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Predictors of 30-Day Serious Events in Older Patients With Syncope

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Study objective: We identify predictors of 30-day serious events after syncope in older adults.

Methods: We reviewed the medical records of older adults (age ≥60 years) who presented with syncope or near syncope to one of 3 emergency departments (EDs) between 2002 and 2005. Our primary outcome was occurrence of a predefined serious event within 30 days after ED evaluation. We used multivariable logistic regression to identify predictors of 30-day serious events.

Results: Of 3,727 potentially eligible patients, 2,871 (77%) met all eligibility criteria. We excluded an additional 287 patients who received a diagnosis of a serious clinical condition while in the ED. In the final study cohort (n=2,584), we identified 173 (7%) patients who experienced a 30-day serious event. High-risk predictors included age greater than 90 years, male sex, history of an arrhythmia, triage systolic blood pressure greater than 160 mm Hg, abnormal ECG result, and abnormal troponin I level. A low-risk predictor was a complaint of near syncope rather than syncope. A risk score, generated by summing high-risk predictors and subtracting the low-risk predictor, can stratify patients into low- (event rate 2.5%; 95% confidence interval [CI] 1.4% to 3.6%), intermediate- (event rate 6.3%; 95% CI 5.1% to 7.5%), and high-risk (event rate 20%; 95% CI 15% to 25%) groups.

Conclusion: We identified predictors of 30-day serious events after syncope in adults aged 60 years and greater. A simple score was able to stratify these patients into distinct risk groups and, if externally validated, might have the potential to aid ED decisionmaking. [Ann Emerg Med. 2009;54:769-778.]

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INTRODUCTION

Background

Syncope is a common complaint among individuals treated in the emergency department (ED) and is responsible for 1% to 3% of all ED visits and hospital admissions.[1-3] Because of comorbid illnesses, concurrent medications, cognitive impairment, and age-related physiologic changes,[4,5] older adults experience a higher incidence of syncope, related health-services use, and associated serious events compared with younger adults.[6-10] As a result, patients aged 60 and older are often hospitalized after syncope,[1] and consensus guidelines suggest a decreased threshold for admission in patients of advanced age.[11,12]

Existing patterns of care are nevertheless characterized by high variance[13,14] and low diagnostic and therapeutic yield. Between 39% and 50% of admitted patients are discharged without an explanation for syncope,[15] and in one study 60% of older patients received no specific therapies during their inpatient stay.[16] Existing admission practices consume significant health resources, and the total annual costs of syncope-related admissions exceed $2 billion.[2]

Importance

Improved risk prediction has the potential to safely reduce practice variation and hospitalizations. Several investigators have

Editor's Capsule Summary

What is already known on this topic

The disposition of syncope patients is controversial because hospitalization is seldom helpful but some patients will have bad outcomes if discharged.

What question this study addressed

This 3-emergency department, 2,584-patient retrospective study identified age-specific risk factors for 30-day adverse events in older patients with syncope or near syncope.

What this study adds to our knowledge

Seven factors were noted to be associated with adverse events, and a risk score was created that stratified patients into low (2.5%), intermediate (6.3%), and high risk (20%) for adverse events.

How this might change clinical practice

The score needs to be validated. Even when it is validated, however, the ability to discharge patients will depend on clinician acceptance of a 2.5% risk of serious 30-day adverse events.

described predictors of serious clinical events after syncope,[7-9,17-20] but these studies enrolled relatively small numbers of patients ($n<800$), and the clinical utility of prediction instruments has been limited by wide confidence intervals (CIs) for false-negative classifications (95% CI 0% to 14%). Some prediction instruments focus on 1-year outcomes, which may not be relevant to ED decisionmaking.[7-9] Attempts to externally validate existing syncope instruments have yielded mixed results.[21-23] Finally, several reports assess age as a dichotomous risk factor (eg, age ≥60 years),[8,9,17] but to our knowledge there have been no published attempts to further risk-stratify older adults who present with syncope. The lack of age-specific risk stratification represents an important gap in the literature because syncope-related health resource use is concentrated in older adults.[2]

Goals of This Investigation

To address this knowledge gap, we reviewed the medical records of older adults (age ≥60 years) who presented with syncope or near syncope to one of 3 EDs. The goal of this report is to identify predictors of 30-day serious events after syncope in such patients. To maximize sample size, data quality, and outcomes detection, all data were collected from a regional, integrated managed care system.

MATERIALS AND METHODS

Study Design and Setting

We performed a structured medical record review of patients who presented to one of 3 EDs within a regional managed care system (Kaiser Permanente–Southern California), from January 2002 to December 2005, with a complaint of syncope or near syncope and for whom a serious underlying cause was not apparent during their ED stay. Annual ED visit volumes ranged from 39,000 to 153,000 at the 3 sites. All care was provided by an attending emergency physician, and none of the sites was a trauma or emergency medicine residency training center. The 3 sites were selected because data on ED visits, hospitalizations, and laboratory and ECG testing during the study period were routinely available through an electronic medical records system. The Kaiser Permanente–Southern California and UCLA institutional review boards approved this study.

Administrative discharge codes for ED visits were used to identify potentially eligible patients. Three research associates performed all chart reviews for eligibility screening, outcomes identification, and covariate abstraction. Two of the abstractors were nonphysician research project managers with at least 2 years of experience. One of the abstractors was a foreign medical school graduate. All research associates were trained on a practice set of 10 charts. Standardized abstraction forms were used for cohort screening, chart abstraction, and identification of serious outcomes (see Appendices E1 to E5, available online at http://www.annemergmed.com). Variables in the abstraction forms were explicitly defined in a study codebook.

