Risk Stratification of Older Adults Who Present to the Emergency Department With Syncope: The FAINT Score

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Study objective: Older adults with syncope are commonly treated in the emergency department (ED). We seek to derive a novel risk-stratification tool to predict 30-day serious cardiac outcomes.

Methods: We performed a prospective, observational study of older adults (≥60 years) with unexplained syncope or near syncope who presented to 11 EDs in the United States. Patients with a serious diagnosis identified in the ED were excluded. We collected clinical and laboratory data on all patients. Our primary outcome was 30-day all-cause mortality or serious cardiac outcome.

Results: We enrolled 3,177 older adults with unexplained syncope or near syncope between April 2013 and September 2016. Mean age was 73 years (SD 9.0 years). The incidence of the primary outcome was 5.7% (95% confidence interval [CI] 4.9% to 6.5%). Using Bayesian logistic regression, we derived the FAINT score: 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 T. A FAINT score of 0 versus greater than or equal to 1 had sensitivity of 96.7% (95% CI 92.9% to 98.8%) and specificity 22.2% (95% CI 20.7% to 23.8%), respectively. The FAINT score tended to be more accurate than unstructured physician judgment: area under the curve 0.704 (95% CI 0.669 to 0.739) versus 0.630 (95% CI 0.589 to 0.670).

Conclusion: Among older adults with syncope or near syncope of potential cardiac cause, a FAINT score of zero had a reasonably high sensitivity for excluding death and serious cardiac outcomes at 30 days. If externally validated, this tool could improve resource use for this common condition. [Ann Emerg Med. 2020;75:147-158.]

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INTRODUCTION

Background

Emergency department (ED) visits for syncope (transient loss of consciousness) in the United States are common[1] and increasing yearly,[2] resulting in greater than $2.4 billion in annual hospital costs.[3] Because of the wide range of potential serious causes, particularly in older adults, the clinical management and disposition of these patients is often challenging.[4]

Importance

The quest for an accurate risk-stratification tool has been the holy grail of syncope research for the last 2 decades.[5-14] Despite these efforts, significant uncertainty remains in regard to which patients with syncope can be safely discharged from the ED.[7,15,16] None of the published risk-stratification rules have gained widespread adoption, largely because of small sample sizes, failure of external validation, or lack of face validity.[7,17-22] Moreover, these tools have not been compared with unstructured physician judgment,[16] a necessary comparison before investment in implementation efforts.[23]

Editor's Capsule Summary

What is already known on this topic

Syncope is a common reason for emergency department visits. Identifying who can be safely discharged remains a challenge, particularly with older patients.

What question this study addressed

Among older patients with syncope or near syncope, what characteristics identify patients at high risk for 30-day mortality or serious cardiac outcome?

What this study adds to our knowledge

In a sample of 3,177 patients aged 60 years and older, history of heart failure, abnormal ECG result, history of arrhythmia, elevated B-type natriuretic peptide level, and elevated troponin level defined the FAINT score, with a sensitivity of 96.7% (95% confidence interval 92.9% to 98.8%) and specificity of 22.2% (95% confidence interval 20.7% to 23.8%) for predicting death or serious cardiac outcome at 30 days.

How this is relevant to clinical practice

External validation and comparison with clinician gestalt and other prediction tools are needed to determine the value of this tool as well as the value of routine biomarker testing for older adults with syncope.

Approximately 30% of patients presenting to the ED with syncope are hospitalized[1,2]; for older adults (≥60 years), it is greater than 50%.[24] If a serious diagnosis is found in the ED, these patients may be hospitalized for specific therapeutic reasons (eg, pacemaker insertion, blood transfusion). However, many older adults with syncope, despite having an unremarkable ED evaluation result, are still admitted to inpatient or observation units solely for observation or further testing.[2,25,26] These diagnostic admissions are costly[3] and may be of little to no clinical benefit.[27-30] An accurate, easy-to-use, syncope risk-stratification tool focused on older adults could help decrease low-yield hospitalizations and diagnostic testing while maintaining patient safety.

Goals of This Investigation

Using a large sample size and Bayesian methodology, we sought to derive a novel clinical risk-stratification tool to predict 30-day all-cause mortality and serious cardiac outcomes in older adults with unexplained syncope or near syncope of potential cardiac cause. If externally validated in a new data set, such a tool could guide the ED clinical management and disposition of these patients to optimize resource use and improve clinical outcomes.

MATERIALS AND METHODS

Study Design and Setting

We conducted a multicenter, prospective, observational study of older adults who presented to an ED with syncope or near syncope. The study was conducted at 11 academic EDs, all located in nonprofit hospitals, across the United States (Table E1, available online at http://www.annemergmed.com), recruiting a diverse patient population from April 28, 2013, to September 21, 2016. Ten out of 11 of the EDs were teaching hospitals with a trauma center; ED volume ranged from 47,000 to 120,000 visits per year. The institutional review boards at each site approved the study and study staff obtained written, informed consent from all participating subjects or their legally authorized representatives.

Selection of Participants

Our inclusion criteria were aged 60 years or older with an ED complaint of syncope or near syncope. Syncope was defined as transient loss of consciousness, associated with postural loss of tone, with immediate, spontaneous, and complete recovery. Near syncope was defined as the sensation of impending loss of consciousness without actual loss of it. We excluded patients if their symptoms were thought to be due to intoxication, seizure, stroke, transient ischemic attack, head trauma, or hypoglycemia. Additional exclusion criteria were the need for medical intervention to restore consciousness (eg, defibrillation), new or worsening confusion, and inability to obtain informed consent from the patient or a legally authorized representative.

For this analysis, we also excluded all patients who had a new serious diagnosis identified in the ED: death, significant cardiac arrhythmia, myocardial infarction, significant structural heart disease, stroke, pulmonary embolism, aortic dissection, hemorrhage or anemia requiring blood transfusion, subarachnoid hemorrhage, cardiopulmonary resuscitation, or major traumatic injury (Table E2, available online at http://www.annemergmed.com). We identified serious diagnoses through ED chart review performed by trained research assistants and confirmed by the local physician site investigator.

Methods of Measurement

All patients underwent standardized history, physical examination, cardiac biomarker testing, and 12-lead ECG

testing. Any additional diagnostic testing was performed at the discretion of the treating providers, and availability of diagnostic testing was similar across sites. Trained research assistants screened for eligible patients by using standard definitions, approached potential subjects, collected data variables consistent with reporting guidelines for ED-based syncope research,[31] and directly questioned patients about symptoms associated with the syncopal or near-syncopal episode. Research assistants prospectively collected data on the patients' medical history, medications, and physical examination by querying treating ED providers. A subsample of data was collected a second time by another provider who was blinded to the first evaluation to allow assessment of interrater agreement with a κ statistic.

