinical prediction rule has merit, prior research suggests that independent clinician judgment may outperform these tools. Constantino and colleagues compared syncope risk prediction rules with clinical judgment in an individual patient meta-analysis of 3681 patients and found that rules did not have better prognostic accuracy for short-term serious outcome after syncope.20 Similarly, Schriger and colleagues noted that clinical prediction rules rarely outperform a physician’s judgment.21 Rationale for the differences between prediction rules and unstructured clinician judgment can be debated, but simply put, current clinical prediction rules cannot replace clinician judgment.

Of the rules evaluated in our cohort, the modified FAI(N)T score has shown the most promising results for the risk stratification of older ED adults, but no meaningful differences were seen when compared with other tools. Nevertheless, existing rules seem to be suboptimal to predict 30-day serious outcomes in older adults presenting with syncope or near syncope to the ED. Risk stratification of older adult patients with syncope should not rely on clinical prediction rules alone.

AUTHOR CONTRIBUTIONS
Richard D. Voigt, Fernanda Bellolio, James E. Colleti, Ronna L. Campbell, and Lucas Oliveira J. e Silva conceived and designed the study. Richard D. Voigt, Momen Alsayed, and Lucas Oliveira J. e Silva conducted the acquisition of the data. Fernanda Bellolio, Ronna L. Campbell, and Lucas Oliveira J. e Silva provided methodological expertise. Aidan Mullan analyzed the data. Richard D. Voigt and Lucas Oliveira J. e Silva drafted the manuscript, and all authors contributed substantially to its revision with critical revisions of the manuscript for important intellectual content.

CONFLICT OF INTEREST
The authors declare no conflict of interest.

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REFERENCES
1. Sun BC, Emond JA, Camargo CA. Characteristics and admission patterns of patients presenting with syncope to U.S. emergency departments. Acad Emerg Med. 2004;11(10):1992-2000.
2. Probst MA, Kanzarla HK, Gbedemah M, Richardson LD, Sun BC. National trends in resource utilization associated with ED visits for syncope. Am J Emerg Med. 2015;33(8):998-1001.
3. Soteriades ES, Evans JC, Larson MG, et al. Incidence and prognosis of syncope. N Engl J Med. 2002;347(12):878-885.
4. Quinn JV, Stiell IG, McDermott DA, Sellers KL, Kohn MA, Wells GA. Derivation of the San Francisco Syncope Rule to predict patients with short-term serious outcomes. Ann Emerg Med. 2004;43(2):224-232.
5. Thiruganasambandamoorthy V, Kwong K, Wells GA, et al. Development of the Canadian Syncope Risk Score to predict serious adverse events after emergency department assessment of syncope. CMAJ. 2016;188(12):E289-E298.
6. Serrano LA, Hess EP, Bellolio MF, et al. Accuracy and quality of clinical decision rules for syncope in the emergency department: a systematic review and meta-analysis. Ann Emerg Med. 2010;56(4):362-373.
7. Thiruganasambandamoorthy V, Sivitlotti MLA, Le Sage N, et al. Multi-center emergency department validation of the Canadian syncope risk score. JAMA Intern Med. 2020;180(5):737-744.
8. Solbiati M, Taleric G, Villa P, et al. Multicentre external validation of the Canadian Syncope Risk Score to predict adverse events and comparison with clinical judgement. Emerg Med J. 2021;38(9):701-706.
9. Chan J, Ballard E, Brain D, et al. External validation of the Canadian Syncope Risk Score for patients presenting with undifferentiated syncope to the emergency department. Emerg Med Australas. 2021;33(3):418-424.
10. Shen WK, Sheldon RS, Benditt DG, et al. ACC/AHA/HRS guideline for the evaluation and management of patients with syncope: a report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines and the Heart Rhythm Society [published correction appears in Circulation. 2017 Oct 17;136(16):e271-e272]. Circulation. 2017;136(5):e60-e122.
11. Costantino G, Sun BC, Barbic F, et al. Syncope clinical management in the emergency department: a consensus from the first international workshop on syncope risk stratification in the emergency department. Eur Heart J. 2016;37(19):1493-1498.
12. Brignole M, Moya A, de Lange FJ, et al. ESC guidelines for the diagnosis and management of syncope. Eur Heart J. 2018;39(21):1883-1948.
13. Gibson TA, Weiss RE, Sun BC. Predictors of short-term outcomes after syncope: a systematic review and meta-analysis. West J Emerg Med. 2018;19(3):517-523.
14. Probst MA, Gibson T, Weiss RE, et al. Risk stratification of older adults who present to the emergency department with syncope: the FAINT score. Ann Emerg Med. 2019;17-22.
15. Von Elm E, Altman DG, Egger M, Pocock SJ, Gotzsche PC, Vandenbroucke JP. The strengthening the reporting of observational studies in epidemiology (STROBE) statement: guidelines for reporting observational studies. Ann Intern Med. 2007;147(8):573-577.
16. Bossuyt PM, Reitsma JB, Bruns DE, et al. STARD 2015: an updated list of essential items for reporting diagnostic accuracy studies. BMJ. 2015:351:h5527. Published 2015 Oct 28. doi:10.1136/bmj.h5527.
17. Sun BC, Thiruganasambandamoorthy V, dela Cruz J. Standardized reporting guidelines for emergency department syncope risk stratification research. Acad Emerg Med. 2012;19(6):694-702.
18. Kaji AH, Schriger D, Green S. Looking through the retrospectoscope: reducing bias in emergency medicine chart review studies. Ann Emerg Med. 2014;64(3):292-298.
19. Sacciotto RT, Nickel CH, Bucher HC, Steyerberg EW, Bingisser R, Koller MT. San Francisco Syncope Rule to predict short-term serious outcomes: a systematic review. CMAJ. 2011;183(15):E1116-E1126.
20. Costantino G, Casazza G, Reed M, et al. Syncope risk stratification tools vs clinical judgment: an individual patient data meta-analysis. Am J Med. 2014;127(11):1126.e13-1126.e25.
21. Schriger DL, Elder JW, Cooper RJ. Structured clinical decision aids are seldom compared with subjective physician judgment, and are seldom superior. Ann Emerg Med. 2017;70(3):338-344.e3.
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Supporting Information
Additional supporting information can be found online in the Supporting Information section at the end of this article.

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