To minimize missing data, research associates reviewed available ED, admitting, and consulting notes in a hierarchic fashion, with only the ED chart being used if it provided the information being sought; if such information was missing from the ED record, the research associate would attempt to find the information in admitting or consulting notes. Any ambiguous chart data were referred to the principal investigator, who made the final coding decision in such cases. The research associates were blinded to study objectives. Research associate performance was monitored monthly by the principal investigator.

In pilot work, we assessed the validity of screening and chart abstraction methods. To assess positive and negative predictive value of discharge code screening, a physician-investigator (B.C.S.) blinded to the ED discharge code reviewed 200 charts (100 consecutive charts with an ED discharge code consistent with syncope and 100 consecutive charts without an ED discharge code for syncope) to assess the presence or absence of syncope.

To assess interrater reliability of chart review for study eligibility, outcomes identification, and covariate abstraction, all research associates independently reviewed a validation set of 100 charts. Research associate reviews were compared with reviews performed by a physician-investigator (B.C.S.), and the physician chart review was considered the criterion standard. The interrater reliability between research associate and physician reviews for study eligibility and covariate abstraction were estimated with the κ statistic. We also estimated the sensitivity of research associates to identify serious outcomes.

Finally, we assessed interphysician reliability in identifying and classifying serious events. We identified a subset of 60 charts that were flagged as potentially documenting a serious event after research associate review. Two physicians (B.C.S., G.G.) independently reviewed these charts to identify the occurrence and type of serious event.

Selection of Participants

Adult patients aged 60 years or older with an ED complaint of syncope or near syncope were eligible for enrollment. We defined syncope as a sudden, transient loss of consciousness and near syncope as a sensation of imminent loss of consciousness, without actual syncope.

We excluded patients who did not clearly present with syncope or near syncope,[3,8,24] including those who presented with a generalized seizure, intoxication, and no spontaneous return to baseline mental status, and patients who experienced loss of consciousness as a result of head trauma. We required patients to have regained consciousness spontaneously and excluded those who required electrical or pharmacologic treatment at initial presentation. If a patient had more than 1 visit for syncope during the study period, then we considered only the first visit as eligible for study inclusion. We excluded all nonmembers of the health plan because we did not have postdischarge outcome information on these patients. Finally, we excluded patients in whom a serious underlying cause of the syncope was evident during the index ED visit.

We identified the study cohort by using a 3-stage screening process. First, we identified all Kaiser Permanente–Southern California patients aged 60 years or older who had an ED visit from January 1, 2002, to December 31, 2005, and an ED discharge diagnosis of *International Classification of Diseases, Ninth Revision* (*ICD-9*) code 780.2 (syncope and collapse: blackout; fainting; (near) (pre) syncope; vasovagal attack), using administrative data.

Second, 3 trained Kaiser Permanente–Southern California research associates reviewed *ICD-9*-flagged ED charts for inclusion and exclusion criteria (Appendix E1, available online at http://www.annemergmed.com). ED visits were eligible only if there was explicit documentation of syncope or near syncope. Other conditions, including weakness, dizziness, seizures, vertigo, and confusion, were ineligible for inclusion. All indeterminate cases of study eligibility were reviewed by a physician-investigator (B.C.S.).

Finally, research associates identified all visits in which a serious condition was diagnosed in the ED. These charts were overread by an emergency physician (see below) and excluded from further analysis.

Outcomes Measures

Our primary outcome was any predefined serious clinical event that occurred during the 30-day period after the initial ED evaluation (Appendix E2, available online at http://www.annemergmed.com). We classified outcomes according to the recommendations of a working group of emergency physicians, internists, geriatricians, and cardiologists who identified syncope-related conditions for which hospital admission may be beneficial.[25] Serious events included death, arrhythmias, myocardial infarction, a new diagnosis of structural heart disease thought to be related to syncope, pulmonary embolism, aortic dissection, stroke/transient ischemic attack, subarachnoid or nontraumatic cerebral hemorrhage, and significant hemorrhage or anemia requiring blood transfusion. Admitted patients who required any of several predefined cardiac interventions during their stay were also considered to have a serious outcome. Cardiac interventions included pacemaker/defibrillator insertion, coronary angioplasty, and open heart surgery for ischemic or valvular heart disease.

We used professional society guidelines,[26] existing arrhythmia research,[3,8,17] and input from local electrophysiologists to define clinically significant arrhythmias. These include ventricular tachycardia, sinus pause greater than 3 seconds, third-degree atrioventricular block, Mobitz II atrioventricular block, symptomatic supraventricular tachycardia (pulse rate greater than 100 beats/min), or symptomatic bradycardia (pulse rate less than 60 beats/min). We subclassified ventricular tachycardia into ventricular tachycardia terminated by an implanted defibrillator, sustained ventricular tachycardia (duration greater than 30 seconds), and nonsustained ventricular tachycardia (duration greater than 3 beats but less than 30 seconds). "Symptomatic" refers to the simultaneous occurrence of dizziness, lightheadedness, hypotension (systolic blood pressure $<$90 mm Hg), or syncope with an arrhythmia on ECG monitoring. We also include electrophysiologic findings that represent risk factors for a dangerous arrhythmia, including inducible, sustained ventricular tachycardia; H-V intervals greater than 100 ms; symptomatic supraventricular tachycardia; infra-Hisian block; and prolonged corrected sinus node recovery time ($>$550 ms).