Research staff obtained blood samples for testing at a core laboratory (University of Rochester, Rochester, NY). Two assays were performed with the Roche Elecsys platform: N-terminal pro B-type natriuretic peptide (NT-proBNP) and the fifth-generation high-sensitivity cardiac troponin T (hs-cTnT). NT-proBNP was classified as abnormal above a cutoff of 125 pg/mL and hs-cTnT was classified as abnormal above the 99th percentile for a reference population (ie, 19 ng/L). Core laboratory results for NT-proBNP and hs-cTnT were not available at the ED evaluation; however, the ED providers were free to order local B-type natriuretic peptide and troponin testing. We abstracted objective quantitative data, such as age, vital signs, and laboratory test results, from the electronic medical record. The first obtained ECG was abstracted by 1 of 5 research study physicians blinded to all clinical data. Research study physicians demonstrated high interrater reliability ($\kappa>0.80$) in distinguishing normal from abnormal ECGs in a training set of 50 ECGs. Abnormal ECG interpretations included nonsinus rhythms (including paced rhythms), multiple premature ventricular complexes, sinus bradycardias ($\leq$40 beats/min), ventricular hypertrophies, short PR-segment intervals (<100 ms), axis deviations, first-degree blocks (>200 ms), complete bundle branch blocks, Brugada's patterns, Wolff-Parkinson-White's patterns, abnormal QRS-interval duration (>120 ms) or abnormal QTc-interval prolongations (>450 ms), and Q/ST/T-segment abnormalities suggestive of acute or chronic ischemia. The disposition of the patients (admission versus observation versus discharge) was decided by the treating providers in accordance with usual care.

To compare our final risk score with unaided physician gestalt,[32] we also prospectively collected unstructured physician risk assessment by asking the treating ED attending physician to estimate the probability that the patient would experience cardiac death or serious cardiac event at 30 days (0% to 100%).

Outcome Measures

Our primary outcome was 30-day all-cause death or serious cardiac outcome. Serious cardiac outcomes included significant cardiac arrhythmia, myocardial infarction, new diagnosis of significant structural heart disease, or cardiac intervention. Significant cardiac arrhythmias included ventricular fibrillation, ventricular tachycardia, sick sinus disease, Mobitz II atrioventricular heart block, complete heart block, symptomatic supraventricular tachycardia, symptomatic bradycardia, and pacemaker malfunction. Structural heart disease included aortic stenosis with valve area less than or equal to 1 cm^2, hypertrophic cardiomyopathy with outflow tract obstruction, severe pulmonary artery hypertension (mean arterial pressure >30 mm Hg), left atrial myxoma or thrombus with protrusion, and outflow tract obstruction. Cardiac interventions were defined as placement of a pacemaker or automated internal cardiac defibrillator, coronary artery bypass graft, percutaneous transluminal coronary angioplasty, or other invasive cardiac surgery. These outcomes are consistent with standardized research reporting and clinical management guidelines.[15,31]

We determined occurrence of the primary outcome by using data collected through a review of the electronic medical records, conducted by local research staff, as well as telephone calls to enrolled patients at 30 days to identify out-of-hospital deaths, ED visits, and hospitalizations that occurred outside the study sites. To minimize outcome bias, research assistants performing chart review were blinded to the clinical outcomes determined by telephone follow-up at 30 days. Multiple strategies were used to maximize follow-up rates, including patient incentives, electronic follow-up tracking, real-time confirmation of telephone numbers, and continuing performance monitoring, as previously described.[33] If a patient or his or her authorized representative reported an ED or hospital visit that occurred outside of the study site, then we obtained and reviewed the medical charts associated with those visits. If research staff were unable to contact a patient at 30 days, we queried the Social Security Death Index Master File 16 months after enrollment completion.

To assess interrater reliability of chart review, records for the first 5 sequentially enrolled patients at each of the 10 external sites (excluding the coordinating center) were independently reviewed by local research staff and the coordinating center. The number of charts chosen (50) for this training set was limited by availability of research staff resources. All 10 serious ED diagnoses and 30-day serious outcomes in the training set were identified by local site reviewers.

We identified candidate predictors by using a previously published systematic review and meta-analysis of the existing syncope risk-stratification literature.[34] We then performed a Bayesian meta-analysis allowing the possibility of exact zero effects. We excluded variables that the Bayesian meta-analysis found to have little chance of being predictive of a serious cardiac outcome (eg, co-occurring palpitations, history of stroke, syncope occurring while the patient was supine) and variables deemed irrelevant by expert physician judgment (eg, Hispanic ethnicity). This left 13 variables: age, sex, hypotension, dyspnea, abnormal ECG result, history of heart disease, history of arrhythmia, history of heart failure, low hematocrit level (<30%), elevated hs-cTnT level, elevated NT-proBNP level, elevated blood urea nitrogen level, and elevated creatinine level. More detailed descriptions of the selection of candidate predictors can be found in Appendix E1 (available online at http://www.annemergmed.com).

Primary Data Analysis

Using the 13 candidate variables as predictors, we fit a Bayesian logistic regression to the primary outcome variable. We chose to use a Bayesian approach over a conventional frequentist analysis because the former allows the incorporation of previously reported empirical data pertaining to syncope risk stratification.[35,36] In particular, the Bayesian approach allowed us to incorporate both shrinkage and variable selection through choice of prior and also incorporated a component that performed multiple imputation of missing predictors. This model was fit to the entire data set. Complete details of the model are given in Appendix E1 (available online at http://www.annemergmed.com). Interrater agreement was assessed with a κ statistic with 95% confidence intervals (CIs), using normal approximation methods.

Five variables were identified as having a high probability of being predictive of a serious cardiac outcome. We fit the same Bayesian logistic model with selection/shrinkage priors and multiple imputation using just these 5 variables to ensure all 5 remained important in the absence of the excluded variables. With this final subset of 5 important variables, we performed Bayesian logistic regression with shrinkage but without model selection to obtain our final model.

We created the final syncope risk score by dividing posterior means of all regression coefficients by the smallest posterior mean and rounding to the nearest integer, as has been done for other health-related risk scores.[37] For each score cutoff, we calculated sensitivity, specificity, positive predictive value, and negative predictive value, with 95% CI, using the exact binomial method. To account for overoptimism of the internal results, we performed cross validation on the entire model selection and score creation procedure to obtain cross-validated estimates for sensitivity, specificity, positive predictive value, and negative predictive value. A *c* statistic and positive and negative likelihood ratios were calculated for a risk-score cutoff of zero. We assessed the calibration of the model by comparing the observed versus expected risk at each level of the score, as well as the Hosmer-Lemeshow goodness-of-fit statistic. We compared the predictive accuracy of the risk score with unstructured physician judgment, using the area under the receiver operating characteristic (ROC) curve with 95% CIs, as done in previous studies.[38,39] Finally, we assessed the net reclassification improvement statistic by comparing the performance of the final risk score with the disposition decision made by the treating physician. This was calculated by taking the percentage of correctly reclassified patients and subtracting the percentage of incorrectly reclassified ones. Correctly reclassified patients were defined as those who were risk-score positive, had a serious outcome, and yet were discharged by the treating physician (ie, inappropriate discharge), and those who were risk-score negative, had no serious outcome, and yet were admitted by the treating physician (ie, unnecessary admission/observation unit stay). Incorrectly reclassified patients were defined as those who were risk-score positive, had no serious outcome, and were discharged by the treating physician, and those who were risk-score negative, had a serious outcome, and were admitted by the treating physician.

RESULTS

Characteristics of Study Subjects

Between April 2013 and September 2016, there were 6,930 eligible patients screened, of whom 3,686 (53.2%) consented to participate in the study (Figure 1). Of patients who consented, 396 were excluded from this analysis for a serious diagnosis found during the ED visit (10.7%), 103 (2.8%) were lost to follow-up, and 10 (0.3%) were withdrawn, leaving 3,177 with complete follow-up data at 30 days. The mean age of the study sample was 72.7 years (SD 8.97), 50.6% were men, and 82.9% reported white race. The majority of patients experienced syncope (n=1,965, 61.9%), whereas the remainder (38.1%) had near syncope. Slightly greater than half of patients (53.3%) had an abnormal initial ECG result, and 29.3% had an elevated hs-cTnT level. See Table 1 for further baseline characteristics.

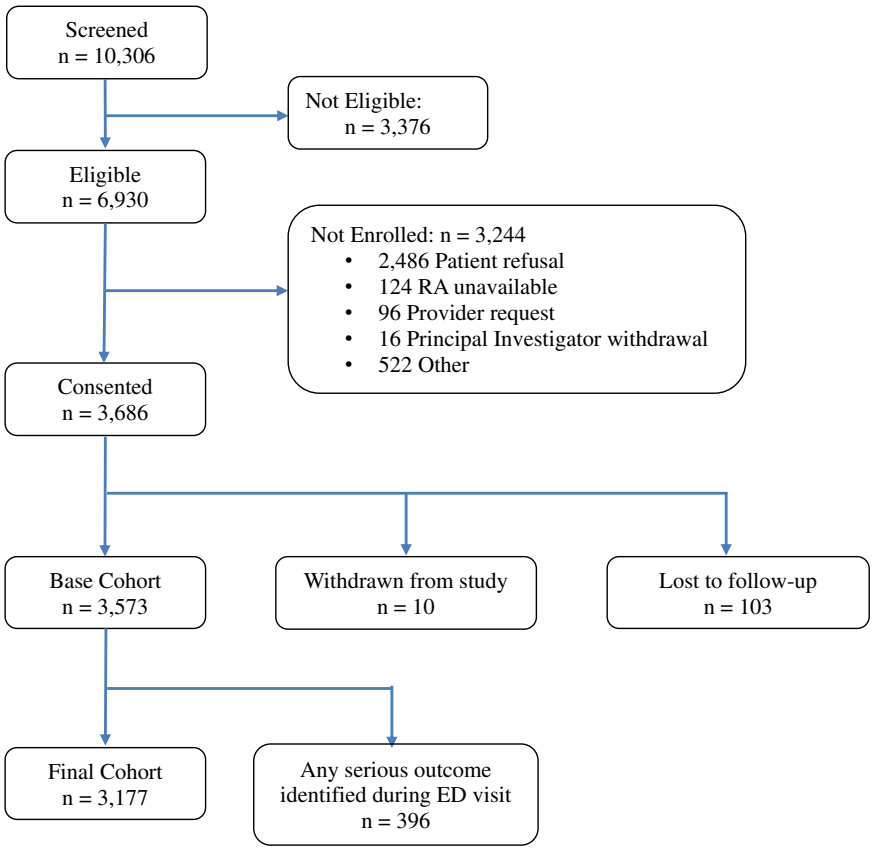

Figure 1. Patient flow diagram. *RA*, Research assistant.

By 30 days after the index ED visit, 180 patients (5.7%) had experienced the primary outcome; 65 of them experienced an event after discharge. The most common outcome was a serious cardiac arrhythmia (n=94/180, 52.2%), of which symptomatic supraventricular tachycardia was the most common (n=35/180, 19.4%). Overall mortality at 30 days was 0.82% (26/3,177). Further data on 30-day serious outcomes are presented in Table 2. Missing data for predictor variables ranged from 0% to 7.6% for predictor variable (hs-cTnT 7.6%, NT-proBNP 4.9%, and dyspnea 2.2%). After multiple imputation, all 3,177 subjects were included in the analysis.

Main Results

Our model selection process, using Bayesian logistic regression, resulted in 5 variables' being significantly associated with the primary outcome: history of heart failure, history of cardiac arrhythmia, abnormal initial ECG result, elevated NT-proBNP level, and elevated hs-cTnT level. The odds ratios and corresponding CIs are presented in Table 3. These 5 variables make up the FAINT score (*f*ailure, *a*rrhythmia, *i*nitial ECG result abnormal, abnormal *n*atriuretic peptide level, and abnormal high-sensitivity *t*roponin level). The κ statistic was good for all 3 of the nonnumeric variables, heart failure 0.70 (95% CI 0.55 to 0.85), arrhythmia 0.77 (95% CI 0.66 to 0.87), and abnormal ECG result 0.65 (95% CI 0.55 to 0.74). An older adult with unexplained syncope or near syncope would be considered at low risk if none of the 5 FAINT variables were present during the ED evaluation (ie, a FAINT score of zero). The sensitivity, specificity, and positive and negative predictive values of a FAINT score of more than zero were 96.7%, 22.2%, 6.9%, and 99.1%, respectively (Table 4). The risk of death or serious cardiac outcome at 30 days for a patient with a FAINT score of zero was 0.9% (95% CI 0.3% to 1.9%) and 6.9% (95% CI 6% to 8%) if the score was greater than zero. The positive and negative likelihood ratios for a FAINT score of 1 or more were 1.24 (95% CI 1.156 to 1.336) and 0.15 (95% CI 0.068 to 0.329), respectively.