Data Collection and Processing

We identified all deaths by linking patient records to California vital statistics files and the Social Security Death Index (Appendices E2 and E3, available online at http://www.annemergmed.com).[27] Research associates reviewed all available medical records of study subjects to identify nonfatal serious events. Member patients receive most of their care within the regional managed care network. Member patients who are treated in a non-network ED and require hospitalization are typically transferred to a network hospital. All health resources use within the regional managed care network are captured by the electronic medical system. If an electronic transcript within the managed care network describing a health encounter was unavailable, then research associates obtained and reviewed the paper chart. All events flagged by a research associate were reviewed by a physician-investigator, who made final determination of occurrence, timing, and classification of a serious event.

We reviewed previous studies to identify potential candidate predictors for arrhythmias, sudden cardiac death, and other

serious events (Appendices E4 and E5, available online at http://www.annemergmed.com).[8,16,17,28-32] Additional variables were considered according to the input of a local panel of emergency physicians, internists, a geriatrician, and a cardiologist. In pilot work, we identified variables with either high rates of missing data (eg, documented orthostatic vital signs) or low interrater reliability (eg, complaint of new neurologic symptoms) and excluded them from our final abstraction form.

Research associates used structured data forms to collect demographic, comorbidity, symptom, examination, and test information from ED, admitting, and consultant notes. All notes were dictated by an attending physician. For comorbidity variables, we assumed that there was no comorbidity in the absence of supportive documentation. For symptom, physical examination, and test variables, we recorded whether the data were explicitly present, absent, or missing. If a test was not ordered by the treating physician, then the test variable was coded as missing. Research associates noted whether there was evidence of associated traumatic injury, and presence of trauma was confirmed by physician review. We defined traumatic injury as the presence of traumatic intracranial injury, long bone fracture, or thoracoabdominal visceral injury.

For test variables, we abstracted ECG results from cardiologist overread and classified them as normal, nonspecific changes, or abnormal. The study team did not attempt to reinterpret ECGs. We did not compare these ECGs to previous ECGs. We considered the following changes to represent abnormal ECG findings: nonsinus rhythm, sinus rhythm with pulse rate less than 40 beats/min, Q/ST/T changes consistent with acute or chronic ischemic heart disease, abnormal conduction intervals (QRS>0.1 ms, QTc>450 ms), left or right ventricular hypertrophy, left axis deviation, and bundle branch block. We collected hematocrit and troponin I values from laboratory data systems and considered a hematocrit value less than 30% as abnormal. We classified troponin I values greater than or equal to 0.04 ng/mL as abnormal. Although serum tests were performed at each study site, rather than at a central facility, all EDs used similar laboratory protocols and had the same reference ranges for hematocrit and troponin I. Finally, the presence of pyuria (>5 WBCs per high-powered field) on urinalysis testing was noted by research associates and confirmed by a physician-reviewer.

At the completion of all chart review, we linked the study database to administrative data to determine whether patients were admitted after their ED evaluation. Because we discovered that the administrative variable for admission status was frequently inaccurate, we reabstracted a sample of charts to estimate the overall admission rate. A study physician (B.C.S.) reviewed charts of all patients who experienced the primary outcome and a random sample of 100 charts of patients who did not experience the primary outcome. We then used these data to calculate a weighted estimate of the overall admission rate.

Data Analysis

We generated frequencies for demographic, comorbidity, symptom, examination, and test characteristics, overall and stratified by occurrence of a 30-day serious event. We use χ^2 tests to analyze binary and categorical variables.

In exploratory bivariate analyses, we used logistic regression to assess the shape of the relationship between continuous variables and the outcome. We identified nonlinear, bivariate relationships between the outcome and age, triage systolic blood pressure, and triage pulse. There was a step increase in risk associated with age greater than 90 years, and high and low extremes of blood pressure and pulse were associated with increased risk. We converted these continuous predictors to categorical variables, and we used the results of exploratory bivariate analyses to identify cut points for these conversions.

To identify independent predictors of the primary outcome, we performed multivariable logistic regression. We coded all missing data as representing absence of the variable. We then used variable-specific binary indicators to flag missing data. In exploratory work, we generated a "complete" model that included all predictor variables. We then created a "reduced" model, using a backward selection algorithm that retained variables at a threshold of $P<.15$. We found no important qualitative differences in coefficient values or P values between the complete and reduced models, and we present the reduced model to improve interpretability.

We used bootstrapping methods to assess the stability of the reduced model. Using random sampling from actual study patients, we generated 1,000 hypothetical study populations of equivalent size to the original cohort. We estimated coefficient point estimates with the reduced model for each hypothetical population. We estimated the bootstrapped effect size and 95% CIs for each coefficient. We assessed goodness of fit using the Hosmer-Lemeshow test.

We assessed 2 different weighting schemes to generate a risk score from significant variables identified by regression modeling. These included weighting by regression coefficients rounded to the nearest integer and simple summation of the presence or absence of each variable. Receiver operating characteristics curve and area under the receiver operating characteristics curve for each scheme were generated with bootstrap methods. The 95% CIs of the area under the receiver operating characteristics curve and differences in area under the receiver operating characteristics curve between the weighting schemes were obtained according to 1,000 bootstrap samples.

Data management and statistical analyses were conducted with SAS software, version 9.1 (SAS Institute, Inc., Cary, NC) and the publicly available statistical software R (R Development Core Team).

RESULTS

Compared with blinded physician chart review, *ICD-9* screening demonstrated a positive predictive value of 92% (n=100 consecutive ED charts with a positive *ICD-9* screen result) and a negative predictive value of 100% (n=100

consecutive ED charts with a negative *ICD-9* screen result) for identifying patients with syncope or near syncope.

In a validation subsample of 100 selected charts, research associate review for study eligibility demonstrated good interrater reliability (κ=0.64; absolute agreement 84%) compared with blinded physician chart review. Research associates demonstrated high interrater reliability (κ=0.5 to 0.9; absolute agreement 73% to 96%) on all elements of chart abstraction compared with blinded physician review. Research associates were 100% sensitive in identifying serious events compared with blinded physician review.