We modified the regression coefficients to obtain the point score associated with each variable, which resulted in point value of +2 for elevated NT-proBNP and +1 for all others. Total FAINT scores ranged from 0 to 6. Our model was well calibrated, demonstrating good agreement between observed and predicted risk at various score levels

Table 1. Characteristics of older adults presenting to the ED with syncope or near syncope.

Variable	Overall (N=3,177)	With Serious Outcome at 30 Days (n=180)	No Serious Outcome at 30 Days (n=2,997)	Missing Data, No. (%)
Age, mean (SD), y	72.74 (8.97)	73.52 (9.14)	72.69 (8.96)	0
Age category, No. (%)				0
60–<70	1,384 (43.6)	70 (38.9)	1,314 (43.8)	
70–<80	1,013 (31.9)	61 (33.9)	952 (31.8)	
80–<90	643 (20.2)	39 (21.7)	604 (20.2)	
≥90	137 (4.3)	10 (5.6)	127 (4.2)	
Sex, men	1,608 (50.6)	103 (57.2)	1,505 (50.2)	
Race				19 (0.6)
White	2,618 (82.9)	151 (83.9)	2,467 (82.8)	
Black	442 (14.0)	25 (13.9)	417 (14.0)	
Other	98 (3.1)	4 (2.2)	94 (3.2)	
Near syncope	1,212 (38.1)	67 (37.2)	1,145 (38.2)	
Syncope	1,965 (61.9)	113 (62.8)	1,852 (61.8)	
Medical history				
Congestive heart failure	376 (11.8)	45 (25.0)	331 (11.1)	3 (0.1)
Coronary artery disease	847 (26.7)	68 (37.8)	779 (26.0)	3 (0.1)
Arrhythmia	630 (19.8)	63 (35.0)	567 (18.9)	3 (0.1)
Dyspnea	617 (19.9)	44 (25.3)	573 (19.5)	71 (2.2)
Chest discomfort	268 (8.4)	20 (11.1)	248 (8.3)	0
Hypotension	313 (9.9)	26 (14.5)	287 (9.6)	20 (0.6)
Abnormal ECG	1,665 (53.3)	128 (72.7)	1,537 (52.1)	51 (1.6)
Physician risk assessment, mean (IQR)	5.0 (2.0–10.0)	8.0 (5.0–15.0)	5.0 (2.0–10.0)	90 (2.8)
Cardiac biomarkers				
NT-proBNP >125 pg/mL	1,928 (63.8)	152 (87.4)	1,776 (62.4)	156 (4.9)
NT-proBNP, median (IQR)	213.0 (82.0–661.0)	874.0 (227.5–1,846.5)	200.0 (80.0–597.0)	
hs troponin T >19 ng/L	863 (29.4)	90 (53.3)	773 (27.9)	240 (7.6)
hs troponin T, median (IQR)	11.0 (6.0–22.0)	21.0 (11.0–41.0)	11.0 (6.0–21.0)	

IQR, Interquartile range; *hs*, high-sensitivity.

(Figure 2*A* and *B*). Adequacy of calibration was confirmed by a nonsignificant Hosmer-Lemeshow goodness-of-fit statistic (χ^2=6.21; 3 *df*; *P*=.10).

The test characteristics for each level of the FAINT score (0 to 6) are presented in Table 4. Results of our cross validation are presented in Table E3 (available online at http://www.annemergmed.com) and discussed in Appendix E1, section 5 (available online at http://www.annemergmed.com). The FAINT score had a significantly better area under the curve statistic (0.704; 95% CI 0.669 to 0.739) compared with that of unstructured physician risk assessment (0.630; 95% CI 0.589 to 0.670) (DeLong's test for 2 correlated ROC curves, Z=3.13, *P*=.002). The ROC curves are presented in Figure 3. Accounting for the optimism of internal validation, the cross-validated *c* statistic of the FAINT score was 0.653 (95% CI 0.534 to 0.765). The total number of correctly reclassified patients was 466: 11 who were FAINT score positive, with a serious outcome, but discharged, and 455 who were FAINT score negative, without a serious outcome, but were hospitalized by the treating physician. The total number of incorrectly reclassified patients was 456, 450 who were FAINT score positive, without a serious outcome and were discharged, and 6 who were FAINT score negative, with a serious outcome, and were admitted by the treating physician. The percentage of correctly and incorrectly reclassified patients was 466 of 3,174 (14.68%) and 456 of 3,174 (14.37%), respectively, for a net reclassification improvement of 0.31% favoring the FAINT score (not significant; *P*=.33).

The FAINT score failed to predict the serious outcomes of 6 patients: complete heart block leading to insertion of a pacemaker, structural heart disease, percutaneous

Table 2. All-cause death and serious cardiac outcomes at 30 days.

Outcome Variable	Overall	Postdischarge	Inhospital
Any 30-day serious outcome	180	56	124*
30-day death	26	24	2
Serious cardiac arrhythmias			
Any cardiac arrhythmia	94	24	70
Ventricular fibrillation	3	1	2
Ventricular tachycardia (>30 s)	10	2	8
Symptomatic ventricular tachycardia (<30 s)	3	1	2
Sick sinus disease with alternating sinus bradycardia and tachycardia	14	3	11
Sinus pause >3 s	4	0	4
Mobitz II atrioventricular heart block	5	3	2
Complete heart block	8	2	6
Symptomatic supraventricular tachycardia	35	9	26
Symptomatic bradycardia	11	3	8
Pacemaker or AICD malfunction with cardiac pauses	1	0	1
Cardiac intervention			
Any	74	22	52
Pacemaker	36	10	26
AICD	9	2	7
CABG	8	4	4
PTCA	11	4	7
Other	10	2	8
Other serious outcomes			
Myocardial infarction	24	9	15
New diagnosis of structural heart disease	26	3	23

AICD, Automated implantable cardioverter-defibrillator; *CABG*, coronary artery bypass graft; *PTCA*, percutaneous transluminal coronary angioplasty.
*Nine patients had events both inhospital and postdischarge; these were counted in the "inhospital" column.

transluminal coronary angioplasty, symptomatic bradycardia, sick sinus syndrome leading to the insertion of a pacemaker, and death. Conversely, the FAINT score would have identified 11 patients who were not admitted to the hospital as being at high risk; these outcomes were 2 cases of symptomatic bradycardia, 2 cases of myocardial infarction, a case of ventricular tachycardia and coronary artery bypass graft, a pacemaker insertion, a coronary artery bypass graft, and 4 deaths (Table E4, available online at http://www.annemergmed.com).

Table 3. Results of Bayesian logistic regression (FAINT score).

Predictor	Point Score	Odds Ratio	95% CI
F: history of heart failure	1	1.59	(1.09–2.27)
A: history of arrhythmia	1	1.55	(1.10–2.14)
I: initial ECG result abnormal	1	1.58	(1.11–2.26)
N: elevated NT-proBNP	2	2.54	(1.58–4.13)
T: elevated hs-troponin T	1	1.85	(1.32–2.59)

LIMITATIONS

Because we did not enroll patients younger than 60 years, the FAINT score was not designed to be applied to adults younger than this cutoff age, which may limit its clinical utility. In light of the high patient refusal rate and low enrollment rate (53.2%), it is possible that sampling bias occurred. Our score requires the use of 2 assays that may not be readily available in all EDs (hs-cTnT and NT-proBNP), which may limit its use in such clinical settings. Our score would likely exhibit decreased sensitivity if used with a contemporary troponin assay. Our data apply only to the specific brand of these cardiac biomarkers (Roche Elecsys) and our result may not hold true with other commercially available high-sensitivity troponin assays (eg, those manufactured by Abbott, Beckman, Siemens). These various assays have different limits of detection and imprecisions at the 99th percentile.[40] However, we anticipate that high-sensitivity troponin assay will become increasingly common in the United States.[41,42] Substituting a conventional B-type natriuretic peptide assay for the NT-proBNP assay could be considered reasonable in EDs where only the former is available.[43,44] Our composite primary outcome included diagnoses with a wide range of severity, from atrial fibrillation to death. When applying this score, clinicians should remember that certain diagnoses may be less serious and time sensitive than others. Although we did perform an internal cross validation, an external validation was not within the scope of this project. We intend to pursue such a study to validate this score in a distinct population of ED syncope patients. Although the specificity and positive likelihood ratio of a FAINT score above zero are not markedly high, the purpose of this score is primarily to rule out serious cardiac outcomes and was derived with this objective in mind. Clinicians should focus on the high sensitivity and low negative likelihood ratio of this score.

Table 4. Test characteristics of the FAINT score to predict serious clinical outcomes at 30 days.*

Score	No. of Patients	No. of Bad Outcomes	Estimated Risk, %	Sensitivity	Specificity	PPV	NPV
0	672	6	0.9	NA	NA	NA	NA
1	447	14	3.1	0.97 (0.93–0.99)	0.22 (0.21–0.24)	0.07 (0.06–0.08)	0.99 (0.98–1.00)
2	499	18	3.6	0.89 (0.83–0.93)	0.37 (0.35–0.38)	0.08 (0.07–0.09)	0.98 (0.97–0.99)
3	684	45	6.6	0.79 (0.72–0.85)	0.53 (0.51–0.55)	0.09 (0.08–0.12)	0.98 (0.97–0.98)
4	561	59	10.5	0.54 (0.46–0.61)	0.74 (0.72–0.76)	0.11 (0.09–0.13)	0.96 (0.96–0.97)
5	235	19	8.1	0.21 (0.15–0.28)	0.91 (0.90–0.92)	0.12 (0.09–0.16)	0.95 (0.94–0.96)
6	79	19	24.1	0.12 (0.07–0.16)	0.98 (0.97–0.99)	0.24 (0.15–0.35)	0.95 (0.94–0.96)
Total	3,177	180					

PPV, Positive predictive value; *NPV*, negative predictive value; *NA*, not applicable.
*Sensitivity, specificity, PPV, and NPV were calculated by defining "at risk" as having that score or greater (eg, score ≥1 gives sensitivity=0.967).

DISCUSSION

Using prospectively collected data from a large, multicenter sample of older adults presenting to the ED with syncope or near syncope, we were able to derive an objective, 5-variable, syncope risk score to predict the occurrence of serious cardiac outcomes at 30 days. This tool, if externally validated, could be used as a "one-way rule"[45] to guide clinical management for these patients by empowering clinicians to discharge low-risk patients (FAINT score=0) and consider further testing or observation for nonlow-risk patients (FAINT score ≥1).

The FAINT score differs from previous syncope risk-stratification tools in the following 5 important ways. First, it was developed with the subset of syncope patients for whom resource use is greatest, those aged 60 years or older, whereas other tools have been developed with samples that included adolescents and adults of all ages.[6,8-11] Adolescents and young adults (<30 years) with syncope are at much lower risk for serious cardiac outcomes than middle-aged or older adults, and often have different causes of their syncope.[15,25] Inclusion of younger adults in such a study sample would reduce the rate of serious outcomes; application of a syncope risk score to an inherently very-low-risk cohort could lead to overtesting and false-positive screening results. Second, our risk score incorporated novel cardiac biomarkers (ie, NT-proBNP and hs-cTnT, both processed at a single, central laboratory, eliminating assay-to-assay variability). Although the hs-cTnT assay was not approved by the Food and Drug Administration at the study onset, we anticipated it would receive approval and eventually be integrated into clinical care (the Food and Drug Administration granted approval in January 2017). Third, the components of our risk score are relatively simple and objective (ie, does the patient have a history of

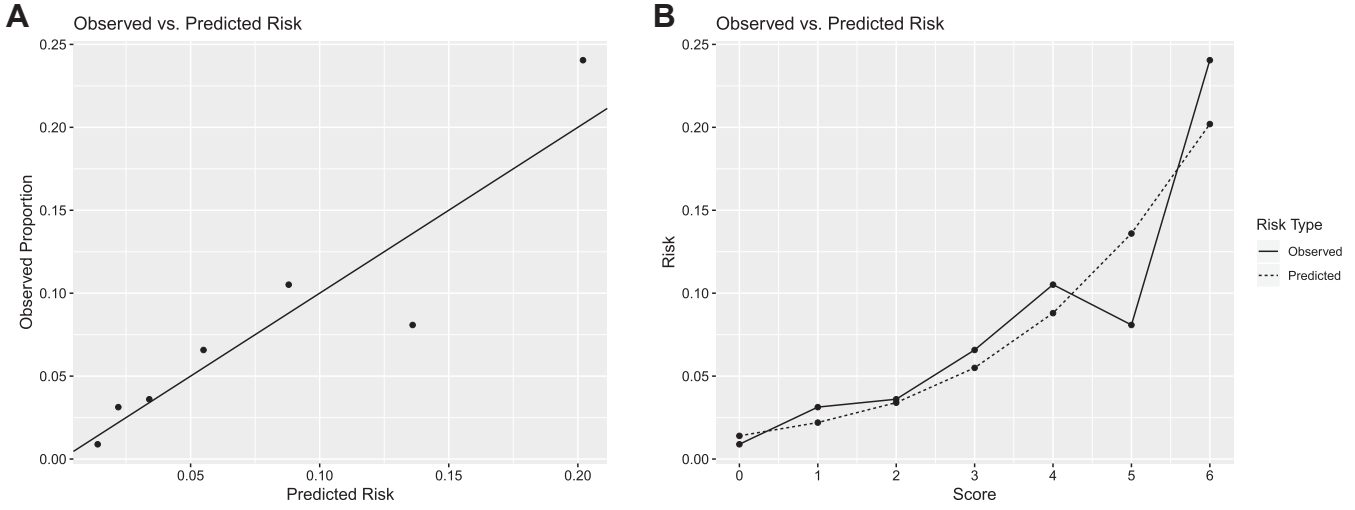

Figure 2. Observed versus predicted risk plot.