To assess reliability of physician overreadings, 2 physicians independently reviewed a subsample of 60 consecutive charts flagged by research associates as potentially documenting a serious event. Agreement of physician reviewers was high for the occurrence of serious events (κ=0.8; absolute agreement 90%), and there was complete agreement in event classification.

We identified 3,727 patients aged 60 years or older with an ED discharge diagnosis of syncope. We excluded 321 nonmember patients. Of the remaining 3,406 patients, 2,972 had available medical chart information and explicit documentation of syncope or near syncope. We excluded 101 patients who had documentation of ongoing confusion (n=34), witnessed seizure (n=22), loss of consciousness after head trauma (n=16), or need for electrical or pharmacologic intervention to restore consciousness (n=32); some patients met more than 1 exclusion criterion. There were 2,871 (84%) patients without any exclusion criteria. Of these patients, we excluded an additional 287 patients who were diagnosed with a serious condition during the ED visit.

The final study cohort includes 2,584 patients, and study sample characteristics are presented in Table 1. The mean age of the cohort was 75 years, with a range of 60 to 102 years. The estimated overall admission rate was 43%, and 86% of patients who experienced the primary outcome were admitted after the initial ED evaluation. Of patients with an abnormal troponin level, the median troponin I value was 0.07 ng/mL, with an interquartile range of 0.04 to 0.2 ng/mL.

Table 2 describes the categories and frequencies of 30-day serious events, both diagnosed in the ED and in the study cohort. There were 173 patients (7% of the final study cohort) who received a diagnosis of a serious condition within 30 days after their initial ED evaluation. An arrhythmia was the most common cause of a serious event, as diagnosed both in the ED and after the ED evaluation. Gastrointestinal hemorrhage/anemia requiring transfusion was the second most common serious condition detected in the ED, but this was rarely diagnosed after the ED evaluation.

Of patients who were admitted at the index ED evaluation, a serious condition was identified during the initial hospitalization in 124 patients. An additional 26 patients were initially hospitalized and discharged without a serious outcome but later were rehospitalized with a 30-day serious outcome or experienced out-of-hospital death. There were 23 patients who were discharged after the initial ED evaluation and later were rehospitalized with a 30-day serious outcome or experienced out-of-hospital death.

Adjusted odds ratios from a reduced, multivariable logistic regression model are presented in Table 3. There were no qualitative differences when the model included indicators for missing data. There were no qualitative changes to the model with bootstrapping techniques. Using predetermined significance thresholds, we identified 6 variables associated with increased risk, including age greater than 90 years, male sex, history of an arrhythmia, triage systolic blood pressure greater than 160 mm Hg, an abnormal ECG result, and an abnormal troponin I level. A complaint of near syncope, compared with syncope, was associated with decreased risk.

These 7 variables were then used to construct a syncope risk score. Different weighting schemes to generate a risk score yielded equivalent area under the receiver operating characteristics curves: (weighting by rounded regression coefficients: area under the receiver operating characteristics curve 0.61, 95% CI 0.57 to 0.65; simple summation: area under the receiver operating characteristics curve 0.61, 95% CI 0.57 to 0.66). A simplified syncope risk score can be calculated by summing high-risk factors and subtracting the low-risk variable (Figure 1). There is a linear increase in risk with higher values of the syncope risk score (Figure 2). The syncope risk score can discriminate patients into low-, medium-, and high-risk groups (Table 4), with a 10-fold range of risk and nonoverlapping 95% CIs.

LIMITATIONS

Strengths of this study include the relatively large cohort size, exclusion of events diagnosed during the ED evaluation, and stability of predictor-outcome associations to a number of internal validation techniques. Chart abstraction was performed by highly trained research associates, and we performed extensive assessments of interrater reliability; these should mitigate threats to the reliability of data derived from chart review. There are nevertheless potential limitations inherent to any retrospective study.

Data elements were not prospectively collected, and missing data may introduce bias into our results. For example, there may be selection bias by patient acuity for tests such as ECG and troponin, and this may inflate the importance of such tests. We attempted to minimize missing data by using information from multiple provider notes. We found no qualitative differences when regression modeling was performed with and without controls for missing data, although future validation studies should minimize missing information through standardized testing data collection.

Patients in our study are all enrolled in a managed health care system, and provider practices and patient characteristics may differ from those in other settings. The estimated admission rate in this sample (43%) is lower than the age-matched rates reported from a national ED sample (54%)[1] and a single academic center (85%).[25] It is possible that discharged patients experienced undiagnosed

Table 1. Study sample characteristics.

Characteristic	Overall Cohort (n=2,584)	30-Day Serious Event (n=173)	No 30-Day Serious Event (n=2,411)	Missing Data
Demographics, %				
Age, y*				
60–69	32	22	33	
70–79	38	38	38	
80–89	26	32	26	
>90	4	9	4	
Male*	46	59	41	
Nonwhite*	20	12	21	7
Hispanic	12	10	12	7
Comorbidities, %				
Coronary artery disease	22	25	21	
Congestive heart failure†	9	17	8	
Ejection fraction <40%*	1	6	1	
Aortic stenosis	1	1	1	
Arrhythmia*	13	30	12	
Pacemaker/automatic implantable cardioverter defibrillator	5	8	5	
Stroke	15	20	15	
Previous syncope in 30 days	2	2	2	
Diabetes	20	23	20	
Hypertension	61	61	62	
Dementia	9	13	9	
Symptoms, %				
Near syncope*†	31	20	32	
Chest pain	7	11	7	16
Shortness of breath	8	13	7	32
No prodromal symptoms†	16	23	16	13
Physical Examination, %				
Triage vital signs				
Pulse rate <60 beats/min†	18	17	17	11
Pulse rate 60–100 beats/min	73	70	76	
Pulse rate >100 beats/min	7	13	7	
SBP <90 mm Hg	2	3	2	11
SBP 90–160 mm Hg	78	72	78	
SBP >160 mm Hg	20	26	19	
Cardiac murmur	11	14	11	12
Abnormal neurologic examination result	4	6	4	15
Major traumatic injury*	4	8	3	
Tests				
Abnormal ECG result*	51	71	50	5
Nonsinus rhythm*	11	10	26	
ST/T changes*	23	23	32	
Abnormal intervals*	8	8	16	
Ventricular hypertrophy	10	9	12	
Left axis deviation	14	14	15	
Left bundle-branch block	4	4	4	
Right bundle-branch block	7	7	11	
Hematocrit <30%	5	5	5	14
Pyuria	7	5	7	
Abnormal troponin level*	11	25	10	30
Admitted*§	43	86	40	

*Comparison between serious event and no-serious-event groups: $P<.01$.
†Comparison between serious event and no-serious-event groups: $P<.05$.
‡Compared with syncope.
§Weighted estimate; see "Materials and Methods" section.

arrhythmias that might have been identified had they been admitted. As a consequence, we may be underestimating the number of patients with causes of syncope that could be potentially identified during an inpatient admission, and in turn could be misestimating the utility of individual risk criteria. Future validation studies should mitigate these limitations by standardizing duration of cardiac monitoring and include patients in nonmanaged care settings.

Table 2. Distribution of serious events.*

Serious Event Type	Serious Event Identified During ED Evaluation,† No. (%)	30-Day Serious Event Occurred After ED Evaluation,‡ No. (%)
Any	287 (10)	173 (7)
Death	0	41 (1)
Cardiac event	198 (7)	120 (4)
Arrhythmia	175 (6)	92 (3)
Ventricular tachycardia	25 (0.9)	10 (0.4)
Ventricular tachycardia terminated by automatic implantable cardioverter defibrillator	10 (0.3)	0
Sustained ventricular tachycardia	5 (0.2)	2 (0.1)
Nonsustained ventricular tachycardia	10 (0.3)	8 (0.3)
Symptomatic paroxysmal supraventricular tachycardia	9 (0.3)	6 (0.2)
Symptomatic atrial fibrillation/flutter with rapid ventricular response	41 (1.4)	18 (0.7)
Sick sinus syndrome/sinus pause	23 (0.8)	30 (1)
Third or Mobitz II heart block	15 (0.5)	9 (0.4)
Symptomatic bradycardia	76 (2.6)	20 (0.8)
Abnormal electrophysiology study	2 (0.1)	5 (0.2)
Myocardial infarction	14 (0.5)	6 (0.2)
Cardiac procedure	0	54 (2)
Pacemaker		40 (2)
Implantable defibrillator		7 (4)
Coronary angioplasty		3 (4)
Coronary bypass surgery		4 (4)
Structural heart disease	5 (0.2)	10 (0.4)
Pulmonary embolism	7 (0.2)	6 (0.3)
Stroke/transient ischemic attack	9 (0.3)	11 (0.4)
Gastrointestinal bleed/anemia	85 (3)	8 (0.3)
Subarachnoid hemorrhage	1 (0.03)	0

*Some patients experienced more than 1 event.
†These patients were excluded from further analysis. Denominator includes 2,871 patients who met initial eligibility criteria.
‡Denominator includes 2,584 patients in the study cohort.

Table 3. Multivariate regression model for 30-day serious events after ED evaluation.

Variable	β Coefficient	Bootstrapped OR	Bootstrapped 95% CI
Age >90 y*	0.85	2.3	1.2–4.4
Male sex	0.6	1.8	1.3–2.6
Near syncope†	−0.62	0.5	0.3–0.8
Ejection fraction <40%	0.72	2.0	0.8–5.0
History of arrhythmia	0.87	2.4	1.6–3.6
Complaint of chest pain	0.47	1.6	0.9–2.8
Complaint of shortness of breath	0.41	1.5	0.8–2.6
Triage systolic blood pressure <90 mm Hg	0.45	1.6	0.9–2.6
Triage systolic blood pressure >160 mm Hg	0.49	1.6	1.1–2.4
Triage pulse >100 beats/min	0.5	1.6	0.9–2.8
Major traumatic injury	0.64	1.8	0.8–4.2
Abnormal ECG result	0.65	1.9	1.3–2.8
Abnormal troponin I level (≥0.04 ng/mL)	0.63	1.9	1.2–2.9

Likelihood ratio test for model: χ^2=124; P<.0001. c-Statistic: 0.73. Hosmer-Lemeshow goodness-of-fit statistic=5.6; P=.7.
*Reference group: aged younger than 90 years.
†Reference group: syncope.

Presence of:	Add:
Age>90 Years	+1
Male Sex	+1
History of Arrhythmia	+1
Triage Systolic Blood Pressure>160	+1
Abnormal Electrocardiogram	+1
Abnormal Troponin I	+1
Near-Syncope	-1

Figure 1. Calculating a syncope risk score.

Although we defined a low-risk group with a 2.5% frequency of 30-day risk for serious events, the optimum risk threshold for discharging patients is undefined. It may be possible that a "no-risk" group of older patients with syncope cannot be reliably identified. As did we, other investigators have identified "low"-risk patients with a 2% to 4% frequency of syncope-related events.[17,28] One possible approach to identify an appropriate risk threshold for discharge is to determine the baseline 30-day serious event rate in an age-, sex-, and comorbidity-matched population of patients without syncope, although this analysis is beyond the scope of this current study.