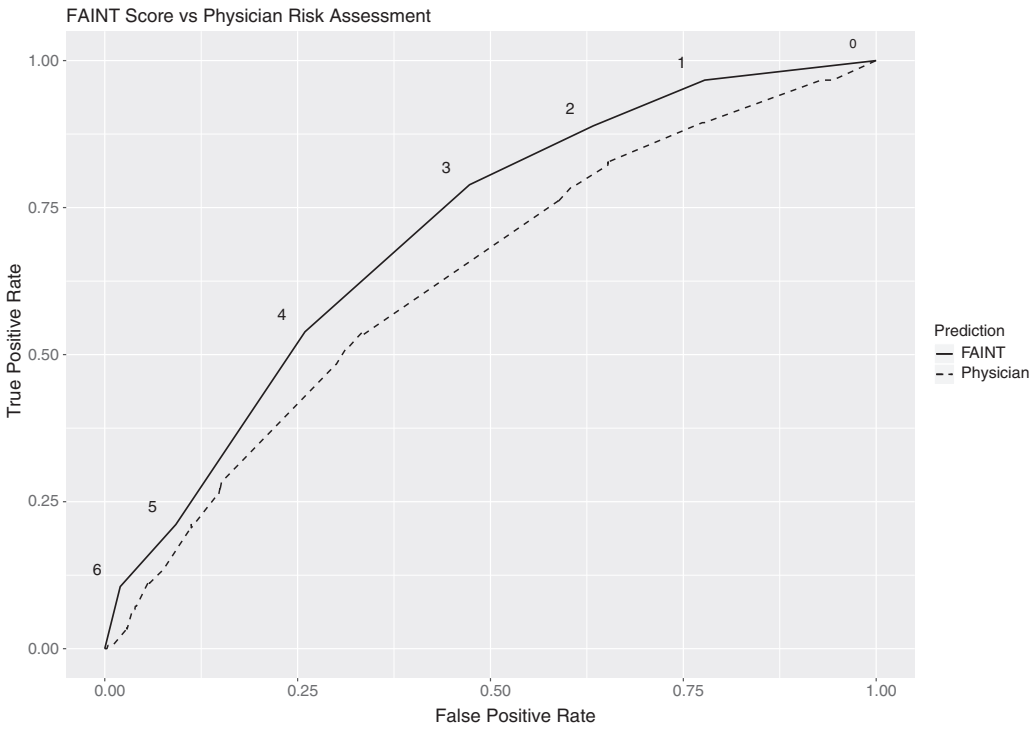

Figure 3. Comparison of the ROC curves for the FAINT score versus physician risk assessment.

heart failure or arrhythmia, and are the NT-proBNP or hs-cTnT levels elevated?). These straightforward questions are less operator dependent and more likely to show high interrater agreement than questions that require clinical gestalt.[9] Fourth, our sample was one of the largest prospectively collected cohorts of ED syncope patients published, much larger than that used to derive previous risk-stratification tools.[5,6,8,10] Fifth, our study set out to predict death and serious cardiac outcomes, and not all serious clinical outcomes, as other authors have done.[6,8,9] We excluded noncardiac outcomes a priori (eg, ischemic stroke, subarachnoid hemorrhage, gastrointestinal hemorrhage, aortic dissection, pulmonary embolism). Although the best definition of the primary outcome for a study of this nature is debatable, we believe that limiting the primary outcome to death and serious cardiac outcomes only is more suitable for the clinical scenario in question (ie, unexplained syncope/near syncope). There are already several risk-stratification tools available to predict the likelihood of pulmonary embolism,[46,47] subarachnoid hemorrhage,[48,49] aortic dissection,[50,51] upper gastrointestinal hemorrhage,[52,53] and ischemic stroke.[54,55] The FAINT score should be used only after these other diagnoses have been excluded during the initial ED evaluation, using clinical gestalt, relevant risk-stratification tools, or both, and potential cardiac causes remain. Moreover, the factors that predict cardiac arrhythmia, subarachnoid hemorrhage, occult gastrointestinal bleeding, and pulmonary embolism are likely to be very different, as has been argued previously.[16] Thus, a syncope risk score should predict serious cardiac outcomes and death, analogous to the History, ECG, Age, Risk Factors, and Troponin score for low-risk chest pain.[56,57]

As with any clinical decision rule that maximizes sensitivity, our corresponding specificity was less than desired. This creates the potential for application of the rule to paradoxically increase resource use if used in a 2-way fashion (ie, admitting all patients with a positive FAINT score).[32] Thus, we caution clinicians to not use this rule before external validation, and, if validated, to use it as a tool to justify the discharge of low-risk patients.

Our results add to the increasing body of literature supporting the utility of B-type natriuretic peptide as a predictor of serious cardiac outcomes after an episode of syncope.[6,58-63] An elevated NT-proBNP level had an odds ratio of 2.5, greater than that of any other clinical predictor we collected (Table 3). This suggests that a B-type natriuretic peptide assay should be strongly considered in the ED evaluation of older adults presenting with syncope or near syncope. Given the score's reliance on cardiac biomarkers, implementation could lead to an increase in laboratory testing, with a concomitant increase in costs, but could potentially lead to a decrease in admissions for unexplained syncope. A formal cost analysis would be required to determine the net effect.