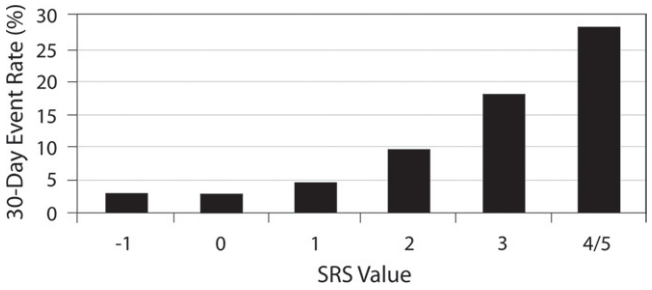

Figure 2. Syncope risk score.

Table 4. Syncope risk score.

Risk Category	Syncope Risk Score Value	Proportion of Patients, %	30-Day Risk, % (95% CI)
Low	−1, 0	31	2.5 (1.4–3.6)
Intermediate	1, 2	58	6.3 (5.1–7.5)
High	3 to 6	11	20 (15–25)

We calculated a weighted estimate of the hospital admission rate, and we do not have complete admission data on all cohort patients because of problems with administrative data. This limits our ability to assess the hypothetical effect on admission rates if varying thresholds of the syncope risk score were used to admit or discharge patients. It is likely that the effect of the syncope risk score will vary by setting and be strongly associated with baseline clinical practices and admission rates. Future validation studies should prospectively collect disposition data.

Finally, this study is unable to assess whether patients at risk for a serious event will benefit from immediate hospitalization. For example, it is possible that some 30-day serious events were not related to the initial episode of syncope or would have occurred regardless of hospital admission (eg, cancer-related mortality). Future interventional trials of inpatient evaluation compared with a rapid, standardized ED observation protocol may clarify the benefit of admission in risk-stratified patients.

DISCUSSION

Professional society guidelines[12,15,33] suggest that most patients who are younger than 60 years and without an obvious treatable cause of syncope, or evidence of cardiac or ECG abnormality, can be treated as outpatients. There is a dearth of evidence, on the other hand, to guide the evaluation of older adults. If externally validated, our prediction instrument may supplement clinical decisionmaking in this group. All elements of the syncope risk score can be rapidly and reliably measured during an ED evaluation. We characterized 31% of study cohort patients as "low risk" with a 2.5% 30-day serious event rate, and these patients may be candidates for discharge or a brief observation unit evaluation. In contrast, "high-risk" patients had a 20% 30-day serious event rate, and inpatient evaluation should be considered for this group. The effect of applying the syncope risk score will likely vary by practice setting and baseline admission rates, and future studies should assess this prediction instrument in different ED environments. The syncope risk score may also be used as a case-mix adjustment measure in future observational and interventional studies.

Cardiac events, and particularly arrhythmias, represented the majority of serious outcomes. Increased age,[8,17] male sex,[19,34] history of arrhythmia,[8,17] and an abnormal ECG result[8,9,17,19,28] have previously been found to be associated with increased risk of a cardiac event. Although several studies have questioned the routine ordering of cardiac enzyme tests,[32,35] we found that an abnormal troponin I level was associated with serious outcomes, even after controlling for ECG abnormalities. In our cohort, the majority of abnormal troponin I levels were in an indeterminate range between 0.04 ng/mL and 0.2 ng/mL. Increased systolic blood pressure may either reflect poorly controlled hypertension or adrenergic surge related to an underlying serious condition. Finally, we report the novel finding that near syncope is less frequently associated with a serious outcome compared with syncope.

At least 3 other groups have derived predictors of short-term events after syncope, although none have specifically studied older adults. A multisite Italian cohort enrolled 676 ED patients with a mean age of 59 years, and 41 patients experienced 10-day mortality or required a major therapeutic procedure.[19] Correlates of 10-day outcomes included an abnormal ECG result, concurrent trauma, lack of prodromal symptoms, and male sex. The San Francisco Syncope Rule investigators enrolled 684 ED patients with a mean age of 62 years, and 79 patients experienced a 7-day serious outcome, including those who received a diagnosis in the ED. Predictors of 7-day outcomes included an abnormal ECG result, a complaint of shortness of breath, hematocrit level less than 30%, systolic blood pressure less than 90 mm Hg, and a history of congestive heart failure.[28] Finally, a single-center Swiss study enrolled 175 patients with a mean age of 66 years, and 30 patients were diagnosed with an arrhythmia during an inpatient evaluation.[17] Predictors of arrhythmias included age greater than 60 years, an abnormal ECG result, and a history of congestive heart failure.

Discrepancies between the findings of our study and those of previous investigations may be in part attributable to differences in cohort age and outcomes definitions. Previous studies suggest that symptoms are poorly predictive of outcomes,[36] particularly among the elderly.[37] A history of congestive heart failure has been associated with increased mortality after syncope.[8,38] However, Kapoor et al[10] reported a negative interaction effect between increasing age and a history of congestive heart failure for predicting death. This finding suggests that the age-stratified mortality risk associated with congestive heart failure for older patients is smaller compared with that of younger patients. Finally, routine hematocrit testing may be indicated to identify older patients with gastrointestinal

hemorrhage or severe anemia.[28] In our study cohort, however, this test appears to have limited power to identify patients who will experience a serious event that is not diagnosed in the ED.