Although the area under the curve for the FAINT score was modest (0.704), it did outperform unstructured physician judgment (0.63), a statistically significant difference. The FAINT score did not result in a statistically significant improvement in correct reclassifications compared with the physician's disposition decision. The score did fail to predict a small number of serious clinical outcomes, and the lower bound of the 95% CI was less than optimal. However, no risk-stratification tool should be used in isolation, but rather should be used to inform clinical decisionmaking while taking overall clinical gestalt and other nonclinical factors into account (eg, social support of the patient, ability to obtain expedited follow-up care, values and preferences of the patient, feasibility of returning to the ED promptly). The FAINT score provides an objective, structured approach to risk stratification that can be used by clinicians at all levels of skill and experience, which could reduce unwanted variation in the clinical management of syncope.[27,64,65] The risk-stratification tool is meant to inform, not replace, clinical judgment while potentially decreasing cognitive load for clinicians.

In summary, we used a large, multicenter, prospective data set of older adults with syncope or near syncope to derive a clinical risk score to identify patients at very low risk for death or serious cardiac outcomes at 30 days. Our score requires external validation before clinical implementation. If validated in a separate cohort of patients, the FAINT score has the potential to help guide clinical management by safely reducing low-yield hospitalizations.

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REFERENCES

1. Probst MA, Kanzaria HK, Gbedemah M, et al. National trends in resource utilization associated with ED visits for syncope. *Am J Emerg Med*. 2015;33:998-1001.
2. Anderson TS, Thombley R, Dudley RA, et al. Trends in hospitalization, readmission, and diagnostic testing of patients presenting to the emergency department with syncope. *Ann Emerg Med*. 2018;72:523-532.
3. Sun BC, Emond JA, Camargo CA Jr. Direct medical costs of syncope-related hospitalizations in the United States. *Am J Cardiol*. 2005;95:668-671.
4. Kapoor WN. Evaluation and management of the patient with syncope. *JAMA*. 1992;268:2553-2560.
5. Costantino G, Perego F, Dipaola F, et al. Short- and long-term prognosis of syncope, risk factors, and role of hospital admission: results from the STePS (Short-Term Prognosis of Syncope) study. *J Am Coll Cardiol*. 2008;51:276-283.
6. Reed MJ, Newby DE, Coull AJ, et al. The ROSE (Risk Stratification of Syncope in the Emergency Department) study. *J Am Coll Cardiol*. 2010;55:713-721.
7. 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;56:362-373.e361.
8. Quinn JV, Stiell IG, McDermott DA, et al. Derivation of the San Francisco Syncope Rule to predict patients with short-term serious outcomes. *Ann Emerg Med*. 2004;43:224-232.
9. 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:E289-E298.
10. Colivicchi F, Ammirati F, Melina D, et al. Development and prospective validation of a risk stratification system for patients with syncope in the emergency department: the OESIL risk score. *Eur Heart J*. 2003;24:811-819.
11. Grossman SA, Fischer C, Lipsitz LA, et al. Predicting adverse outcomes in syncope. *J Emerg Med*. 2007;33:233-239.
12. Martin TP, Hanusa BH, Kapoor WN. Risk stratification of patients with syncope. *Ann Emerg Med*. 1997;29:459-466.
13. Sun BC, Derose SF, Liang LJ, et al. Predictors of 30-day serious events in older patients with syncope. *Ann Emerg Med*. 2009;54:769-778; e761-765.
14. Del Rosso A, Ungar A, Maggi R, et al. Clinical predictors of cardiac syncope at initial evaluation in patients referred urgently to a general hospital: the EGSYS score. *Heart*. 2008;94:1620-1626.
15. Shen WK, Sheldon RS, Benditt DG, et al. 2017 ACC/AHA/HRS guideline for the evaluation and management of patients with syncope: executive summary: a report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines and the Heart Rhythm Society. *J Am Coll Cardiol*. 2017;70:620-663.
16. Sun BC, Costantino G, Barbic F, et al. Priorities for emergency department syncope research. *Ann Emerg Med*. 2014;64:649-655.e642.
17. Birnbaum A, Esses D, Bijur P, et al. Failure to validate the San Francisco Syncope Rule in an independent emergency department population. *Ann Emerg Med*. 2008;52:151-159.
18. Probst MA, Sun BC. How can we improve management of syncope in the emergency department? *Cardiol J*. 2014;21:643-650.
19. Sun BC, Mangione CM, Merchant G, et al. External validation of the San Francisco Syncope Rule. *Ann Emerg Med*. 2007;49:420-427, 427.e1-4.
20. Tan C, Sim TB, Thng SY. Validation of the San Francisco Syncope Rule in two hospital emergency departments in an Asian population. *Acad Emerg Med*. 2013;20:487-497.
21. Thiruganasambandamoorthy V, Hess EP, Alreesi A, et al. External validation of the San Francisco Syncope Rule in the Canadian setting. *Ann Emerg Med*. 2010;55:464-472.
22. Reed MJ, Henderson SS, Newby DE, et al. One-year prognosis after syncope and the failure of the ROSE decision instrument to predict one-year adverse events. *Ann Emerg Med*. 2011;58:250-256.
23. 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;70:338-344.e333.
24. Sun BC, Emond JA, Camargo CA Jr. Characteristics and admission patterns of patients presenting with syncope to US emergency departments, 1992-2000. *Acad Emerg Med*. 2004;11:1029-1034.
25. Huff JS, Decker WW, Quinn JV, et al. Clinical policy: critical issues in the evaluation and management of adult patients presenting to the emergency department with syncope. *Ann Emerg Med*. 2007;49:431-444.
26. Baugh CW, Liang LJ, Probst MA, et al. National cost savings from observation unit management of syncope. *Acad Emerg Med*. 2015;22:934-941.
27. Baugh CW, Sun BC. Syncope Risk Stratification Study Group. Variation in diagnostic testing for older patients with syncope in the emergency department. *Am J Emerg Med*. 2019;37:810-816.
28. Morag RM, Murdock LF, Khan ZA, et al. Do patients with a negative emergency department evaluation for syncope require hospital admission? *J Emerg Med*. 2004;27:339-343.
29. Shiyovich A, Munchak I, Zelingher J, et al. Admission for syncope: evaluation, cost and prognosis according to etiology. *Isr Med Assoc J*. 2008;10:104-108.
30. Canzoniero JV, Afshar E, Hedian H, et al. Unnecessary hospitalization and related harm for patients with low-risk syncope. *JAMA Intern Med*. 2015;175:1065-1067.
31. Sun BC, Thiruganasambandamoorthy V, Cruz JD; Consortium to Standardize Department Syncope Risk Stratification Reporting. Standardized reporting guidelines for emergency department syncope risk-stratification research. *Acad Emerg Med*. 2012;19:694-702.
32. Green SM, Schriger DL, Yealy DM. Methodologic standards for interpreting clinical decision rules in emergency medicine: 2014 update. *Ann Emerg Med*. 2014;64:286-291.
33. Nicks BA, Shah MN, Adler DH, et al. Minimizing attrition for multisite emergency care research. *Acad Emerg Med*. 2017;24:458-466.
34. Gibson TA, Weiss RE, Sun BC. Predictors of short-term outcomes after syncope: a systematic review and meta-analysis. *West J Emerg Med*. 2018;19:517-523.
35. Weiss RE. Bayesian methods for data analysis. *Am J Ophthalmol*. 2010;149:187-188.e181.
36. Gurrin LC, Kurinczuk JJ, Burton PR. Bayesian statistics in medical research: an intuitive alternative to conventional data analysis. *J Eval Clin Pract*. 2000;6:193-204.