In summary, we identified 7 predictors of 30-day serious events after syncope in adults aged 60 years and older. A simple score was able to stratify the patients we studied into distinct low-, intermediate-, and high-risk groups, with a 10-fold difference in serious event rates. If validated in an external cohort, this syncope risk score would have the potential to aid in clinical decisionmaking. Low-risk patients may be candidates for discharge or a brief observation unit evaluation, whereas high-risk patients may benefit from evaluation in a cardiac monitored setting. The syncope risk score can also be used as a case-mix adjustment measure for future interventional studies of syncope to assess the relative benefits of inpatient evaluation compared with a rapid, standardized, ED observation protocol.

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APPENDIX 1. Cohort Screening Form

XXXX ID:_____ Index Date:_____
Study ID:_____
Name of Abstractor:_____

1a. Is there documentation of transient loss of consciousness?

☐ Yes ☐ No ☐ Unsure [FLAG FOR MD REVIEW]

1b. Is there documentation of near-syncopal states WITHOUT loss of consciousness
☐ Yes ☐ No ☐ Unsure [FLAG FOR MD REVIEW]

2. Is there documentation of any exclusion criteria:

2a. No spontaneous return to baseline mental status
☐ Yes ☐ No ☐ Unsure [FLAG FOR MD REVIEW]

2b. Patient requiring pharmacologic or electrical treatment at initial presentation
☐ Yes ☐ No ☐ Unsure [FLAG FOR MD REVIEW]

2c. Loss of consciousness due to generalized seizure
☐ Yes ☐ No ☐ Unsure [FLAG FOR MD REVIEW]

2d. Loss of consciousness due to head trauma
☐ Yes ☐ No ☐ Unsure [FLAG FOR MD REVIEW]

Appendix E2. Outcomes definitions.

Arrhythmia

- ventricular tachycardia more than 3 beats
- sick sinus disease with alternating sinus bradycardia and tachycardia
- sinus pause greater than 3 seconds
- third-degree atrioventricular block
- Mobitz II atrioventricular block
- symptomatic supraventricular tachycardia (pulse rate greater than 100 beats/min)
- Atrial flutter or fibrillation with rapid ventricular response (pulse rate greater than 100 beats/min)
- symptomatic bradycardia (pulse rate less than 60 beats/min), OR pulse rate less than 40 beats/min
- ***"Symptomatic" refers to the simultaneous occurrence of dizziness, lightheadedness, hypotension (systolic blood pressure <90 mm Hg), or syncope with an arrhythmia on ECG monitoring.
- Abnormal electrophysiology study; includes:
  - inducible, sustained ventricular tachycardia;
  - His-ventricular intervals >100 ms;
  - symptomatic supraventricular tachycardia
  - infra-Hisian block
  - prolonged corrected sinus node recovery time (>550 ms)

Myocardial Infarction

- Requires increase of troponin level or ECG change AND
- Cardiology consultant concurs with diagnosis of myocardial infarction

Stroke

- Requires confirmatory testing (eg, head computed tomography [CT] or brain magnetic resonance imaging [MRI])
- Neurology consultant concurs with diagnosis of stroke

Structural Heart Disease

- Structural heart disease thought to be the cause of syncope (eg, aortic stenosis, cardiomyopathy) by the admission team

Pulmonary Embolism

- Requires confirmatory testing (high-probability perfusion-ventilation scan, chest CT angiogram, pulmonary angiography, or new deep venous thrombosis noted on duplex ultrasound WITH a non-normal perfusion-ventilation scan result OR non-normal chest CT angiogram OR non-normal pulmonary angiography result)

Aortic Dissection

- Requires confirmatory testing (chest CT, transesophageal echocardiogram, MRI, or angiography)

Subarachnoid Hemorrhage (Nontraumatic)

- Requires confirmatory neurologic imaging or lumbar puncture results
- Requires that neurology or neurosurgical consultant concur with diagnosis

Internal Hemorrhage/Anemia Requiring Transfusion

- Any source of bleeding (gastrointestinal, vaginal, ruptured abdominal aortic aneurysm) or anemia requiring blood transfusion (includes patients who refuse recommended transfusion, eg, Jehovah's Witnesses)

APPENDIX 3. Outcomes Screening Form

XXXX ID:_____ Name of Abstractor:_____

Study ID:_____ Index Date:_____

ANY 30-Day Dangerous Clinical Outcomes? ☐ Yes ☐ No

Occurrence and Cause of Death

Patient died within 30 days: ☐ Yes ☐ No

If yes, indicate number of days after index ED visit that death occurred:_____

Cardiac Death: ☐ Yes ☐ No ☐ Unknown

Sudden death: ☐ Yes ☐ No ☐ Unknown

Nonfatal Dangerous Clinical Outcomes

Indicate occurrence of the following dangerous clinical outcomes. For dangerous outcomes, please indicate whether the diagnosis was made at ED evaluation. For delayed dangerous outcomes, indicate the time of diagnosis in days after initial ED evaluation. Finally, indicate your opinion about whether the dangerous outcome was related to initial episode of syncope.

☐ Arrhythmia: specify type
- ☐ Ventricular Tachycardia/Fibrillation
- ☐ Sick sinus disease/ sinus pause
- ☐ Mobitz II or Type III block
- ☐ Symptomatic Supraventricular Tachycardia (SVT)
- ☐ Symptomatic Bradycardia OR pulse<40
- ☐ Atrial fibrillation or flutter with pulse>100
- ☐ Abnormal electrophysiology study

Diagnosis made at ED evaluation: ☐ Yes ☐ No
If no, indicate time of diagnosis in days after index ED evaluation:_____
Was this event related to initial syncope? ☐ Yes ☐ No ☐ Unknown

☐ Myocardial Infarction

Diagnosis made at ED evaluation: ☐ Yes ☐ No
If no, indicate time of diagnosis in days after index ED evaluation:_____
Was this event related to initial syncope? ☐ Yes ☐ No ☐ Unknown

☐ Cardiac Intervention. Indicate type of intervention (e.g. Pacemaker, AICD, CABG, PTCA, etc):_____

Indicate time of procedure in days after index ED evaluation:_____
Was this event related to initial syncope? ☐ Yes ☐ No ☐ Unknown

☐ Stroke (CVA) or Transient Ischemic Attack (TIA)

Diagnosis made at ED evaluation: ☐ Yes ☐ No
If no, indicate time of diagnosis in days after index ED evaluation:_____
Was this event related to initial syncope? ☐ Yes ☐ No ☐ Unknown

☐ Structural Heart Disease. Indicate type (e.g. aortic stenosis, cardiomyopathy, etc):_____

Diagnosis made at ED evaluation: ☐ Yes ☐ No
If no, indicate time of diagnosis in days after index ED evaluation:_____
Was this event related to initial syncope? ☐ Yes ☐ No ☐ Unknown

☐ Pulmonary Embolism

Diagnosis made at ED evaluation: ☐ Yes ☐ No
If no, indicate time of diagnosis in days after index ED evaluation:_____
Was this event related to initial syncope? ☐ Yes ☐ No ☐ Unknown

☐ Aortic Dissection

Diagnosis made at ED evaluation: ☐ Yes ☐ No
If no, indicate time of diagnosis in days after index ED evaluation:_____
Was this event related to initial syncope? ☐ Yes ☐ No ☐ Unknown

☐ Subarachnoid Hemorrhage (Non-traumatic)

Diagnosis made at ED evaluation: ☐ Yes ☐ No
If no, indicate time of diagnosis in days after index ED evaluation:_____
Was this event related to initial syncope? ☐ Yes ☐ No ☐ Unknown

☐ Internal Hemorrhage/Anemia requiring transfusion. Indicate type of hemorrhage (e.g. GI bleed, ruptured AAA, etc):_____

Diagnosis made at ED evaluation: ☐ Yes ☐ No
If no, indicate time of diagnosis in days after index ED evaluation:_____
Was this event related to initial syncope? ☐ Yes ☐ No ☐ Unknown

☐ Other unusual events. Please describe:_____

Diagnosis made at ED evaluation: ☐ Yes ☐ No
If no, indicate time of diagnosis in days after index ED evaluation:_____
Was this event related to initial syncope? ☐ Yes ☐ No ☐ Unknown

APPENDIX 4: ED Chart Abstraction Form

XXXX ID:_____ Index Date:_____
Study ID:_____
Name of Abstractor:_____

SYMPTOMS			
Chest discomfort	☐ Yes	☐ No	☐ Unknown
Shortness of breath	☐ Yes	☐ No	☐ Unknown
Lack of warning symptoms	☐ Yes	☐ No	☐ Unknown

COMORBIDITIES		
Coronary artery disease	☐ Yes	☐ No
Congestive heart failure	☐ Yes	☐ No
Pacemaker and/or AICD	☐ Yes	☐ No
Arrhythmia	☐ Yes	☐ No
Ventricular Arrhythmia	☐ Yes	☐ No
Sick Sinus Syndrome	☐ Yes	☐ No
Type II or III Block	☐ Yes	☐ No
PSVT	☐ Yes	☐ No
Atrial fibrillation or flutter	☐ Yes	☐ No
Other- please describe:		
Structural heart disease	☐ Yes	☐ No
Severe aortic stenosis (<1cm^2)	☐ Yes	☐ No
Ejection fraction <40%	☐ Yes	☐ No
Other structural heart disease	☐ Yes	☐ No
If yes, describe:		
Prior stroke/ TIA	☐ Yes	☐ No
Diabetes mellitus	☐ Yes	☐ No
Hypertension	☐ Yes	☐ No
Dementia/ cognitively impaired	☐ Yes	☐ No

PHYSICAL EXAMINATION

Triage Vital Signs: SBP___ DBP___ HR_____ Room Air O2Sat_____

Cardiac murmur	☐ Yes	☐ No	☐ Unknown
Abnormal cranial nerve or motor exam	☐ Yes	☐ No	☐ Unknown
If yes, describe (please indicate new vs. old deficits):			

DISCHARGE SUMMARY MISSING ☐ Yes

30-DAY ADVERSE EVENT*

Chart requires further review by physician ☐ Yes

*Please flag for any major adverse events, including death, MI, cardiac procedures, stroke/TIA, pulmonary embolism, intracranial hemorrhage, internal bleeding or anemia, traumatic injuries, infections, or any other unusual events.

APPENDIX 5: EKG Abstraction Form

XXXX ID:_____
Study ID:_____
Name of Abstractor:_____

ECG Source
☐ MUSE ☐ Other (KPDS, chart, etc)

ECG Interpretation (Select one)
☐ Normal: includes sinus tachycardia, first degree block, sinus bradycardia>40, premature atrial contractions, premature ventricular contractions, incomplete right bundle branch block
☐ Non-specific ST/T wave changes
☐ Abnormal. Check all the following that apply:
- ☐ Non-sinus rhythms (includes pacemaker, Mobitz II and complete heart block)
- ☐ Sinus rhythm, HR<40
- ☐ Q/ST/T changes consistent with acute or chronic ischemic heart disease
- ☐ Abnormal conduction intervals excluding first degree block*
- ☐ LVH or RVH
- ☐ Left axis deviation
- ☐ Complete left bundle branch block
- ☐ Complete right bundle branch block
- ☐ Other:_____

*Includes intraventricular conduction delay (QRS>0.1ms), prolonged QTc interval (QTc>450ms in men, >470ms in women)