37. Sullivan LM, Massaro JM, D'Agostino RB Sr. Presentation of multivariate data for clinical use: the Framingham Study risk score functions. *Stat Med*. 2004;23:1631-1660.
38. Bandiera G, Stiell IG, Wells GA, et al. The Canadian C-Spine Rule performs better than unstructured physician judgment. *Ann Emerg Med*. 2003;42:395-402.
39. Quinn JV, Stiell IG, McDermott DA, et al. The San Francisco Syncope Rule vs physician judgment and decision making. *Am J Emerg Med*. 2005;23:782-786.
40. Apple FS, Collinson PO. Analytical characteristics of high-sensitivity cardiac troponin assays. *Clin Chem*. 2012;58:54-61.
41. Nowak RM, Gandolfo CM, Jacobsen G, et al. Ultrarapid rule-out for acute myocardial infarction using the generation 5 cardiac troponin T assay: results from the REACTION-US study. *Ann Emerg Med*. 2018;72:654-664.
42. Hollander JE. High-sensitivity troponin: time to implement. *Ann Emerg Med*. 2018;72:665-667.
43. Weber M, Hamm C. Role of B-type natriuretic peptide (BNP) and NT-proBNP in clinical routine. *Heart*. 2006;92:843-849.
44. Mueller T, Gegenhuber A, Poelz W, et al. Diagnostic accuracy of B type natriuretic peptide and amino terminal proBNP in the emergency diagnosis of heart failure. *Heart*. 2005;91:606-612.
45. Rodriguez RM, Hendey GW. The case for 1-way clinical decision rules in emergency medicine. *Ann Emerg Med*. 2015;66:689.
46. Kline JA, Mitchell AM, Kabrhel C, et al. Clinical criteria to prevent unnecessary diagnostic testing in emergency department patients with suspected pulmonary embolism. *J Thromb Haemost*. 2004;2:1247-1255.
47. Wolf SJ, McCubbin TR, Feldhaus KM, et al. Prospective validation of Wells criteria in the evaluation of patients with suspected pulmonary embolism. *Ann Emerg Med*. 2004;44:503-510.
48. Perry JJ, Sivilotti MLA, Sutherland J, et al. Validation of the Ottawa Subarachnoid Hemorrhage Rule in patients with acute headache. *CMAJ*. 2017;189:E1379-E1385.
49. Perry JJ, Stiell IG, Sivilotti ML, et al. Clinical decision rules to rule out subarachnoid hemorrhage for acute headache. *JAMA*. 2013;310:1248-1255.
50. Lovy AJ, Bellin E, Levsky JM, et al. Preliminary development of a clinical decision rule for acute aortic syndromes. *Am J Emerg Med*. 2013;31:1546-1550.
51. Nazerian P, Mueller C, Soeiro AM, et al. Diagnostic accuracy of the Aortic Dissection Detection Risk Score plus D-dimer for acute aortic syndromes: the ADvISED prospective multicenter study. *Circulation*. 2018;137:250-258.
52. Blatchford O, Murray WR, Blatchford M. A risk score to predict need for treatment for upper-gastrointestinal haemorrhage. *Lancet*. 2000;356:1318-1321.
53. Chen IC, Hung MS, Chiu TF, et al. Risk scoring systems to predict need for clinical intervention for patients with nonvariceal upper gastrointestinal tract bleeding. *Am J Emerg Med*. 2007;25:774-779.
54. Yang J, Fu JH, Chen XY, et al. Validation of the ABCD2 score to identify the patients with high risk of late stroke after a transient ischemic attack or minor ischemic stroke. *Stroke*. 2010;41:1298-1300.
55. Purroy F, Jimenez Caballero PE, Gorospe A, et al. Prediction of early stroke recurrence in transient ischemic attack patients from the PROMAPA study: a comparison of prognostic risk scores. *Cerebrovasc Dis*. 2012;33:182-189.
56. Backus BE, Six AJ, Kelder JC, et al. Chest pain in the emergency room: a multicenter validation of the HEART Score. *Crit Pathw Cardiol*. 2010;9:164-169.
57. Laureano-Phillips J, Robinson RD, Aryal S, et al. HEART score risk stratification of low-risk chest pain patients in the emergency department: a systematic review and meta-analysis. *Ann Emerg Med*. 2018;72:523-532.
58. Isbitan A, Hawatmeh A, Elnahar Y, et al. Utility of brain natriuretic peptide assay as a predictor of short term outcomes in patients presenting with syncope to the emergency department. *Cardiovasc Diagn Ther*. 2016;6:234-240.
59. Tanimoto K, Yukiiri K, Mizushige K, et al. Usefulness of brain natriuretic peptide as a marker for separating cardiac and noncardiac causes of syncope. *Am J Cardiol*. 2004;93:228-230.
60. Pfister R, Diedrichs H, Larbig R, et al. NT-pro-BNP for differential diagnosis in patients with syncope. *Int J Cardiol*. 2009;133:51-54.
61. Reed MJ, Newby DE, Coull AJ, et al. Role of brain natriuretic peptide (BNP) in risk stratification of adult syncope. *Emerg Med J*. 2007;24:769-773.
62. Costantino G, Solbiati M, Casazza G, et al. Usefulness of N-terminal pro-B-type natriuretic peptide increase as a marker for cardiac arrhythmia in patients with syncope. *Am J Cardiol*. 2014;113:98-102.
63. Thiruganasambandamoorthy V, Ramaekers R, Rahman MO, et al. Prognostic value of cardiac biomarkers in the risk stratification of syncope: a systematic review. *Intern Emerg Med*. 2015;10:1003-1014.
64. Thiruganasambandamoorthy V, Taljaard M, Stiell IG, et al. Emergency department management of syncope: need for standardization and improved risk stratification. *Intern Emerg Med*. 2015;10:619-627.
65. 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;37:1493-1498.